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Hospital Universitario Clínica Puerta de Hierro, Madrid, Spain. dabejon@telefonica.net

METHODS: A retrospective analysis of 54 consecutive patients. RESULTS: A decrease in the NRS score was observed in patients with HD ($P < 0.05$) and SS ($P < 0.001$), but not in those with FBSS.

PMID: 17305674

Rating: 4c

"Radiofrequency (RF) thermolesioning adjacent to the dorsal root ganglion (DRG) has been employed for pain relief in patients with cervicobrachial pain, thoracic radiculopathy, and chronic lumbar radicular pain (LRP)," write David Abejón, MD, FIPP, from Hospital Universitario Clínica Puerta de Hierro in Madrid, Spain, and colleagues. "Despite its widespread use and well-documented efficacy, this option does not appear to be an ideal modality of treatment for LRP because neurodestructive methods for the treatment of neuropathic pain are in principle generally considered inappropriate.... Authors noted this is a small retrospective study and prospective randomized studies are needed to confirm the findings before adding pulsed radiofrequency to the armamentarium for lumbar radicular pain treatment.

Abrahm JL; Snyder L. Pain assessment and management. Primary Care: Clinics in Office Practice. 01-Jun-2001; 28(2): 269-97.

With appropriate assessment and management, often using home health or hospice teams, pain can be controlled in more than 90% of patients.

Rating: 5b

Ackerman WE, Zhang JM. Efficacy of stellate ganglion blockade for the management of type 1 complex regional pain syndrome. South Med J. 2006 Oct;99(10):1084-8.

Pain Medicine Consultants PA, Little Rock, AR, USA. William.Ackerman@bhsi.com

METHODS: 25 subjects. RESULTS: Compared with the normal control hand, the skin perfusion in the CRPS I affected hand was greater in group I and decreased in groups II and III. DISCUSSION: The results of our study demonstrate that an inverse relationship exists between hand perfusion and the duration of symptoms of CRPS I. On the other hand, a positive correlation exists between SGB efficacy and how soon SGB therapy is initiated. A duration of symptoms greater than 16 weeks before the initial SGB and/or a decrease in skin perfusion of 22% between the normal and affected hands adversely affects the efficacy of SGB therapy.

PMID: 17100029

Rating: 4c

Aetna Clinical Policy Bulletins. Chronic Pain Programs Number 0237. Reviewed: May 5, 2006.

Aetna considers a screening examination medically necessary for members who are being considered for admission into a chronic pain program.

Rating: 8b

Aetna Clinical Policy Bulletins. Electrical Stimulation for Pain. Number 0011. February 22, 2005. Updated 2007.

Aetna considers transcutaneous electrical nerve stimulators (TENS) medically necessary durable medical equipment (DME) when used as an adjunct or as an alternative to the use of drugs in the treatment of acute post-operative pain in the first 30 days after surgery, or chronic, intractable pain not responsive to other methods of treatment.

Rating: 8b
Agency for Healthcare Research and Quality. Washington, DC. Management of Cancer Pain. AHRQ Publication No. 01-E033, January 2001. Agency for Healthcare Research and Quality, Rockville, MD.

In framing this request, the American Pain Society observed that a significant amount of scientific evidence had been published on this topic since the 1994 release of the clinical practice guideline Management of Cancer Pain.

Rating: 8b

Airaksinen O, Brox JI, Cedraschi C, Hildebrandt J, Klaber-Moffett J, Kovacs F, Mannion AF, Reis S, Staal JB, Ursin H, Zanoli G; On behalf of the COST B13 Working Group on Guidelines for Chronic

Low Back Pain. Chapter 4 European guidelines for the management of chronic nonspecific low back pain. Eur Spine J. 2006 Mar;15(Supplement 2):s192-s300.

Physical examination and case history: The use of diagnostic triage, to exclude specific spinal pathology and nerve root pain, and the assessment of prognostic factors (yellow flags) are recommended. We cannot recommend spinal palpatory tests, soft tissue tests and segmental range of motion or straight leg raising tests (Lasegue) in the diagnosis of nonspecific
CLBP.
Imaging: We do not recommend radiographic imaging (plain radiography, CT or MRI), bone scanning, SPECT, discography or facet nerve blocks for the diagnosis of nonspecific CLBP unless a specific cause is strongly suspected.
• Conservative treatments: Cognitive behavioural therapy, supervised exercise
therapy, brief educational interventions, and multidisciplinary (bio-psycho-social) treatment can each be recommended for nonspecific CLBP. Back schools (for short-term improvement), and short courses of manipulation/mobilisation can also be considered. The use of physical therapies (heat/cold, traction, laser, ultrasound, short wave, interferential, massage, corsets) cannot be recommended. We do not recommend TENS.
• Pharmacological treatments: The short term use of NSAIDs and weak opioids can be recommended for pain relief. Noradrenergic or noradrenergic-serotoninergic antidepressants, muscle relaxants and capsicum plasters can be considered for pain relief. We cannot recommend the use of Gabapentin.
• Invasive treatments: Acupuncture, epidural corticosteroids, intra-articular
(facet) steroid injections, local facet nerve blocks, trigger point injections, botulinum toxin, radiofrequency facet denervation, intradiscal radiofrequency lesioning, intradiscal electrothermal therapy, radiofrequency lesioning of the dorsal root ganglion, and spinal cord stimulation cannot be recommended for nonspecific CLBP. Intradiscal injections and prolotherapy are not recommended. Percutaneous electrical nerve stimulation (PENS) and neuroreflexotherapy can be considered where available. Surgery for nonspecific CLBP cannot be recommended unless 2 years of all other recommended conservative treatments – including multidisciplinary approaches with combined programs of cognitive intervention and exercises – have failed, or such combined programs are not available, and only then in carefully selected patients with maximum 2-level degenerative disc disease.
Overarching comments
• CLBP is not a clinical entity and diagnosis, but rather a symptom in patients with very different stages of impairment, disability and chronicity. Therefore assessment of prognostic factors before treatment is essential.
• The most promising approaches seem to be cognitivebehavioural interventions encouraging activity/exercise.

PMID: 16550448

Rating: 8a

Alvarez DJ, Rockwell PG. Trigger points: diagnosis and management. Am Fam Physician. 2002 Feb 15;65(4):653-60.

Department of Family Medicine, University of Michigan Medical School, Ann Arbor, USA. dalvarez@umich.edu

Trigger points are discrete, focal, hyperirritable spots located in a taut band of skeletal muscle. These include muscles used to maintain body posture, such as those in the neck, shoulders, and pelvic girdle. Trigger points may also manifest as tension headache, tinnitus, temporomandibular joint pain, decreased range of motion in the legs, and low back pain. Palpation of a hypersensitive bundle or nodule of muscle fiber of harder than normal consistency is the physical finding typically associated with a trigger point. Palpation of the trigger point will elicit pain directly over the affected area and/or cause radiation of pain toward a zone of reference and a local twitch response. Trigger-point injection has been shown to be one of the most effective treatment modalities to inactivate trigger points and provide prompt relief of symptoms.

PMID: 11871683

Rating: 5b

Ambler N; Williams AC; Hill P; Gunary R; Cratchley G. Sexual difficulties of chronic pain patients. Clinical Journal of Pain. 01-Jun-2001; 17(2): 138-45.

Pain Management Center, Frenchay Hospital, North Bristol NHS Trust, United Kingdom. Nicholas.Ambler@north-bristol.swest.nhs.uk

Conclusion: "The range of problems and patients' expressed preferences for help suggest that multidisciplinary intervention is required. "

PMID: 11444715

Rating: 4b

American Academy of Pain Medicine. The Necessity for Early Evaluation of the Chronic Pain Patient. (February 6, 2001).

The diagnosis and management of chronic pain is a complex process requiring intensive, comprehensive, and interdisciplinary services for optimum treatment outcomes.

Rating: 5b

American Academy of Pain Medicine. Use of Opioids for the Treatment of Chronic Pain. (February 6, 2001).

These publications, which have been endorsed by AAPM and APS, state that opioids, sometimes called "narcotic analgesics", are an essential part of a pain management plan. There is currently no nationally accepted consensus for the treatment of chronic pain not due to cancer, yet the economic and social costs of chronic pain are substantial, with estimates ranging in the tens of billions of dollars annually.

Rating: 5b

AAPM. Definitions related to the use of opioids for the treatment of chronic pain. A consensus document from the American Academy of Pain Medicine, The American Pain Society, and the American Society of Addiction Medicine, 2001. www.ampainsoc.org.

Rating: 5c

Abs R, Verhelst J, Maeyaert J, Van Buyten JP, Opsomer F, Adriaensen H, Verlooy J, Van Havenbergh T, Smet M, Van Acker K. Endocrine consequences of long-term intrathecal administration of opioids. J Clin Endocrinol Metab. 2000;85:2215-22.

Department of Endocrinology, University Hospital Antwerp, Belgium.

Decreased libido or impotency was present in 23 of 24 men receiving opioids. The serum testosterone level was below 9 nmol/L in 25 of 29 men and was significantly lower than that in the control group ($P < 0.001$). The serum LH level was less than 2 U/L in 20 of 29 men and was significantly lower than that in the control group ($P < 0.001$). Serum FSH was comparable in both groups. Decreased libido was present in 22 of 32 women receiving opioids. All 21 premenopausal females developed either amenorrhea or an irregular menstrual cycle, with ovulation in only 1. Supplementation with gonadal steroids improved sexual function in most patients. These findings suggest that further investigations are required to determine the need for systematic endocrine work-up in these patients and the necessity for substitutive therapy.

PMID: 10852454

Rating: 3c

Ackerman LL, Follett KA, Rosenquist RW. Long-term outcomes during treatment of chronic pain with intrathecal clonidine or clonidine/opioid combinations. J Pain Symptom Manage. 2003 Jul;26(1):668-77.

Department of Neurosurgery, University of Iowa Hospitals and Clinics, Iowa City, Iowa 52242, USA.

15 patients. In this population, intrathecal clonidine was of limited utility for most patients.

PMID: 12850649

Rating: 5b

Ackermann, L., Follett, K., Rosenquist, R. "Long-Term Outcomes During Treatment of Chronic Pain with Intrathecal Clonidine or Clonidine/Opioid Combinations" Journal of Pain and Symptom Management. 2003; July, Volume 26: 668-76.

Rating: 2c

Quality: Low. Total Rating: 1.0. Comment: Does not meet inclusion criteria for evidence-based review. [CA DWC]

ACOEM. Chronic Pain. Update to Chapter 6 in the Occupational Medicine Practice Guidelines, 2nd Edition. American College of Occupational and Environmental Medicine. 2008.

In the recently released update to Chapter 6 (Chronic Pain) in the Occupational Medicine Practice Guidelines, 2nd Edition, NSAIDs are recommended for treatment over acetaminophen, although acetaminophen is a reasonable alternative, or can be used as an adjunct, they conclude that evidence suggests it is modestly less efficacious. (page 71)

Rating: 6a

Adams LL, Gatchel RJ, Robinson RC, Polatin P, Gajraj N, Deschner M, Noe C. Development of a self-report screening instrument for assessing potential opioid medication misuse in chronic pain patients. J Pain Symptom Manage. 2004 May;27(5):440-59

The Eugene McDermott Center for Pain, The University of Texas Southwestern Medical Center at Dallas, 75390, USA.

This study constituted the first step in the psychometric development of a self-report screening instrument for risk of opioid medication misuse among chronic pain patients. A 26-item instrument, the Pain Medication Questionnaire (PMQ), was constructed.

PMID: 15120773

Rating: 4a

Aetna Clinical Policy Bulletin. Ultra Rapid Detoxification (UROD). Number: 0317. 06/20/2006.

Aetna considers ultra rapid detoxification (UROD) experimental and investigational as a clinical detoxification treatment and for all other indications.

Rating: 8b

AHFS Drug Information. © Copyright, 1959-2008, Selected Revisions March 2008, American Society of Health-System Pharmacists, Inc. Bethesda, MD. 2008.

Rating: 9a

Akbik H, Butler SF, Budman SH, Fernandez K, Katz NP, Jamison RN. Validation and Clinical Application of the Screener and Opioid Assessment for Patients with Pain (SOAPP). J Pain Symptom Manage. 2006 Sep;32(3):287-293.

Departments of Anesthesiology and Pain Medicine (H.A.), University of Cincinnati, Cincinnati, Ohio.

The Screener and Opioid Assessment for Patients with Pain (SOAPP) is a brief, self-administered screening instrument used to assess suitability of long-term opioid therapy for chronic pain patients. A combined factor analysis of the SOAPP revealed five factors labeled 1) history of substance abuse, 2) legal problems, 3) craving medication, 4) heavy smoking, and 5) mood swings.

PMID: 16939853

Rating: 4a

Altmaier EM, Lehmann TR, Russell DW, Weinstein JN, Kao CF. The effectiveness of psychological interventions for the rehabilitation of low back pain: a randomized controlled trial evaluation. Pain. 1992 Jun;49(3):329-35.

Division of Psychological and Quantitative Foundations, University of Iowa, Iowa City 52242.

Forty-five low back pain patients. 81% of the patients had returned to work or were engaged in active job retraining by the follow-up. Patient improvement, however, was not differentially affected by

treatment group assignment, suggesting that the psychological treatment failed to add to the effectiveness obtained by the standard rehabilitation program.

PMID: 1408299

Rating: 2b

Altman RD, Aven A, Holmburg CE, Pfeifer LM, Sack M, Young GT. Capsaicin Cream 0.025% as Monotherapy for Osteoarthritis: A Double-Blind Study. Seminars in Arthritis and Rheumatism, June 1994;23: Suppl 3:25-33.

Patients (113). These results support the beneficial effects of 0.025% capsaicin cream as a first-line therapy for OA pain.

Rating 2c

AltMedDex®. AltMedDex® System [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. 1974-2008. Accessed July 2008

Rating: 9b

American Diabetes Association American Academy of Neurology. Consensus statement: Report and recommendations of the San Antonio conference on diabetic neuropathy. Diabetes Care. 1988 Jul-Aug;11(7):592-7.

What Is Diabetic Neuropathy? Diabetic neuropathy is a nerve disorder caused by diabetes. Symptoms of neuropathy include numbness and sometimes pain in the hands, feet, or legs.

PMID: 3060328

Rating: 5a

American Medical Association (AMA). Thermography update. H-175.988. Dec 23, 2005.

"(1) In view of the lack of sufficient proof of effectiveness, it is the policy of the AMA that the use of thermography for diagnostic purposes cannot be recommended at this time." (CSA Rep. C, A-93; Reaffirmed: CSA Rep. 8, A-03)

Rating: 8b

American Psychiatric Association, Diagnostic and Statistical Manual for Mental Disorders. 4th ed. Washington: APA Press, 1994.

Rating: 9a

Andersen JH, Kaergaard A, Frost P, Thomsen JF, Bonde JP, Fallentin N, Borg V, Mikkelsen S. Physical, psychosocial, and individual risk factors for neck/shoulder pain with pressure tenderness in the muscles among workers performing monotonous, repetitive work. Spine. 2002 Mar 15;27(6):660-7.

Department of Occupational Medicine, Herning Hospital, Herning, Denmark. hecjha@ringamt.dk

CONCLUSIONS: "Work-related physical and psychosocial factors, as well as several individual risk factors, are important in the understanding of neck/shoulder pain. The findings suggest that neck/shoulder pain has a multifactorial nature. Reduced health-related quality of life is associated with subjective pain and clinical signs from the neck and shoulders."

Rating: 4a Publication Type: Case Control, 3123 Cases

PMID: 11884915

Anderson VC, Cooke B, Burchiel KJ. Intrathecal hydromorphone for chronic nonmalignant pain: a retrospective study. Pain Med. 2001 Dec;2(4):287-97.

Department of Neurological Surgery, Oregon Health Sciences University, Portland, Oregon 97201, USA.

DESIGN: A retrospective review of 37 patients with chronic nonmalignant pain managed with intrathecal hydromorphone after failure of intraspinal morphine. RESULTS: Morphine was replaced with hydromorphone because of pharmacological complications (21/37; 57%) or inadequate analgesic response (16/37; 43%) after an average of 11 months +/- 11 SD of intrathecal therapy. Pharmacological complications, particularly nausea and vomiting, pruritus, and sedation were reduced by hydromorphone in most patients. Peripheral edema was improved by hydromorphone but tended to recur with prolonged hydromorphone exposure. Analgesic response was improved by at least 25% in six of 16 patients who were switched to hydromorphone because of poor pain relief.

PMID: 15102233

Rating: 3c

Anderson VC, Burchiel KJ. A prospective study of long-term intrathecal morphine in the management of chronic nonmalignant pain. Neurosurgery. 1999;4:289-300; discussion 300-1

Department of Neurological Surgery, Oregon Health Sciences University, Portland 97201, USA.

METHODS: Thirty participants reported successful pain relief during trial and were implanted with an intraspinal delivery system. RESULTS: Overall, 50% (11 of 22 patients) of the population reported at least a 25% reduction in visual analog scale pain after 24 months of treatment. Pharmacological side effects were managed medically by morphine dose reduction, addition of bupivacaine, or replacement of morphine with hydromorphone. Device-related complications requiring repeat operations were experienced by 20% of the patients.

PMID: 9932882

Rating: 3c

Angel IF, Gould HJ Jr, Carey ME. Intrathecal morphine pump as a treatment option in chronic pain of nonmalignant origin. Surg Neurol. 1998 Jan;49(1):92-8; discussion 98-9.

Department of Neurosurgery, Louisiana State University Medical Center, New Orleans 70112, USA.

BACKGROUND: Implantable pumps for the delivery of intrathecal morphine have become a common option for administering opiate medication for the management of pain in patients with terminal cancer. Options for treating chronic pain of non-malignant origin are more controversial. METHODS: Eleven patients. CONCLUSIONS: The morphine pump was found to be a viable alternative in the management of failed back syndrome. Its use in long-term therapy, however, is not without limitations and should be a last choice option.

PMID: 9428901

Rating: 4c

ANS, product literature, Indications for stimulator implantation, 2004

Neurostimulation - Who Can it Help? Neurostimulation is not for everyone.

First, you may be able to obtain relief from more conservative, less invasive or less expensive treatment options. Many doctors believe that other pain therapies — including analgesics, NSAIDs, and sometimes even surgery — should be tried and fail before offering patients the opportunity to try neurostimulation.

Second, you may have a type of pain that does not respond well to neurostimulation. Neurostimulation — in particular, spinal cord stimulation (dorsal column stimulation) — works best for neuropathic pain. Neurostimulation is generally considered to be ineffective in treating nociceptive pain.

Rating: 5c

Antman EM, Bennett JS, Daugherty A, Furberg C, Roberts H, Taubert KA. Use of Nonsteroidal Antiinflammatory Drugs. An Update for Clinicians. A Scientific Statement From the American Heart Association. Circulation. 2007 Feb 26.

PMID: 17325246

Rating: 6a

From Medscape:
The AHA recommends acetaminophen and aspirin as the best initial choices for analgesia of musculoskeletal pain. NSAIDs should be used at the smallest dose for the shortest course possible, and COX-2 inhibitors should be avoided if there is an alternative analgesic available.
starting with nonpharmacologic treatments, such as physical therapy and exercise, weight loss to reduce stress on joints, and heat or cold therapy. If this does not provide enough pain relief, acetaminophen, aspirin, and even short-term use of narcotic analgesics are recommended as first-line drugs. Then,
Some Question Narcotics as First-Line Treatment
While all appear to support the recommendation that COX-2 inhibitors should be last on the list, some experts have questioned the advice to give a narcotic before a non-COX-2 selective NSAID, particularly naproxen.
Appelboom T. Calcitonin in reflex sympathetic dystrophy syndrome and other painful conditions. Bone. 2002 May;30(5 Suppl):84S-86S.

Division of Rheumatology and Physical Medicine, Erasmus University Hospital, University of Brussels, Brussels, Belgium. tappelbo@ulb.ac.be

Salmon calcitonin (especially intranasal) provides an interesting analgesic effect in a series of painful conditions including reflex sympathetic dystrophy syndrome.

PMID: 12008165

Rating: 5b

Argoff CE. Topical agents for the treatment of chronic pain. Curr Pain Headache Rep. 2006 Feb;10(1):11-9.

North Shore University Hospital/NYU School of Medicine, Cohn Pain Management Center, Bethpage, NY 11714, USA. pargoff@optonline.net

Unlike systemic analgesics, topical analgesics exert their analgesic activity locally and without significant systemic absorption. This is in contrast to transdermal analgesics,

PMID: 16499825

Rating: 5b

Argoff CE, Katz N, Backonja M. Treatment of postherpetic neuralgia: a review of therapeutic options. J Pain Symptom Manage. 2004;28:396-411.

Cohn Pain Management Center, North Shore University Hospital, Cohn Pain Management Center, Bethpage, New York 11714, USA.

Postherpetic neuralgia (PHN) is a disabling consequence of the reactivation of the varicella zoster infection. Physicians can either add another agent to the current regimen or switch to a new type of monotherapy if there is inadequate response to initial therapy.

PMID: 15471658

Rating: 5b

Arnold LM, Goldenberg DL, Stanford SB, Lalonde JK, Sandhu HS, Keck PE Jr, Welge JA, Bishop F, Stanford KE, Hess EV, Hudson JI. Gabapentin in the treatment of fibromyalgia: a randomized, double-blind, placebo-controlled, multicenter trial. Arthritis Rheum. 2007 Apr;56(4):1336-44.

University of Cincinnati College of Medicine, Cincinnati, Ohio 45219, and Newton-Wellesley Hospital, Newton, MA, USA. Lesley.Arnold@uc.edu

METHODS: A 12-week, randomized, double-blind study was designed to compare gabapentin (1,200-2,400 mg/day) (n=75 patients) with placebo (n=75 patients) RESULTS: Gabapentin-treated patients displayed a significantly greater improvement in the BPI average pain severity score.

PMID: 17393438

Rating: 2a

American Society of Addiction Medicine (ASAM). Public policy statement on rapid and ultra rapid opioid detoxification (Formerly Public Policy Statement on Opioid Antagonist Agent Detoxification under Sedation or Anesthesia (OADUSA). www.asam.org. April 2005.

1. Opioid detoxification alone is not a treatment of opioid addiction. ASAM does not support the initiation of acute opioid detoxification interventions unless they are part of an integrated continuum of services that promote ongoing recovery from addiction.
2. Ultra-Rapid Opioid Detoxification (UROD) is a procedure with uncertain risks and benefits, and its use in clinical settings is not supportable until a clearly positive risk-benefit relationship can be demonstrated. Further research on UROD should be conducted.
3. Although there is medical literature describing various techniques of Rapid Opioid Detoxification (ROD), further research into the physiology and consequences of ROD should be supported so that patients may be directed to the most effective treatment methods and practices.
4. Prior to participation in any particular modality of opioid detoxification, a patient should be provided with sufficient information by which to provide informed consent, including information about the risks of termination of a treatment plan of prescribed agonist medications such as methadone or Buprenorphine, as well as the need to comply with medical monitoring of their clinical status for a defined period of time following the procedure to ensure a safe outcome. Patients should also be informed of the risks, benefits and costs of alternative methods of treatment available.

Rating: 6b

Arnold LM, Rosen A, Pritchett YL, D'Souza DN, Goldstein DJ, Iyengar S, Wernicke JF. A randomized, double-blind, placebo-controlled trial of duloxetine in the treatment of women with fibromyalgia with or without major depressive disorder. Pain. 2005 Dec 15;119(1-3):5-15.

Women's Health Research Program, Department of Psychiatry, University of Cincinnati College of Medicine, Cincinnati, OH 45219, USA. lesley.arnold@uc.edu

354 female patients. In conclusion, both duloxetine 60 mg QD and duloxetine 60 mg BID were effective and safe in the treatment of fibromyalgia in female patients with or without major depressive disorder.

PMID: 16298061

Rating: 2a

Arnold LM. Duloxetine and other antidepressants in the treatment of patients with fibromyalgia. Pain Med. 2007;8:S63-74.

Women's Health Research Program, University of Cincinnati College of Medicine, Cincinnati, Ohio, USA. lesley.arnold@uc.edu

OBJECTIVE: To review the use of duloxetine, a new selective serotonin and norepinephrine reuptake inhibitor (SNRI), and other antidepressants in the treatment of patients with fibromyalgia. DESIGN: Two randomized, placebo-controlled, double-blind, parallel-group, 12-week trials of duloxetine in the treatment of fibromyalgia were reviewed. Other published, randomized, placebo-controlled, double-blind trials, and meta-analyses of antidepressant treatment of fibromyalgia were identified by a PubMed search that was augmented by reference cross-check. RESULTS: Duloxetine has been shown to be an effective and safe treatment for many of the symptoms associated with fibromyalgia, particularly for women. Other selective SNRIs also show promise in the treatment of fibromyalgia. Until recently, tricyclic agents that have serotonin and norepinephrine reuptake inhibitory activity had been the most commonly studied group of antidepressants, and they are effective in treating pain and other symptoms associated with fibromyalgia, although their use may be limited by safety and tolerability concerns. There are few randomized, controlled studies of selective serotonin reuptake inhibitors in fibromyalgia, and the results have been mixed. CONCLUSIONS: Antidepressants play an important role in the treatment of patients with fibromyalgia. Agents with dual effects on serotonin and norepinephrine appear to have more consistent benefits than selective serotonin antidepressants for the treatment of persistent pain associated with fibromyalgia.

PMID: 17714117

Rating: 5a

Asfour SS, Khalil TM, Waly SM, Goldberg ML, Rosomoff RS, Rosomoff HL. Biofeedback in back muscle strengthening. Spine. 1990 Jun;15(6):510-3.

Comprehensive Pain and Rehabilitation Center, University of Miami Medical School, Florida.

This study was undertaken to investigate the use of electromyography (EMG) biofeedback as an add-on therapy to standard exercise in the restoration of the functional abilities of the trunk extensor muscles in patients suffering from chronic low-back pain (CLBP). A controlled experimental investigation was conducted to study the effectiveness of using the proposed treatment modality in the management of the low-back pain problem. The results obtained indicate that the proposed methodology was an effective tool to achieve a significant improvement in the strength of lumbar paraspinal muscles of chronic low-back pain patients.

PMID: 2144915

Rating: 2c

The study included 30 patients, and found that the increase in strength was greater in the biofeedback group (81.3%) versus the control group (16.9%).

Ashburn MA and Staats PS. Management of Chronic Pain. Lancet 1999;353:1865-69.
Department of Anesthesiology, University of Utah Health Sciences Center, Salt Lake City 84132, USA.
Publication Type: Review
PMID: 10359427

Ashton H. The diagnosis and management of benzodiazepine dependence. Curr Opin Psychiatry. 2005 May;18(3):249-55.

Department of Psychiatry, University of Newcastle upon Tyne, Royal Victoria Infirmary, Newcastle upon Tyne, UK. c.h.ashton@ncl.ac.uk

PURPOSE OF REVIEW: Despite repeated recommendations to limit benzodiazepines to short-term use (2-4 weeks), doctors worldwide are still prescribing them for months or years. This over-prescribing has resulted in large populations of long-term users who have become dependent on benzodiazepines and has also led to leakage of benzodiazepines into the illicit drug market. This review outlines the risks of long-term benzodiazepine use, gives guidelines on the management of benzodiazepine withdrawal and suggests ways in which dependence can be prevented. RECENT FINDINGS: Recent literature shows that benzodiazepines have all the characteristics of drugs of dependence and that they are inappropriately prescribed for many patients, including those with physical and psychiatric problems, elderly residents of care homes and those with comorbid alcohol and substance abuse. Many trials have investigated methods of benzodiazepine withdrawal, of which the keystones are gradual dosage tapering and psychological support when necessary. Several studies have shown that mental and physical health and cognitive performance improve after withdrawal, especially in elderly patients taking benzodiazepine hypnotics, who comprise a large proportion of the dependent population. SUMMARY: Benzodiazepine dependence could be prevented by adherence to recommendations for short-term prescribing (2-4 weeks only when possible). Withdrawal of benzodiazepines from dependent patients is feasible and need not be traumatic if judiciously, and often individually, managed.

PMID: 16639148

Rting: 5b

Asmundson GJ, Norton PJ, Norton GR. Beyond pain: the role of fear and avoidance in chronicity. Clin Psychol Rev. 1999 Jan;19(1):97-119. Review.
Regina Health District, Clinical Research and Development Program, Saskatchewan, Canada. gasmundson@reginahealth.sk.ca
The purpose of the present article is to provide unification to a number of somewhat disparate themes in the chronic pain and phobia literature. First, we present a summary review of the early writings and current theoretical perspectives regarding the role of avoidance in the maintenance of chronic pain. Second, we present an integrative review of recent empirical investigations of fear and avoidance in

patients with chronic musculoskeletal pain, relating the findings to existing cognitive-behavioral theoretical positions. We also discuss several new and emerging lines of investigation, specifically related to information processing and anxiety sensitivity, which appear to be closely linked to pain-related avoidance behavior. Finally, we discuss the implications of the recent empirical findings for the assessment and treatment of individuals who experience disabling chronic musculoskeletal pain and suggest possible avenues for future investigation.

Publication Types:
- Review
- Review, Tutorial

PMID: 9987586

Asnis GM, Kohn SR, Henderson M, Brown NL. SSRIs versus non-SSRIs in post-traumatic stress disorder: an update with recommendations. Drugs. 2004;64(4):383-404.

Department of Psychiatry and Behavioral Sciences, Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, New York 10467, USA. asnisarts@aol.com

Post-traumatic stress disorder (PTSD) is a highly prevalent (7.8% lifetime rate) anxiety disorder with impairment in daily functioning, frequent suicidal behaviour and high rates of co-morbidity. Fortunately, PTSD is responsive to pharmacotherapy and psychotherapy. The selective serotonin reuptake inhibitors (SSRIs) are the most studied medications for PTSD, with the largest number of double-blind, placebo-controlled trials. Of the SSRIs, sertraline, paroxetine and fluoxetine have been the most extensively studied, with sertraline and paroxetine being US FDA-approved for PTSD. These studies have demonstrated that SSRIs are effective in short-term trials (6-12 weeks). Furthermore, continuation and maintenance treatment for 6-12 months decrease relapse rates. Besides being the most studied and effective drugs for PTSD, SSRIs have a favourable adverse effect profile, making them the first-line treatment for PTSD. If SSRIs are not tolerated or are ineffective, non-SSRIs should be considered. Serotonin-potentiating non-SSRIs, such as venlafaxine, nefazodone, trazodone and mirtazapine, have been evaluated in PTSD only in open-label and case studies. Because of their promising results and relatively good safety profile, they should be considered as second-line treatment. Monoamine oxidase inhibitors (MAOIs) and tricyclic antidepressants (TCAs) have both been evaluated in a small number of double-blind, placebo-controlled studies. The results have been inconsistent but promising. In the limited comparative studies, MAOIs appeared superior to TCAs but patients continued to have residual symptoms. These drugs have significant adverse effects, such as cardiovascular complications, and safety issues, such as ease of overdose. Therefore, TCAs and MAOIs should be considered as third-line treatment. Anticonvulsants have been evaluated in PTSD in open-label studies and results have been positive for carbamazepine, valproic acid, topiramate and gabapentin. A small double-blind, placebo-controlled study demonstrated efficacy of lamotrigine for PTSD. Anticonvulsants should be considered where co-morbidity of bipolar disorder exists, and where impulsivity and anger predominate. Bupropion

(amfebutamone), a predominantly noradrenergic reuptake inhibitor, was ineffective in PTSD in an open-label study. Benzodiazepines were ineffective in a double-blind, placebo-controlled study despite encouraging case reports. They should be avoided or used only short term because of potential depressogenic effects, and the possibility that they may promote or worsen PTSD. Buspirone, a non-benzodiazepine anxiolytic, was found to be effective in PTSD only in open-label studies. Recently, atypical antipsychotics were as effective as monotherapy and as an augmenter to SSRIs in open-label/case studies and small double-blind, placebo-controlled trials; atypical antipsychotics should be considered in PTSD where paranoia or flashbacks are prominent and in potentiating SSRIs in refractory cases.

Publication Types:
- Review
- Review, Tutorial

PMID: 14969574

Rating: 5b

Astin JA, Shapiro SL, Eisenberg DM, Forys KL, Mind-body medicine: state of the science, implications for practice, J Am Board Fam Pract. 2003 Mar-Apr;16(2):131-47.

California Pacific Medical Center, San Francisco 94115, USA.

BACKGROUND: Although emerging evidence during the past several decades suggests that psychosocial factors can directly influence both physiologic function and health outcomes, medicine had failed to move beyond the biomedical model, in part because of lack of exposure to the evidence base supporting the biopsychosocial model. The literature was reviewed to examine the efficacy of representative psychosocial-mind-body interventions, including relaxation, (cognitive) behavioral therapies, meditation, imagery, biofeedback, and hypnosis for several common clinical conditions. METHODS: An electronic search was undertaken of the MEDLINE, PsycLIT, and the Cochrane Library databases and a manual search of the reference sections of relevant articles for related clinical trials and reviews of the literature. Studies examining mind-body interventions for psychological disorders were excluded. Owing to space limitations, studies examining more body-based therapies, such as yoga and tai chi chuan, were also not included. Data were extracted from relevant systematic reviews, meta-analyses, and randomized controlled trials. RESULTS: Drawing principally from systematic reviews and meta-analyses, there is considerable evidence of efficacy for several mind-body therapies in the treatment of coronary artery disease (eg, cardiac rehabilitation), headaches, insomnia, incontinence, chronic low back pain, disease and treatment-related symptoms of cancer, and improving postsurgical outcomes. We found moderate evidence of efficacy for mind-body therapies in the areas of hypertension and arthritis. Additional research is required to clarify the relative efficacy of different mind-body therapies, factors (such as specific patient characteristics) that might predict more or less

successful outcomes, and mechanisms of action. Research is also necessary to examine the cost offsets associated with mind-body therapies. CONCLUSIONS: There is now considerable evidence that an array of mind-body therapies can be used as effective adjuncts to conventional medical treatment for a number of common clinical conditions.

Publication Types:
- Review
- Review, Academic

PMID: 12665179
Rating: 1c
Atalay A, Arslan S, Dincer F. Psychosocial function, clinical status, and radiographic findings in a group of chronic low back pain patients. Rheumatol Int. 2001 Oct;21(2):62-5.
Hacettepe University, Department of Physical Medicine and Rehabilitation, Ankara, Turkey.
ayce@hacettepe.edu.tr
Abstract:
Low back pain is considered a problem with multiple facets for which the underlying causative factors should be determined. The aim of this study was to evaluate the relationships between depression, clinical status, and radiographic findings in a group of fifty patients with low back pain for more than 6 months. The patients underwent clinical examination and they completed Beck depression inventory (BDI), Aberdeen back pain scale (ABPS) and research questionnaire. Radiographic evaluations were performed. Clinical score and duration of symptoms were found to be positively correlated. The BDI scores were not found to be correlated with the existing variables. The ABPS scores were positively correlated with clinical scores and number of medications used.
Publication Type: Case Control, 50 cases
PMID: 11732860

Atkins D, Best D, Briss PA, Eccles M, Falck-Ytter Y, Flottorp S, Guyatt GH, Harbour RT, Haugh MC, Henry D, Hill S, Jaeschke R, Leng G, Liberati A, Magrini N, Mason J, Middleton P, Mrukowicz J, O'Connell D, Oxman AD, Phillips B, Schunemann HJ, Edejer TT, Varonen H, Vist GE, Williams JW Jr, Zaza S; GRADE Working Group. Grading quality of evidence and strength of recommendations. BMJ. 2004 Jun 19;328(7454):1490.

Users of clinical practice guidelines and other recommendations need to know how much confidence they can place in the recommendations. Systematic and explicit methods of making judgments can reduce errors and improve communication. We have developed a system for grading the quality of evidence and the strength of recommendations that can be applied across a wide range of interventions and contexts. In this article we present a summary of our approach from the perspective of a guideline user. Judgments about the strength of a recommendation require consideration of the balance between benefits and harms, the quality of the evidence, translation of the evidence into specific circumstances, and the certainty of the baseline risk. It is also important to consider costs (resource utilisation) before

making a recommendation. Inconsistencies among systems for grading the quality of evidence and the strength of recommendations reduce their potential to facilitate critical appraisal and improve communication of these judgments. Our system for guiding these complex judgments balances the need for simplicity with the need for full and transparent consideration of all important issues.

PMID: 15205295

Rating: 5b

Attal N, Cruccu G, Haanpää M, Hansson P, Jensen TS, Nurmikko T, Sampaio C, Sindrup S, Wiffen P; EFNS Task Force. EFNS guidelines on pharmacological treatment of neuropathic pain. Eur J Neurol 2006;13:1153-69.

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Neuropathic pain treatment remains unsatisfactory despite a substantial increase in the number of trials. This EFNS Task Force aimed at evaluating the existing evidence about the pharmacological treatment of neuropathic pain. Studies were identified using first the Cochrane Database then Medline. Trials were classified according to the aetiological condition. All class I and II controlled trials (according to EFNS classification of evidence) were assessed, but lower-class studies were considered in conditions that had no top level studies. Only treatments feasible in an outpatient setting were evaluated. Effects on pain symptoms/signs, quality of life and comorbidities were particularly searched for. Most of the randomized controlled trials included patients with postherpetic neuralgia (PHN) and painful polyneuropathies (PPN) mainly caused by diabetes. These trials provide level A evidence for the efficacy of tricyclic antidepressants, gabapentin, pregabalin and opioids, with a large number of class I trials, followed by topical lidocaine (in PHN) and the newer antidepressants venlafaxine and duloxetine (in PPN). A small number of controlled trials were performed in central pain, trigeminal neuralgia, other peripheral neuropathic pain states and multiple-aetiology neuropathic pains. The main peripheral pain conditions respond similarly well to tricyclic antidepressants, gabapentin, and pregabalin, but some conditions, such as HIV-associated polyneuropathy, are more refractory. There are too few studies on central pain, combination therapy, and head-to-head comparison. For future trials, we recommend to assess quality of life and pain symptoms or signs with standardized tools.

PMID: 17038030

Rating: 1A

Avouac J, Gossec L, Dougados M. Efficacy and safety of opioids for osteoarthritis: a meta-analysis of randomized controlled trials. Osteoarthritis Cartilage. 2007 Mar 28; [Epub ahead of print]

René Descartes University, Medicine Faculty, APHP Cochin Hospital, Rheumatology B Department, Paris, France.

OBJECTIVES: To determine the analgesic effectiveness, the effect on physical function and the safety of opioids in patients with osteoarthritis (OA). SEARCH STRATEGY: A systematic literature search was performed in electronic databases up to October 2006. A hand search of references was also performed. SELECTION CRITERIA: All randomized controlled trials evaluating the efficacy and/or the safety of opioids vs placebo or non-opioid analgesics in patients with OA were selected. DATA COLLECTION AND ANALYSIS: Data were collected using a predetermined form. Statistical analysis determined in each trial the effect size to assess the magnitude of treatment effect and the number needed to harm (NNH) to evaluate opioids safety. MAIN RESULTS: Eighteen randomized placebo-controlled trials were analyzed, i.e., a total of 3244 participants who received opioids and 1612 who received placebo. The mean trial duration was 13+/-18 weeks. The pooled effect sizes of all opioids vs placebo for pain intensity and physical function were -0.79 (95% confidence interval, CI, -0.98 to -0.59) and -0.31 (95% CI -0.39 to -0.24), respectively. The NNH was calculated to be 5 vs placebo. The number of studies (n=4) that compared opioids with non-opioid analgesics (paracetamol and non-steroidal anti-inflammatory drugs) was too limited to provide robust data. CONCLUSIONS: Opioids significantly decrease pain intensity and have small benefits on function compared with placebo in patients with OA. Adverse events, although reversible and not life threatening, often cause participants to stop taking the medication and could limit opioid usefulness. Moreover, the long-term efficacy and safety of these drugs for OA is yet to be determined due to the short mean trial duration.

PMID: 17398122

Rating: 1b

Aydin G, Tomruk S, Keles I, Demir SO, Orkun S. Transcutaneous electrical nerve stimulation versus baclofen in spasticity: clinical and electrophysiologic comparison. Am J Phys Med Rehabil. 2005 Aug;84(8):584-92.

Department of Physical Medicine and Rehabilitation, Kirikkale University, Faculty of Medicine, Kirikkale, Turkey.

OBJECTIVES: Clinical and electrophysiologic comparison of the efficacy of transcutaneous electrical nerve stimulation (TENS) and oral baclofen in the treatment of spasticity. DESIGN: Patients with spinal cord injury and spasticity were included in the study. Ten patients were assigned to oral baclofen and 11 to TENS groups. For the comparison of H-reflex variables, 20 healthy individuals were allocated to a control group. TENS was applied to the tibial nerve for 15 days at a frequency of 100 Hz. Clinical (spasm frequency scale, painful spasm scale, lower limb Ashworth score, clonus score, deep tendon reflex score, plantar stimulation response score) and electrophysiologic evaluations (H-reflex response at the highest amplitude, latency of maximum H-reflex, and ratio of H-reflex response at the highest

amplitude to M response at maximum amplitude) of the lower limb and functional evaluations (functional disability score and FIM) were carried out in baclofen and TENS groups before and after treatment. Posttreatment evaluation was made 24 hrs after the 15th session in the TENS group. In addition, clinical spasticity scores and electrophysiologic variables were measured 15 mins after the first application and 15 mins after the 15th session. RESULTS: Significant improvement was detected in lower limb Ashworth score, spasm frequency scale, deep tendon reflex score, functional disability score, and FIM in the baclofen (P = 0.011, P = 0.014, P = 0.025, P = 0.004, and P = 0.005, respectively) and TENS (P = 0.020, P = 0.014, P = 0.025, P = 0.003, and P = 0.003, respectively) group after treatment. Decrease in H-reflex maximum amplitude was significant in the TENS group (P = 0.026). Most marked improvement was observed in the third evaluation, 15 mins after the 15th session, particularly in lower limb Ashworth score (P = 0.006) and H-reflex maximum amplitude (P = 0.006) in the TENS group. The percentage change in clinical, electrophysiologic, and functional variables caused by baclofen was not different from that caused by repeated applications of TENS in the short- and long-term evaluations (P > 0.05). CONCLUSION: TENS may be recommended as a supplement to medical treatment in the management of spasticity.

PMID: 16034227

Rating: 2c

Backonja MM, Serra J. Pharmacologic management part 1: better-studied neuropathic pain diseases. Pain Med. 2004;5:S28-47.

University of Wisconsin Hospital and Clinics, Madison, Wisconsin, USA.

Neuropathic pain impacts millions of people in the United States and around the world. Patients experience one of many symptoms, such as pain, paresthesia, dysesthesia, hyperalgesia, and allodynia, for many years because of unavailable or inadequate treatment. One of the major challenges in treating patients with neuropathic pain syndromes is a lack of consensus concerning the appropriate first-line treatment options for conditions associated with neuropathic pain, including postherpetic neuralgia, diabetic peripheral neuropathy, and trigeminal neuralgia. This review summarizes the published results of randomized trials involving treatment for neuropathic pain conditions. Anticonvulsants, such as gabapentin, carbamazepine, and lamotrigine, and tricyclic antidepressants, including amitriptyline and desipramine, have demonstrated efficacy in relieving pain associated with postherpetic neuralgia, diabetic peripheral neuropathy, and trigeminal neuralgia, in several studies. However, the lack of head-to-head comparison studies of these agents limits the conclusions that can be reached. Clinicians who must make decisions regarding the care of individual patients may find some guidance from the number of randomized trials with a positive outcome for each agent. Using quality-of-life study outcomes, treatment strategies must encompass the impact of therapeutic agents on the comorbid conditions of sleep disturbance and mood and anxiety disorders associated with neuropathic pain. Looking to the future, emerging therapies, such as pregabalin and newer N-methyl-D-aspartate-receptor blockers, may

provide physicians and patients with new treatment options for more effective relief of pain. Copyright American Academy of Pain Medicine

PMID: 14996228

Rating: 5a

Backonja MM. Use of anticonvulsants for treatment of neuropathic pain. Neurology. 2002. 10:59:s14-7.

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Emerging evidence from animal models of neuropathic pain suggests that many pathophysiologic and biochemical changes occur in the peripheral and central nervous system. Similarities between the pathophysiologic phenomena observed in some epilepsy models and in neuropathic pain models justify the use of anticonvulsants in the symptomatic management of neuropathic pain. Positive results from laboratory and clinical trials further support such use. Carbamazepine was the first of this class of drugs to be studied in clinical trials and has been longest in use for treatment of neuropathic pain. Clinical trial data support its use in treating trigeminal neuralgia, but data for treatment of painful diabetic neuropathy are less convincing. Use of newer anticonvulsants has marked a new era in the treatment of neuropathic pain. Gabapentin has demonstrated efficacy, specifically in painful diabetic neuropathy and postherpetic neuralgia. Lamotrigine has been reported to be effective in relieving pain from trigeminal neuralgia refractory to other treatments, HIV neuropathy, and central post-stroke pain. Results from clinical trials of phenytoin are equivocal. Zonisamide's mechanisms of action suggest that it would be effective in controlling neuropathic pain symptoms. Other anticonvulsants, including lorazepam, valproate, topiramate, and tiagabine, have also been under investigation. Anecdotal experience provides support for studies with oxcarbazepine and levetiracetam for treating neuropathic pain. Evidence supporting the efficacy of anticonvulsants in treatment of such pain is evolving. Additional clinical trials should provide information that will better define their role in neuropathic pain.

PMID: 12221151

Rating: 1b

Backonja M, Beydoun A, Edwards KR, Schwartz SL, Fonseca V, Hes M, LaMoreaux L, Garofalo E. Gabapentin for the symptomatic treatment of painful neuropathy in patients with diabetes mellitus: a randomized controlled trial. JAMA. 1998 Dec 2;280(21):1831-6.

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CONTEXT: Pain is the most disturbing symptom of diabetic peripheral neuropathy. As many as 45% of patients with diabetes mellitus develop peripheral neuropathies. OBJECTIVE: To evaluate the effect of gabapentin monotherapy on pain associated with diabetic peripheral neuropathy. DESIGN: Randomized, double-blind, placebo-controlled, 8-week trial conducted between July 1996 and March 1997. SETTING: Outpatient clinics at 20 sites. PATIENTS: The 165 patients enrolled had a 1- to 5-year history of pain attributed to diabetic neuropathy and a minimum 40-mm pain score on the Short-Form McGill Pain Questionnaire visual analogue scale. INTERVENTION: Gabapentin (titrated from 900 to 3600 mg/d or maximum tolerated dosage) or placebo. MAIN OUTCOME MEASURES: The primary efficacy measure was daily pain severity as measured on an 11-point Likert scale (0, no pain; 10, worst possible pain). Secondary measures included sleep interference scores, the Short-Form McGill Pain Questionnaire scores, Patient Global Impression of Change and Clinical Global Impression of Change, the Short Form-36 Quality of Life Questionnaire scores, and the Profile of Mood States results. RESULTS: Eighty-four patients received gabapentin and 70 (83%) completed the study; 81 received placebo and 65 (80%) completed the study. By intent-to-treat analysis, gabapentin-treated patients' mean daily pain score at the study end point (baseline, 6.4; end point, 3.9; n = 82) was significantly lower (P<.001) compared with the placebo-treated patients' end-point score (baseline, 6.5; end point, 5.1; n = 80). All secondary outcome measures of pain were significantly better in the gabapentin group than in the placebo group. Additional statistically significant differences favoring gabapentin treatment were observed in measures of quality of life (Short Form-36 Quality of Life Questionnaire and Profile of Mood States). Adverse events experienced significantly more frequently in the gabapentin group were dizziness (20 [24%] in the gabapentin group vs 4 [4.9%] in the control group; P<.001) and somnolence (19 [23%] in the gabapentin group vs 5 [6%] in the control group; P = .003). Confusion was also more frequent in the gabapentin group (7 [8%] vs 1 [1.2%]; P = .06). CONCLUSION: Gabapentin monotherapy appears to be efficacious for the treatment of pain and sleep interference associated with diabetic peripheral neuropathy and exhibits positive effects on mood and quality of life.

PMID: 9846777

Rating: 2b

Baillargeon L, Landreville P, Verreault R, Beauchemin JP, Gregoire JP, Morin CM. Discontinuation of benzodiazepines among older insomniac adults treated with cognitive-behavioural therapy combined with gradual tapering: a randomized trial. CMAJ. 2003 Nov 11;169(10):1015-20.

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BACKGROUND: Long-term use of hypnotics is not recommended because of risks of dependency and adverse effects on health. The usual clinical management of benzodiazepine dependency is gradual tapering, but when used alone this method is not highly effective in achieving long-term discontinuation. We compared the efficacy of tapering plus cognitive-behavioural therapy for insomnia with tapering

alone in reducing the use of hypnotics by older adults with insomnia. METHODS: People with chronic insomnia who had been taking a benzodiazepine every night for more than 3 months were recruited through media advertisements or were referred by their family doctors. They were randomly assigned to undergo either cognitive-behavioural therapy plus gradual tapering of the drug (combined treatment) or gradual tapering only. The cognitive-behavioural therapy was provided by a psychologist in 8 weekly small-group sessions. The tapering was supervised by a physician, who met weekly with each participant over an 8-week period. The main outcome measure was benzodiazepine discontinuation, confirmed by blood screening performed at each of 3 measurement points (immediately after completion of treatment and at 3- and 12-month follow-ups). RESULTS: Of the 344 potential participants, 65 (mean age 67.4 years) met the inclusion criteria and entered the study. The 2 study groups (35 subjects in the combined treatment group and 30 in the tapering group) were similar in terms of demographic characteristics, duration of insomnia and hypnotic dosage. Immediately after completion of treatment, a greater proportion of patients in the combined treatment group had withdrawn from benzodiazepine use completely (77% [26/34] v. 38% [11/29]; odds ratio [OR] 5.3, 95% confidence interval [CI] 1.8-16.2; OR after adjustment for initial benzodiazepine daily dose 7.9, 95% CI 2.4-30.9). At the 12-month follow-up, the favourable outcome persisted (70% [23/33] v. 24% [7/29]; OR 7.2, 95% CI 2.4-23.7; adjusted OR 7.6, 95% CI 2.5-26.6); similar results were obtained at 3 months. INTERPRETATION: A combination of cognitive-behavioural therapy and benzodiazepine tapering was superior to tapering alone in the management of patients with insomnia and chronic benzodiazepine use. The beneficial effects were sustained for up to 1 year. Applying this multidisciplinary approach in the community could help reduce benzodiazepine use by older people.

PMID: 14609970

Rating: 2b

Baldwin DS, Anderson IM, Nutt DJ, Bandelow B, Bond A, Davidson JR, den Boer JA, Fineberg NA, Knapp M, Scott J, Wittchen HU; British Association for Psychopharmacology. Evidence-based guidelines for the pharmacological treatment of anxiety disorders: recommendations from the British Association for Psychopharmacology. J Psychopharmacol. 2005; 19:567-96.

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This British Association for Psychopharmacology guidelines covers the range and aims of treatment for anxiety disorders. They are based explicitly on the available evidence and are presented as recommendations to aid clinical decision making in primary and secondary medical care. They may also serve as a source of information for patients and their cares. The recommendations are presented together with a more detailed review of the available evidence. A consensus meeting involving experts in anxiety disorders reviewed the main subject areas and considered the strength of evidence and its clinical implications. The guidelines were constructed after extensive feedback from participants and interested parties. The strength of supporting evidence for recommendations was rated. The guidelines

cover the diagnosis of anxiety disorders and key steps in clinical management, including acute treatment, relapse prevention and approaches for patients who do not respond to first-line treatments.

PMID: 16272179

Rating: 5a

Baliki MN, Geha PY, Apkarian AV, Chialvo DR. Beyond feeling: chronic pain hurts the brain, disrupting the default-mode network dynamics. J Neurosci. 2008 Feb 6;28(6):1398-403.

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Chronic pain patients suffer from more than just pain; depression and anxiety, sleep disturbances, and decision-making abnormalities (Apkarian et al., 2004a) also significantly diminish their quality of life. Recent studies have demonstrated that chronic pain harms cortical areas unrelated to pain (Apkarian et al., 2004b; Acerra and Moseley, 2005), but whether these structural impairments and behavioral deficits are connected by a single mechanism is as of yet unknown. Here we propose that long-term pain alters the functional connectivity of cortical regions known to be active at rest, i.e., the components of the "default mode network" (DMN). This DMN (Raichle et al., 2001; Greicius et al., 2003; Vincent et al., 2007) is marked by balanced positive and negative correlations between activity in component brain regions. In several disorders, however this balance is disrupted (Fox and Raichle, 2007). Using well validated functional magnetic resonance imaging (fMRI) paradigms to study the DMN (Fox et al., 2005), we investigated whether the impairments of chronic pain patients could be rooted in disturbed DMN dynamics. Studying with fMRI a group of chronic back pain (CBP) patients and healthy controls while executing a simple visual attention task, we discovered that CBP patients, despite performing the task equally well as controls, displayed reduced deactivation in several key DMN regions. These findings demonstrate that chronic pain has a widespread impact on overall brain function, and suggest that disruptions of the DMN may underlie the cognitive and behavioral impairments accompanying chronic pain.

PMID: 18256259

Rating: 4c

Ballantyne JC, Mao J, Opioid therapy for chronic pain, N Engl J Med. 2003 Nov 13;349(20): 1943-53.

From: jhchristianmd, Sent: Saturday, January 03, 2004 2:26 PM
To: WorkFitnessandDisabilityRoundtable@yahoogroups.com
Subject: [WFDRoundtable] What can you do? Narcotic use in chronic pain?

What can be done when we see people with chronic non-cancer pain who have become totally dysfunctional or even addicted to pain-killers by their well-meaning (but weak) treating physicians?

Here are some excerpts from a recent article on long-term use of opiates in chronic pain:

Opioid Therapy for Chronic Pain [review article] New England J of Med 2003; 349-1943-53

The recognition that opioid therapy can relief pain and improve mood and functioning in many patients with chronic pain has led experts on paid to recommend that such patients not be denied opioids. . . .Key organizations . . have published consensus statements to guide physicians [that] emphasize the importance of a standardized [and] . . . necessarily elaborate process [which] should be fully documented.

. . . The published trials leave two important questions unawered: Is opioid therapy beneficial in the long term (over a period of years rathern than months)? Does the dose have an effect on the efficacy and the safety of long-term therapy?

. . . Opioid tolerance . . develops with the repeated use of opioids and brings about the need to increase the dose to maintain equipotent [equally effective] analgesic [pain-relieving] effects . . . and may be a reason for dose escalation.

. . . Abnormal pain sensitivity . . . is manifested as increased pain (perceived as tenderness) from noxious stimuli (hyperalgesia) and as pain from previously innocuous stimuli (allodynia). Long-term use of opioids may also be associated with the development of abnormal sensitivity to pain . . . [and] has been observed in patients treated for both pain and addicition.

. . . Repeated administration of opioids not only results in the development of tolerance (a desensitization process) but also leads to a pro-noiceptive (sensitization) process. Together, . . [they] may contribute to an apparent decrease in analgesic efficacy regardless of the progression of the pain.

. . . [A]bnormal pain sensitivity may, at least in part, explain the failure to relieve pain in some patients, despite inreases in the opioid dose. Thus, in some instances, treating increasing pain with increasing doses of opioids may be futile.

. . Paradoxically, opioid treatment may be offered in an attempt to improve pain and funtioning, and thereby reduce the burden of care, but the treatment may actually increase the burden of care, because the management of opioid therapy in patients with complex problems is time-consuming and difficult. When the necessary resources of time, personnel, and multidisciplinary rehabilitation are not available, physicians tend to bypass the principles outlined in the guidelines

and comply with patients' demands for increased opioid doses, even when the treatment goals are not achieved.

. . . . Deterioriation in funtioning or quality of life appears to be closedly associated with lack of motivation to improve; young adults are the most susceptible to this type of deterioration. . . .

. . . Current guidelines recommend a cautious approach to dose escalation and the discontinuation of opioids if treatment goals are not met. However, in busy practice settings, the reality of dealing with patients who have complex problems often forces physicians to compromise. As a consequence, very large doses of opioids are prescribed for patients with chronic pain that is not associated with terminal disease, often in the absence of any real improvement in the patient's pain or level of functioning. Whereas it was was previously thought that unlimited dose escalation was at least safe, evidence now suggests that prolonged, high-dose opioid therapy may be neither safe nor effect. It is therefore important that physicians make every effort to control indiscriminate prescribing, even when they are under pressure by patients to increase the dose of opioids.

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Publication Types:
- Review
- Review, Tutorial

PMID: 14614170

Rating: 5b

Ballantyne JC. Opioids for chronic nonterminal pain. South Med J. 2006;99):1245-55.

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This article first reviews the evidence for and against chronic opioid therapy. Evidence supporting the opioid responsiveness of chronic pain, including neuropathic pain, includes multiple randomized trials conducted over months (up to 8 months). Observational studies are conducted for longer, and many also support opioid analgesic efficacy. Concerns have arisen about loss of efficacy with prolonged use, possibly related to tolerance or opioid-induced hyperalgesia. Mechanisms of tolerance and opioid-induced hyperalgesia are explored. Evidence on other important outcomes such as improvement in function and quality of life is mixed, and is less convincing than evidence supporting analgesic efficacy. It is clear from current evidence that many patients abandon chronic opioid therapy because of the

unacceptability of side effects. There are also concerns about toxicity, especially when opioids are used in high doses for prolonged periods, related to hormonal and immune function. The issue of addiction during opioid treatment of chronic pain is also explored. Addiction issues present many complex questions that have not been satisfactorily answered. Opioid treatment of pain has been, and remains, severely hampered because of actual and legal constraints related to addiction risk. Pain advocacy has focused on placing addiction risk into context so that addiction fears do not compromise effective treatment of pain. On the other hand, denying addiction risk during opioid treatment of chronic pain has not been helpful in terms of providing physicians with the tools needed for safe chronic opioid therapy. Here, a structured goal-directed approach to chronic opioid treatment is suggested; this aims to select and monitor patients carefully, and wean therapy if treatment goals are not reached. Chronic opioid therapy for pain has not been a universal success since it was re-established during the last two decades of the twentieth century. It is now realized that the therapy is not as effective or as free from addiction risk as was once thought. Knowing this, many ethical dilemmas arise, especially in relation to patients' right to treatment competing with physicians' need to offer the treatment selectively. In the future, we must learn how to select patients for this therapy who are likely to achieve improvement in pain, function and quality of life without interference from addiction. Efforts will also be made in the laboratory to identify opioids with lower abuse potential.

PMID: 17195420

Rating: 5b

Bandelow B, Zohar J, Hollander E, Kasper S, Möller HJ; World Federation of Societies of Biological Psychiatry Task Force on Treatment Guidelines for Anxiety, Obsessive-Compulsive and Posttraumatic Stress Disorders. World Federation of Societies of Biological Psychiatry (WFSBP) guidelines for the pharmacological treatment of anxiety, obsessive-compulsive and posttraumatic stress disorders. World J Biol Psychiatry. 2002; 3:171-99

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In this report, recommendations for the pharmacological treatment of anxiety and obsessive-compulsive disorders are presented, based on available randomized, placebo- or comparator-controlled clinical studies. Selective serotonin reuptake inhibitors (SSRIs) are the first-line treatment for panic disorder. Tri2-cyclic antidepressants (TCAs) are equally effective, but they are less well tolerated than the SSRIs. In treatment-resistant cases, benzodiazepines like alprazolam may be used when the patient does not have a history of dependency and tolerance. Due to possible serious side effects and interactions with other drugs and food components, the irreversible monamine oxidase inhibitor (MAOI) phenelzine should be used only when first-line drugs have failed. In generalised anxiety disorder, venlafaxine and SSRIs can be recommended, while buspirone and imipramine may be alternatives. For social phobia, SSRIs are recommended for the first line, and MAOIs, moclobemide and benzodiazepines as second line. Obsessive-compulsive disorder is best treated with SSRIs or clomipramine.

PMID: 12516310

Rating: 5a

Bansal V, Kalita J, Misra UK. Diabetic neuropathy. Postgrad Med J. 2006 Feb;82(964):95-100.

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Diabetic neuropathy (DN) refers to symptoms and signs of neuropathy in a patient with diabetes in whom other causes of neuropathy have been excluded. Distal symmetrical neuropathy is the commonest accounting for 75% DN. Asymmetrical neuropathies may involve cranial nerves, thoracic or limb nerves; are of acute onset resulting from ischaemic infarction of vasa nervosa. Asymmetric neuropathies in diabetic patients should be investigated for entrapment neuropathy. Diabetic amyotrophy, initially considered to result from metabolic changes, and later ischaemia, is now attributed to immunological changes. For diagnosis of DN, symptoms, signs, quantitative sensory testing, nerve conduction study, and autonomic testing are used; and two of these five are recommended for clinical diagnosis. Management of DN includes control of hyperglycaemia, other cardiovascular risk factors; alpha lipoic acid and L carnitine. For neuropathic pain, analgesics, non-steroidal anti-inflammatory drugs, antidepressants, and anticonvulsants are recommended. The treatment of autonomic neuropathy is symptomatic.

Publication Types:
Review

PMID: 16461471

Rating: 5a

Barbui C, Guaiana G, Hotopf M. Amitriptyline for inpatients and SSRIs for outpatients with depression? Systematic review and meta-regression analysis. Pharmacopsychiatry. 2004 May;37(3):93-7.

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BACKGROUND: Although the selective serotonin reuptake inhibitors (SSRIs) are widely used as first-line agents in depression, amitriptyline, a reference tricyclic (TCA) agent, has the edge in terms of efficacy over control antidepressants (ADs), but it is not clear whether this advantage can be attributed to a more favourable profile in inpatients, but not in outpatients, with depression. The aim of this study

was to investigate the contribution of study setting on outcome in clinical trials comparing amitriptyline with any other AD. METHODS: A systematic review and meta-regression analysis of amitryptiline randomised clinical trials was carried out. The electronic search yielded 181 randomised clinical trials, 47% enrolling inpatients and 53% outpatients with depression. RESULTS: Both on a dichotomous and continuous out-come, amitriptyline was more effective than control agents in in-patients [Peto odds ratio (OR): 1.22, 95%, Confidence Interval (CI): 1.04, 1.42; Standardised Mean Difference (SMD): 0.28, 95 %,Cl: 0.08, 0.46], but not in outpatients (Peto OR: 1.01, 95%, CI: 0.88,1.17; SMD: 0.10,95% CI: -0.02,0.23). Among inpatients amitriptyline was significantly more effective than TCA and nonsignificantly more effective than the SSRIs. Among outpatients no statistically significant differences emerged between amitriptyline and TCA and between amitriptyline and the SSRIs. Amitriptylinewas less well tolerated than control agents in outpatients (Peto OR: 0.90, 95%, CI: 0.81, 0.99), but not in inpatients (Peto OR:1.09, 95% CI: 0.95, 1.25). CONCLUSIONS: These data suggest that a reasonable approach could be the first-line prescription of newer agents in the routine outpatient care of depressive subjects, and the use of amitriptyline in inpatients with severe depression.

PMID: 15179966

Rating: 1a

Barolat G, Spinal cord stimulation for chronic pain management, Arch Med Res. 2000 May-Jun;31(3):258-62.

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This article outlines the role of spinal cord stimulation in contemporary chronic pain management. The anatomical and neurophysiological correlates of stimulation of the intraspinal structures are discussed. The most common indications are presented, including failed back syndrome, reflex sympathetic dystrophy, neurogenic thoracic outlet syndrome, and spinal cord injury, etc. The most common complications are presented, including paralysis, infection, electrode migration, cerebrospinal fluid leak, and pain. Spinal cord stimulation is one of the most effective techniques available in the management of severe chronic pain that has been refractory to other more conservative modalities.

PMID: 11036175

Rating: 5b

Barolat G, Sharan AD, Future trends in spinal cord stimulation, Neurol Res. 2000 Apr;22(3):279-84.

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Spinal cord stimulation (SCS) has been available for about 30 years, but only in the past five years has it met with widespread acceptance and recognition by the medical community. Traditionally performed by neurosurgeons, SCS is being increasingly utilized by anesthesiologists, orthopedic surgeons and physiatrists. Pain management continues to be the most widespread application of SCS. More sophisticated technology has allowed the implanters to successfully address more complex pain syndromes such as widespread reflex sympathetic dystrophy and the failed back syndrome. Other applications are being developed, combining the ability to stimulate the spinal cord, the nerve roots and the peripheral nerves. Examples include angina pectoris, urinary incontinence and occipital neuralgia. Computer-interactive programming is gaining popularity, especially due to the extreme complexity of the implanted stimulation devices. The ability to stimulate independently multiple channels as well as multiple arrays of electrodes is today a reality. This has increased greatly the efficacy, safety and reliability of the modality. In the future, SCS will undoubtedly move several steps up in the treatment ladder of chronic pain conditions, while new applications will be discovered. The future of neural implantable technologies is bright, with an increasingly important role in the medical management of chronic conditions affecting the nervous system.

PMID: 10769821

Rating: 5c

Barolat G.; Oakley J.C.; Law J.D.; North R.B.; Ketcik B.; Sharan A. Epidural Spinal Cord Stimulation with a Multiple Electrode Paddle Lead Is Effective in Treating Intractable Low Back Pain. Neuromodulation, Volume 4, Number 2, 1 April 2001, pp. 59-66(8).
The objective of this paper is to examine the outcomes of patients with intractable low-back pain treated with epidural spinal cord stimulation (SCS) utilizing paddle electrodes and a radio frequency (RF) stimulator. A multicenter prospective study was performed to collect data from patients suffering from chronic low-back pain. The study was designed to collect data from 60 patients at four centers and examine their outcomes at, or up to two years post implantation. Patients' participation included written responses to a series of preoperative questionnaires that were designed to collect previous surgical history information, leg and low back pain characteristics, and routine demographic information. Outcome measurements included the visual analog scale (VAS), the Oswestry Disability Questionnaire, the Sickness Impact Profile (SIP), and a patient satisfaction rating scale. Data were collected at each site during patient visits or by mail, at approximately six months, 12 months, and 24 months.

A total of 44 patients have been implanted with a SCS system at the time of this writing. Follow-up data were available for 41 patients. Preoperatively, all patients reported more than 50% of their pain in the low back. All patients had pain in both their backs and legs. All patients showed a reported mean decrease in their 10-point VAS scores compared to baseline. The majority of patients reported fair to excellent pain relief in both the low back and legs. At six months 91.6% of the patients reported fair to

excellent relief in the legs and 82.7% of the patients reported fair to excellent relief in the low back. At one year 88.2% of the patients reported fair to excellent relief in the legs and 68.8% of the patients reported fair to excellent relief in the low back. Significant improvement in function and quality of life was found at both the six-month and one-year follow-ups using the Oswestry and SIP, respectively. The majority of patients reported that the procedure was worthwhile (92% at six months, 88% at one year). No patient indicated that the procedure was not worthwhile. We conclude that SCS proved beneficial at one year for the treatment of patients with chronic low back and leg pain.

Rating: 3c

Barrows KA, Jacobs BP. Mind-body medicine. An introduction and review of the literature. Medical Clinics of North America. 01-Jan-2002; 86(1): 11-31.
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Abstract:
MBM is a well-established phenomenon in modern medicine. If one accepts a model of mind/body that is truly nondualistic, it could be said that the MBM phenomenon is inherent to medicine. Because of its popularity and efficacy for common chronic conditions, MBM may have its greatest presence in primary care medicine. The flourishing of MBM techniques resulting from the public's enthusiastic embrace of these therapies has created a great need for rigorous scientific examination. The MBM literature may be said to be in its adolescence, having grown out of its early years of enthusiastic case reports and small studies, but not yet fully grown into a broad catalogue of large controlled experimental trials. Nevertheless, clinical trials suggest that certain MBM therapies are effective in improving quality of life, anxiety, and pain intensity for a variety of conditions. There is moderate evidence to suggest these techniques improve chronic pain, headache, insomnia, and other common conditions. There is preliminary evidence to suggest these techniques may affect coronary artery disease and cancer. MBM techniques ultimately may prove to be most effective in combinations or in conjunction with traditional treatment.

PMID: 11795084

Bartels S, Sivilotti M, Crosby D, Richard J. Are recommended doses of acetaminophen hepatotoxic for recently abstinent alcoholics? A randomized trial. Clin Toxicol (Phila). 2008;46:243-9.

Department of Emergency Medicine, Brigham and Women's Hospital, Boston, Massachusetts, USA.

Although acetaminophen overdose is a leading cause of fulminant hepatic failure, it is controversial whether therapeutic doses of acetaminophen can cause hepatotoxicity in alcoholics, especially those rendered most vulnerable by recent abstinence. While the mechanism is unclear, these observations do provide some reassurance that short courses of acetaminophen are unlikely to cause subclinical hepatocellular injury in recently abstinent alcoholics.

PMID: 18344107

Rating: 2b

Baumann T. Pain Management. In Pharmacotherapy and Pathophysiologic Approach, 5th ed. Eds. DiPiro J, Talbert R, Yee G, Matze G, Wells B, Posey L. Appleton & Lange. 2002. p. 1103-1117.

Rating: 9a

Benca RM. Diagnosis and treatment of chronic insomnia: a review. Psychiatr Serv. 2005;56:332-43.

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OBJECTIVE: Insomnia has high prevalence rates and is associated with significant personal and socioeconomic burden, yet it remains largely underrecognized and inadequately treated. METHODS: A PubMed search for English-language articles covering randomized controlled trials published between 1970 and 2004 was conducted. Search terms used were "insomnia," "behavioral therapy," and the generic names of agents commonly used to treat insomnia (the Food and Drug Administration-approved benzodiazepines and nonbenzodiazepines, trazodone, and over-the-counter agents). RESULTS: Evidence from epidemiologic studies, physician surveys, and clinical studies suggests that numerous patient and physician factors contribute to the fact that the needs of patients with insomnia remain unmet, including low reporting of insomnia by patients, limited physician training, and office-based time constraints, as well as misconceptions about the seriousness of insomnia, the advantages of treatment, and the risks associated with hypnotic use. Nonpharmacologic therapies produce long-lasting and reliable changes among people with chronic insomnia and have minimal side effects. Pharmacologic therapies have proven effective with improving wake time after sleep onset and sleep maintenance and reducing the number of nighttime awakenings. However, pharmacologic therapy has a greater chance of producing side effects. No conclusive evidence exists to favor either pharmacologic therapy or behavioral therapy. CONCLUSIONS: Insomnia is particularly challenging for clinicians because of the lack of guidelines and the small number of studies conducted in patient populations with behavioral and pharmacologic therapies. Current treatment options do not address the needs of difficult-to-treat patients with chronic insomnia, such as the elderly, and those with comorbid medical and psychiatric conditions. More research is necessary to determine the long-term effects of insomnia treatments.

PMID: 15746509

Rating: 1c

Bendix AF, Bendix T, Labriola M, Boekgaard P. Functional restoration for chronic low back pain. Two-year follow-up of two randomized clinical trials. Spine. 1998 Mar 15;23(6):717-25.

Copenhagen Back Center, University Hospital, Denmark.

STUDY DESIGN: Two randomized, prospective clinical trials involving 238 chronic low back disability patients were carried out. Results at 2-year follow-up are presented. OBJECTIVES: To compare the clinical outcomes of a multidisciplinary functional restoration program with a nontreated control group (Project A) and with two less intensive but different training programs (Project B). SUMMARY OF BACKGROUND DATA: The effectiveness of functional restoration programs has not been firmly established. Results from trials carried out in the United States differ from those in trials conducted in other countries. Only a few of these studies have been carried out as prospective and randomized clinical studies. METHODS: Two hundred thirty-eight patients with chronic low back disability of at least 6 months' duration were included. There were 106 patients in project A and 132 patients in project B. Two years after completion of treatment patients were mailed a questionnaire that included questions regarding their work status, pain and disability levels, number of sick leave days, number of medical care contacts, medication use, physical activity levels, and subjective overall assessment of their "back life situation." RESULTS: Patients in both studies were comparable at inclusion, except that patients in Project A were recruited from all of Denmark, whereas those in Project B were from the greater Copenhagen area. Thirteen patients did not report for treatment after randomization. Of the remaining 225 patients, 20 (9%) did not complete treatment. The questionnaire response rate was 94%. In Project A, those patients receiving treatment (functional restoration) reported significantly less contact with the health care system, fewer sick leave days, and a less disabled life style during the follow-up period, compared with reports of patients in the control group. Other effect parameters did not demonstrate a significant difference between the two groups. In Project B, all effect parameters reported, except leg pain and medication usage, were significantly in favor of functional restoration, compared with reports from the less intensively treated groups. CONCLUSIONS: The functional restoration program seems effective in various parameters compared with the less intensive programs, but the differences in outcome in the two parallel studies indicate the necessity of testing a treatment program in different settings, in that the statistical variation may be a major factor in results of different studies.

PMID: 9549794

Rating: 2b
Benzon HT, Raja SN, Molloy RE, Liu SS, Fishman SM. Essentials of Pain Medicine and Regional Anesthesia. 2nd ed. Elisevier 2005, p. 215.

This second edition of Essentials of Pain Management and Regional Anesthesia, offers an accessible and concise, yet complete, overview of today's theory and practice of pain medicine and regional anesthesia.

From a review of basic considerations through local anesthetics and nerve block techniques, this book provides the reader with an excellent tool for exam review or practice of Pain Management.

Rating: 9a

Bernacki EJ, Guidera JA, Schaefer JA, Tsai S, A facilitated early return to work program at a large urban medical center, J Occup Environ Med 2000 Dec;42(12):1172-7

Division of Occupational and Environmental Medicine, Johns Hopkins University, School of Medicine, 600 N. Wolfe Street, Billings Administration 129, Baltimore, MD 21287-1629, USA.

Publication Types:
- Evaluation Studies

Rating: 5a

Besson JM. The Neurobiology of Pain. Lancet 1999;353:1610-15.

Publication Type: Review

Bigos SJ, McKee JE, Holland JP, Holland CL, Hildebrandt J, Back pain, the uncomfortable truth - assurance and activity problem. Schmerz 2001 Dec;15(6):430-4

Department of Orthopedics, Harborview Medical Center, Seattle, USA.

Back problems are common, expensive, and the few patients who are the crux of the problem are uncomfortable but also an uncomfortable frustration for clinicians and employers alike. We now know that clinicians can greatly improve the patient's response to back symptoms by admitting our diagnostic limitations, demedicalizing the issue, providing assurance, and encouraging a more reasonable approach to improving comfortable activity tolerance.

Rating: 5a

Birklein F. Complex regional pain syndrome. J Neurol. 2005 Feb;252(2):131-8.

Neurologische Klinik, Universitat Mainz, Langenbeckstrasse 1, 55101 Mainz, Germany. birklein@neurologie.klinik.uni-mainz.de

Complex regional pain syndrome (CRPS) may develop after limb trauma and is characterized by pain, sensory-motor and autonomic symptoms. Most important for the understanding of the pathophysiology of CRPS are recent results of neurophysiological research. Major mechanism for CRPS symptoms,

which might be present subsequently or in parallel during the course of CRPS, are trauma-related cytokine release, exaggerated neurogenic inflammation, sympathetically maintained pain and cortical reorganisation in response to chronic pain (neuroplasticity). The recognition of these mechanisms in individual CRPS patients is the prerequisite for a mechanism-oriented treatment.

Publication Types:
Review

PMID: 15729516

Rating: 5b

Biswal S, Medhi B, Pandhi P. Longterm efficacy of topical nonsteroidal antiinflammatory drugs in knee osteoarthritis: metaanalysis of randomized placebo controlled clinical trials. J Rheumatol. 2006;33:1841-4.

Department of Pharmacology, Postgraduate Institute of Medical Education and Research, Chandigarh, India.

OBJECTIVE: To evaluate the longterm efficacy of topical therapies for pain control in primary knee osteoarthritis (OA). METHODS: Systematic literature search was carried out from January 1, 1966, to December 31, 2004, in Pubmed, Medline, Embase, and Cochrane database. Manual searches of related journals in the National Medical Library (New Delhi, India), the library of our institute, and conference abstracts were also carried out. We included randomized controlled clinical trials of 4 weeks or more comparing any topical nonsteroidal antiinflammatory drug (NSAID) with placebo or vehicle. Effect size for pain control was estimated. RESULTS: Out of 172 citations, 4 studies fulfilled all the specified criteria. Four of them compared topical NSAID with placebo or vehicle. Pooled effect of topical NSAID measured at 4 weeks or beyond was superior to placebo/vehicle in pain relief (mean effect size -0.28, 95% CI -0.42 to -0.14). CONCLUSION: Topical NSAID are effective for pain relief in knee OA for a longer duration; however, this may not hold true for all the preparations.

PMID: 16960944

Rating: 1c

Bjordal JM, Klovning A, Ljunggren AE, Slørdal L. Short-term efficacy of pharmacotherapeutic interventions in osteoarthritic knee pain: A meta-analysis of randomised placebo-controlled trials. Eur J Pain. 2007;11:125-38.

Department of Public Health and Primary Health Care, University of Bergen, 5018 Bergen, Norway. jmb@hib.no

BACKGROUND: Pain is the most debilitating symptom in osteoarthritis of the knee (OAK). AIM AND METHODS: To determine the short-term pain-relieving effects of seven commonly used pharmacological agents for OAK pain by performing a systematic review of randomised placebo-controlled trials. RESULTS: In total, 14,060 patients in 63 trials were evaluated. Opioids and oral NSAIDs therapy in patients with moderate to severe pain (mean baseline 64.3 and 72.8 mm on VAS respectively) had maximum efficacies compared to placebo at 2-4 weeks of 10.5 mm [95% CI: 7.4-13.7] and 10.2 mm [95% CI: 8.8-11.2] respectively. The efficacy of opioids may be inflated by high withdrawal rates (24-50%) and "best-case" scenarios reported in intention-to-treat analyses. In patients with moderate pain scores on VAS (mean range from 51 to 57 mm), intra-articular steroid injections and topical NSAIDs had maximum efficacies at 1-3 weeks of 14.5mm [95% CI: 9.7-19.2] and 11.6 mm [95% CI: 7.4-15.7], respectively. Paracetamol, glucosamin sulphate and chondroitin sulphate had maximum mean efficacies at 1-4 weeks of only 4.7 mm or lower. Heterogeneity tests revealed that best efficacy values of topical NSAIDs may be slightly deflated, while data for oral NSAIDs may be slightly inflated due to probable patient selection bias. CONCLUSION: Clinical effects from pharmacological interventions in OAK are small and limited to the first 2-3 weeks after start of treatment. The pain-relieving effects over placebo in OAK are smaller than the patient-reported thresholds for relevant improvement.

PMID: 16682240

Rating 1c

Blier P, Saint-André E, Hébert C, de Montigny C, Lavoie N, Debonnel G. Effects of different doses of venlafaxine on serotonin and norepinephrine reuptake in healthy volunteers. Int J Neuropsychopharmacol. 2007 Feb;10(1):41-50.

Department of Psychiatry, McGill University, Montréal, QC, Canada. pblier@rohcg.on.ca

Venlafaxine is generally considered to be a dual 5-HT and NE reuptake inhibitor when it is used at doses above 75 mg/d in humans. While its 5-HT reuptake-inhibiting property has been demonstrated, some controversy still exists regarding the doses of venlafaxine required to inhibit NE reuptake. Healthy male volunteers received, on a double-blind basis, paroxetine (20 mg/d), desipramine (100 mg/d), nefazodone (300 mg/d), or venlafaxine (150 or 300 mg/d) in the last 5 d of a 7-d period of administration. Inhibition of 5-HT reuptake was estimated by determining the degree of depletion of whole-blood 5-HT, while that of NE was assessed by measuring the attenuation of the systolic blood pressure increases produced by intravenous injections of tyramine. Paroxetine, both regimens of venlafaxine, and to a lesser extent desipramine significantly decreased whole-blood 5-HT content. Nefazodone failed to produce any significant change. Desipramine abolished the tyramine pressor response, whereas all other drug regimens left this parameter unaltered. Venlafaxine and paroxetine acted as potent 5-HT reuptake inhibitors in the present study. In contrast, neither the moderate nor the high dose of venlafaxine

displayed any significant inhibiting activity in this model assessing NE reuptake in peripheral NE terminals. The validity of the model was confirmed by the potent inhibitory action of desipramine on NE reuptake. While the reasons for this unexpected lack of action remain unclear, venlafaxine appeared to be an effective NE reuptake agent in depressed patients using the same approach.

PMID: 16690005

Rating: 2b

Blommel ML, Blommel AL. Pregabalin: an antiepileptic agent useful for neuropathic pain. Am J Health Syst Pharm. 2007;15;64:1475-82.

West Virginia Center for Drug and Health Information, Morgantown, WV 26506-9520, USA.

PURPOSE: The pharmacology, pharmacokinetics, clinical efficacy, adverse effects, and dosage and administration of pregabalin are reviewed. SUMMARY: Pregabalin is the first drug to receive approved labeling from the Food and Drug Administration (FDA) for the treatment of painful diabetic neuropathy and postherpetic neuralgia and is the first antiepileptic agent to receive FDA-approved labeling since 1999. Pregabalin is the pharmacologically active S-enantiomer of racemic 3-isobutyl gamma-aminobutyric acid. Pregabalin has demonstrated efficacy in the management of neuropathic pain associated with diabetic peripheral neuropathy, postherpetic neuralgia, and as adjunctive therapy for adult patients with partial onset seizures. Its exact mechanism of action is unknown. Pregabalin is rapidly absorbed and exhibits linear pharmacokinetics after oral administration. The lack of hepatic metabolism and lack of interaction with cytochrome P-450 isoenzymes explain the absence of drug interactions with pregabalin. Several clinical studies have demonstrated pregabalin's efficacy for each of the FDA-approved indications, with dizziness and somnolence reported as the most common adverse events. Pregabalin has been designated as a Schedule V controlled substance because of its potential for abuse and dependence. The starting dosage for patients with neuropathic pain associated with diabetic peripheral neuropathy is 50 mg three times daily and may be increased to 300 mg daily within one week based on efficacy and tolerability. The starting dosage for patients with partial-onset seizures is 75 mg twice daily or 50 mg three times daily and may be increased to 600 mg daily based on individual response and tolerability. CONCLUSION: Pregabalin may be beneficial for the treatment of neuropathic pain or partial-onset seizures in patients who do not respond to conventional treatments or cannot tolerate their adverse effects.

PMID: 17617497

Rating: 5b

BlueCross BlueShield, Surgery Section - Percutaneous Electrical Nerve Stimulation (PENS), Policy No: 44, 08/03/2004

Description
Percutaneous electrical nerve stimulation (PENS) is similar in concept to transcutaneous electrical nerve stimulation (TENS, see policy, DME11, Electrical Stimulation Devices for Home Use) but differs in that needles are inserted to a depth of 1 to 4 cm either around or immediately adjacent to the nerve serving the painful area and then stimulated. PENS is generally reserved for patients who fail to get pain relief from TENS, apparently due to obvious physical barriers to the conduction of the electrical stimulation (e.g., scar tissue, obesity). PENS must be distinguished from acupuncture with electrical stimulation. In electrical acupuncture, needles are also inserted just below the skin, but the placement of needles is based on specific theories regarding energy flow throughout the human body. Thus in PENS the location of stimulation is determined by proximity to the pain rather than the theories of energy flow that guide placement of stimulation for acupuncture.
Percutaneous neuromodulation therapy is a variant of PENS in which up to 10 fine filament electrodes are temporarily placed at specific anatomical landmarks in the back. Treatment regimens consist of 30-minute sessions, once or twice a week for eight to ten sessions. Percutaneous Neuromodulation Therapy™ (Vertis Neurosciences) received approval to market by the U.S. Food and Drug Administration (FDA) through the 510(k) process in 2002. The labeled indications reads as follows: "Percutaneous neuromodulation therapy (PNT) is indicated for the symptomatic relief and management of chronic or intractable pain and/or as an adjunct treatment in the management of post-surgical pain and post-trauma pain."
Policy/Criteria
PENS using surgically implanted electrodes may be considered medically necessary for treating patients with chronic pain due to disease or injury affecting a peripheral nerve corresponding to the local pathology when all of the following criteria are met: 1) Pain relief from temporarily placed peripheral nerve stimulation needles has been documented prior to permanent placement.
2) Patient was carefully screened, evaluated and diagnosed by a multidisciplinary medical team prior to application of the implanted stimulation therapy.
3) All facilities, equipment, and professional and support personnel required for the proper diagnosis, treatment training, and follow-up of the patient are available.
4) Treatment is used only as a last resort; other non-surgical treatments have been tried and failed or are judged to be unsuitable or contraindicated.
Percutaneous neuromodulation therapy (PNT) is considered investigational.

Rating: 8b

BlueCross BlueShield, Durable Medical Equipment Section - Electrical Stimulation Devices for Home Use, DME Policy No: 11, Approved Date: 04/05/2005. Also Electrical Stimulators for pain, seizures, or cerebral palsy. Policy 003; Posted 4/23/07.

Description
Transcutaneous Electrical Nerve Stimulation Devices (TENS)

Transcutaneous electrical nerve stimulator (TENS) consists of an electrical pulse generator connected by wire to two electrodes that apply electrical stimulation to the surface of the skin at the site of pain. TENS has been used to relieve chronic intractable pain, post-surgical pain, and pain associated with active or post-trauma injury unresponsive to other standard pain therapies. TENS is characterized by biphasic current and selectable parameters. It stimulates sensory nerves to block pain signals and generate endorphins. We cover TENS and PENS/PNT for Medicare HMO Blue and Medicare PPO Blue members only, in accordance with CMS regulations.

Neuromuscular Electrical Stimulation Devices (NMES)

NMES, through multiple channels, attempts to stimulate motor nerves and alternately causes contraction and relaxation of muscles, unlike a TENS device which is intended to alter the perception of pain. NMES devices are used to prevent or retard disuse atrophy, relax muscle spasm, increase blood circulation, maintain or increase range-of-motion, and re-educate muscles.

Functional Neuromuscular Stimulation Devices (FNS or ENS)

Functional neuromuscular stimulation (also called electrical neuromuscular stimulation and EMG-triggered neuromuscular stimulation) attempts to replace stimuli from destroyed nerve pathways with computer-controlled sequential electrical stimulation of muscles to enable spinal-cord-injured or stroke patients to function independently, or at least maintain healthy muscle tone and strength. Also used to stimulate quadriceps muscles following major knee surgeries to maintain and enhance strength during rehabilitation.

Galvanic Stimulation Devices

Galvanic stimulation is characterized by high voltage, pulsed stimulation and is used primarily for local edema reduction through muscle pumping and polarity effect. Edema is comprised of negatively charged plasma proteins, which leak into the interstitial space. The theory of galvanic stimulation is that by placing a negative electrode over the edematous site and a positive electrode at a distant site, the monophasic high voltage stimulus applies an electrical potential which disperses the negatively charged proteins away from the edematous site, thereby helping to reduce edema.

Microcurrent Stimulation Devices (MENS)

MENS is characterized by sub-sensory current that acts on the body's naturally occurring electrical impulses to decrease pain and facilitate the healing process. MENS differs from TENS in that it uses a significantly reduced electrical stimulation. TENS blocks pain, while MENS acts on the naturally occurring electrical impulses to decrease pain by stimulating the healing process.

H-wave Stimulation Devices

H-wave stimulation is a form of electrical stimulation that differs from other forms of electrical stimulation, such as transcutaneous electrical nerve stimulation (TENS), in terms of its waveform. While physiatrists, chiropractors, or podiatrists may perform H-wave stimulation, H-wave devices are also available for home use. H-wave stimulation has been used for the treatment of pain related to a variety of etiologies, such as diabetic neuropathy, muscle sprain's, temporomandibular joint dysfunctions or reflex sympathetic dystrophy. H-wave stimulation has also been used to accelerate healing of wounds, such as diabetic ulcers. H-wave electrical stimulation must be distinguished from the H-waves that are a component of electromyography.

Note: This policy is not intended to address all electrical stimulation devices. Separate medical policies exist for the following services used in the home:

- Functional Neuromuscular Stimulation To Provide Ambulation, TRG Medical Policy, DME 56
- Sympathetic Therapy for the Treatment of Pain, TRG Medical Policy DME 65
- Interferential Therapy, TRG Medical Policy, DME 66
- Electrostimulation and Electromagnetic Therapy for the Treatment of Chronic Wounds, TRG Medical Policy, DME 67

Policy/Criteria

TENS may be considered medically necessary for the treatment of chronic intractable musculoskeletal pain or acute postoperative musculoskeletal pain. A TENS unit is considered not medically necessary for non-musculoskeletal pain, including but not limited to pain associated with: headache, visceral abdominal pain, and pelvic pain.

The Regence Group medical policy for TENS reflects the long-standing accepted standard of care within our medical communities. However, several published evidence-based assessments of TENS have found that evidence is lacking concerning the effectiveness of TENS in the treatment of chronic intractable pain and acute postoperative pain.

The following devices are considered investigational for all indications when used in the home setting:

1. Galvanic stimulation devices
2. Microcurrent stimulation devices. Based on the available evidence conclusions cannot be made concerning the effect of MENS on pain management and objective health outcomes.
3. Functional neuromuscular stimulation devices. The scientific evidence related to electromyography (EMG)-triggered electrical stimulation therapy continues to evolve, and this therapy appears to be useful in a supervised physical therapy setting to rehabilitate atrophied upper extremity muscles following stroke and as part of a comprehensive PT program.
4. H-wave stimulation devices. While 2 small controlled trials provide suggestive evidence about the effectiveness of H-wave electrical stimulation for diabetic neuropathy, their results are insufficient to permit conclusions.
5. Neuromuscular electrical stimulation devices

Rating: 8b

BlueCross BlueShield, Durable Medical Equipment Section - Sympathetic Therapy for the Treatment of Pain, DME Policy No: 65. Effective Date: 03/01/2005

Description

Sympathetic therapy describes a type of electrical stimulation of the peripheral nerves that is designed to stimulate the sympathetic nervous system in an effort to "normalize" the autonomic nervous system and alleviate chronic pain. Unlike TENS (transcutaneous electrical nerve stimulation) or interferential electrical stimulation, sympathetic therapy is not designed to treat local pain, but is designed to induce a systemic effect on sympathetically induced pain. Sympathetic therapy uses four intersecting channels of various frequencies with bilateral electrode placement on the feet, legs, arms, and hands. Based on the

location of the patient's pain and treatment protocols supplied by the manufacturer, electrodes are placed in various locations on the lower legs and feet or the hands and arms. Electrical current is then induced with beat frequencies between 0 and 1000 Hz. Treatment may include daily 1-hour treatments in the physician's office, followed by home treatments if the initial treatment is effective. The Dynatron STS device and a companion home device, Dynatron STS Rx, are devices that deliver sympathetic therapy. These devices received U.S. Food and Drug Administration (FDA) clearance in March 2001 through a 510(k) process. The FDA-labeled indication is as follows: "Electrical stimulation delivered by the Dynatron STS and Dynatron STS Rx is indicated for providing symptomatic relief of chronic intractable pain and/or management of post-traumatic or post-surgical pain."

Policy/Criteria
Sympathetic therapy is considered investigational. The lack of published outcomes from well-designed clinical trials prohibits scientific conclusions concerning the health outcome effects of sympathetic therapy for the treatment of pain.

Rating: 8b

BlueCross BlueShield, Durable Medical Equipment Section - Interferential Stimulation, DME Policy No: 66. Effective Date: 03/01/2005. Updated 2006.

Description
Interferential stimulation is a type of electrical stimulation that uses paired electrodes of two independent circuits carrying medium-frequency alternating currents. The electrodes are aligned on the skin so that the current flowing between each pair intersects at the underlying target, thus maximizing the current permeating the tissues while reducing to a minimum unwanted stimulation of cutaneous nerves. Interferential stimulation has been investigated as a technique to reduce pain, improve range of motion, or promote local healing following various tissue injuries. There are no standardized protocols for the use of interferential therapy; the therapy may vary according to the frequency of stimulation, the pulse duration, treatment time, and electrode-placement technique.
Policy/Criteria
Interferential current stimulation is considered investigational. The results of placebo-controlled trials have reported negative findings of interferential therapy.
The trials are reviewed briefly below.
Taylor and colleagues randomized 40 patients with temporomandibular joint syndrome or myofascial pain syndrome to undergo either active or placebo interferential stimulation. (2) The principal outcomes were pain assessed by a questionnaire and range of motion (ROM). There was no statistically significant difference in the outcomes between the two groups.
Van der Heijden and colleagues randomized 180 patients with soft tissue shoulder disorders to undergo therapy in one of the following groups in addition to a program of exercise therapy:
1) interferential therapy plus ultrasound;
2) active interferential therapy plus dummy ultrasound;

3) dummy interferential therapy plus active ultrasound;
4) dummy interferential therapy plus dummy ultrasound (i.e., the placebo group);
5) no adjuvant therapy. (3)

Principal outcome measures include recovery, functional status, chief complaint, pain, clinical status, and range of motion at six weeks after the therapy was completed and at intervals up to one year. The authors reported that neither interferential therapy nor ultrasound proved to be effective as adjuvants to exercise therapy.

Werners and colleagues reported on the results of a study that randomized 152 patients with low back pain to either treatment with interferential therapy or traction. (4) Therefore, this study was not placebo-controlled. Outcomes were based on the results of the Oswestry Disability Index and a pain visual analog scale. The authors reported that both groups recorded improvements over a 3-month period; there was no statistically significant difference in outcomes between the two groups. Without a placebo group, it is unknown whether the improvement is related to the natural history of the disease or any intervention.

Hurley and colleagues randomly assigned 60 patients with back pain to one of three groups:
1) interferential therapy of the painful area;
2) interferential therapy of the spinal nerve; and
3) a control group, who received no interferential therapy. (5) Therefore, this study was not placebo controlled. All patients received educational materials. Those assigned to active treatment groups received 2–3 treatments per week for variable periods of time. The principal outcome measures were based on results of pain-rating index and the Roland-Morris Disability Questionnaire.

There was no placebo group. All patients received educational materials. Those assigned to active treatment groups received 2–3 treatments per week for variable periods of time. The principal outcome measures were based on results of pain-rating index and the Roland-Morris Disability Questionnaire. Placement of the interferential therapy electrodes over the spinal nerve, compared to the painful area, resulted in a significantly larger reduction in disability scores. However, the lack of a placebo group limits interpretation of these data.

In a randomized trial, Hou and colleagues studied a various combination of therapies in a group of 119 patients with myofascial disease and active trigger points, including hot packs, "stretch and spray," ischemic compression, myofascial release, and interferential therapy. (6) There was no control or placebo group, and thus interpretation of the data is limited.

In summary, the results of placebo-controlled trials have reported negative findings of interferential therapy. An updated search of the MEDLINE database through February 7, 2005 did not reveal any randomized, placebo-controlled, blinded clinical trials on interferential stimulation therapy.

Interferential therapy (such as RS-4i): Is denied experimental/investigational.

References

1) BlueCross and BlueShield Association Medical Policy Reference Manual, Policy No. 1.01.24
2) Taylor K, Newton RA, Personius WJ et al. Effects of interferential current stimulation for treatment of subjects with recurrent jaw pain. Phys Ther 1987;67(3):346-50

3) van der Heijden GJ, Leffers P, Wolters PJ et al. No effect of bipolar interferential electrotherapy and pulsed ultrasound for soft tissue disorders: a randomised controlled trial. Ann Rheum Dis 1999;58(9):530-50
4) Werners R, Pynsent PB, Bulstrode CJ. Randomized trial comparing interferential therapy with motorized lumbar traction and massage in the management of low back pain in a primary care setting. Spine 1999;24(15):1579-84
5) Hurley DA, Minder PM, McDonough SM et al. Interferential therapy electrode placement technique in acute low back pain: a preliminary investigation. Arch Phys Med Rehabil 2001;82(4): 485-93
6) Hou CR, Tsai LC, Cheng KF et al. Immediate effects of various physical therapeutic modalities on cervical myofascial pain and trigger-point sensitivity. Arch Phys Med Rehabil 2002;83(10): 1406-14

Rating: 8b

BlueCross BlueShield, Durable Medical Equipment Section - Biomagnetic Therapy, DME Policy No: 55, Effective Date: 03/01/2005

Description
Biomagnetic therapy is used for the relief of chronic painful conditions. It is proposed that magnets, worn close to the skin, create an electromagnetic field within the body that suppresses pain. The theory is that the magnetic field causes potassium channels to be stimulated, producing repolarization or hyperpolarization.
Policy/Criteria
Biomagnetic therapy is considered investigational.
Scientific Background
Biomagnetic therapy has been investigated for various types of pain, including peripheral neuropathy, chronic low back pain, carpal tunnel syndrome, plantar heel pain and hip and knee pain due to osteoarthritis. As with any therapy for pain, a placebo effect is anticipated, thus randomized placebo-controlled trials are necessary to investigate the extent of the placebo effect and to determine whether any improvement with biomagnetic therapy exceeds that associated with a placebo. The following discussion for each type of pain focuses on results of published randomized, placebo-controlled clinical trials.
Peripheral Neuropathy
Weintraub published results of twenty-four patients with peripheral neuropathy (14 from diabetes and 10 from other etiologies) who received biomagnetic therapy. (1) Patients had a magnetic shoe insert for one foot and a sham insert for the other foot. Patients were instructed to have constant, 24 hrs/day contact with the footpads for the 4-month treatment period. After 30 days the inserts were switched. Patients were blinded to the treatment side in an effort to control for placebo effect. Patients scored their complaints of burning, numbness and tingling pain in both feet twice/day. The primary outcome was comparison of pre- and post-treatment pain scores. Baseline scores were tabulated at the time of entry into the study. Also, nerve conduction studies and EMG were performed.

Outcomes were reported for 19 of the study patients. Results showed that diabetics with peripheral neuropathy (N=10) had a statistically significant better improvement in numbness and tingling neuropathic pain than the non-diabetic peripheral neuropathy patients (N=9). However, results were not reported for 4 (28%) of the 14 diabetic patients originally enrolled in the study. Burning neuropathic pain was not improved, and the follow-up neurologic exam and nerve conduction studies did not change compared to the baseline exams. Overall, there were too few patients in the study to draw conclusions concerning the effectiveness of magnetic therapy for painful diabetic peripheral neuropathy. Also, it is was unclear why magnetic therapy did not work in the non-diabetic patients with peripheral neuropathy. The author noted that while results were promising, they were preliminary and inconclusive and need to be validated in larger longitudinal studies. In 2003, Weintraub and colleagues published results of a randomized placebo controlled clinical trial of 375 patients with diabetic peripheral neuropathy. (2) The authors estimated that a difference between treatment and sham group responses of 17% or more would be statistically significant with 150 subjects per cohort. Results were reported for 141 patients in the active treatment group and 118 patients in the placebo group. Thirty-one percent of patients were excluded from the final analysis due to allodynia, complications, excluded/missing data or loss to follow-up; an intention to treat analysis was not conducted. Improvements in burning, numbness and tingling, and foot pain scores were reported for both the treatment and placebo groups. Although the authors reported statistically significant differences in some scores between the treatment and placebo groups, there were not enough patients in either group to satisfy the criteria originally established for defining statistical significance. The authors note that "only modest clinical improvement was achieved." In addition, outcomes were only followed for four months. The authors stated that long-term studies were needed to establish whether or not the anticipated clinical benefit is more potent at 8 to 12 months (suggested by greater improvement at 2 to 4 months compared to outcomes at 1 to 2 months).

Chronic Low Back Pain

Collacort and colleagues published results of a randomized, double-blind, placebo controlled, cross-over pilot study in 20 patients with chronic low back pain of 19 years duration. (3) Magnets or sham magnets were applied on alternate weeks for 6 hours/day. Mean visual analog scores declined by 0.49 points for the real magnet treatment and 0.44 points for the sham magnet treatment. The authors reported no statistically significant differences in the effect between real and sham magnets.

Carpal Tunnel Syndrome

Carter and colleagues conducted a double-blind, placebo-controlled, randomized clinical trial in which 30 patients with pain attributed to carpal tunnel syndrome had either a 1000 gauss magnet or a placebo metal disk applied to the carpal tunnel area using a Velcro wrap for a period of 45 minutes. (4) The authors reported equally significant pain reduction across the 45-minute period for both groups.

Plantar Heel Pain

Winemiller and colleagues reported results of a randomized, double-blind, placebo-controlled trial assessing the effectiveness of bipolar static magnets in insoles for the treatment of plantar heel pain. (5) In this study, the primary outcome variables were the 4- and 8-week categorical responses to treatment (all/mostly better vs somewhat better/unchanged/worse), as well as VAS scores. Results were reported for 101 enrolled patients, and intention to treat analysis was completed. No statistically significant differences were found between the magnetic and nonmagnetic groups on any of the primary outcome

variables at baseline, 4 weeks or 8 weeks. The authors conclude that static magnets are ineffective in the treatment of plantar pain.

Pain due to Osteoarthritis

Harlow and colleagues reported results of a randomized, blinded, placebo-controlled trial assessing the effectiveness of magnetic bracelets in the treatment of pain due to osteoarthritis of the hip and knee. (6) Participants, researchers and healthcare practitioners were all blinded to the treatment allocation. Participants were randomly allocated to one of three treatment groups who received one of the following: standard magnets, weak (non-therapeutic) magnets, or non-magnetic steel washers. Scores from an index (WOMAC) that assesses pain, disability and joint stiffness in knee and hip osteoarthritis and from a visual analogue scale (VAS) were compared between the three groups at baseline, 4 and 12 weeks. Statistically significant differences in some WOMAC scores were reported between the standard and dummy magnets. However, differences between the standard and weak magnet cohorts and between the weak and dummy magnet cohorts were not significant. It should be noted that a portion of the weak magnets were contaminated with magnets of greater strength, thus compromising study results. In addition, the authors do not provide information concerning what, if any, additional treatments patients were receiving during the study, so it is not possible to determine if any reported treatment effects from the standard magnets can be attributed solely to magnet therapy. In discussing their findings, the authors state, "…we cannot be certain whether our data show a specific effect of magnets, a placebo effect, or both." Summary

The data from the above randomized, placebo-controlled clinical trials fails to demonstrate that biomagnetic therapy results in improved health outcomes for any type of pain. An updated search of the MEDLINE database through February 11, 2005 did not identify any additional studies which alter this conclusion.

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Rating: 8b

BlueCross BlueShield. Surgery Section - Fully Implantable Infusion Pump. Policy No: 18. Effective Date: 04/05/2005

Description: A fully implantable infusion pump (IIP) is intended to provide long-term continuous or intermittent drug infusion. Possible routes of administration include intravenous, intra-arterial, subcutaneous, intraperitoneal, intrathecal, epidural, and intraventricular. The IIP is surgically placed in a subcutaneous pocket under the infraclavicular fossa or in the abdominal wall, and a catheter is threaded into the desired position. Intrathecal and epidural catheter positions are both intraspinal; however, the intrathecal position is located in the subarachnoid space, which is past the epidural space and dura mater and through the theca of the spinal cord. A drug is infused over an extended period of time and may be delivered at a constant or variable rate by calibrating the IIP per physician specifications. The drug reservoir may be refilled as needed by an external needle injection through a self-sealing septum in the IIP. Bacteriostatic water or physiological saline is often used to dilute drugs. A heparinized saline solution may also be used during an interruption of drug therapy to maintain catheter patency. The driving mechanisms of the IIP may include peristalsis, fluorocarbon propellant, osmotic pressure, piezoelectric disk benders, or the combination of osmotic pressure with an oscillating piston.
Policy/Criteria: Fully implantable infusion pumps may be considered medically necessary when used to deliver drugs having FDA approval for this route of access and for the related indication for the treatment of:
1. Primary liver cancer (intrahepatic artery infusion)
2. Metastatic colon, breast, islet cell, or carcinoid tumors with metastasis limited to the liver (intrahepatic artery infusion)
3. Head and neck cancers (intra-arterial infusion)
4. Severe, chronic, intractable pain (intravenous, intrathecal, or epidural infusion of Duramorph, Dilaudid and Clonidine) of malignant or non-malignant origin in patients who have a life expectancy of at least 3 months and who have proven unresponsive to less invasive medical therapy as determined by the following:
a) The clinical history suggests the patient would not respond adequately to non-invasive pain control methods (such as systemic opioids) and
A preliminary trial of opioids with a temporary intrathecal/epidural/intravenous catheter must be undertaken to substantiate acceptable pain relief, degree of side effects, and patient acceptance.
5) Severe spasticity of cerebral or spinal cord origin in patients who are unresponsive to less invasive medical therapy as determined by the following criteria:
a) A trial of at least 6 weeks on oral medication shows that the patient experienced intolerable side effects or that there was a lack of adequate control of the spasticity, and
b) The patient responded favorably to a trial of one intrathecal dose of the antispasmodic drug (baclofen) prior to pump implantation.
Fully implantable infusion pumps are considered investigational for all other indications.

Rating: 8c

BlueCross BlueShield. Medicine Section - Low Level Laser Treatment of Neuromuscular Pain Disorders. Policy No: 105, Effective Date: 03/01/2005

Low level laser therapy has been proposed as a treatment of carpal tunnel syndrome and other painful musculoskeletal disorders such as temporomandibular joint disfunction and low back pain. Carpal tunnel syndrome is the most common entrapment neuropathy and the most commonly performed surgery of the hand. The syndrome is related to the bony anatomy of the wrist. The carpal tunnel is bound dorsally and laterally by the carpal bones and ventrally by the transverse carpal ligament. Through this contained space run the nine flexor tendons and the median nerve. Therefore any space-occupying lesions can compress the median nerve and produce the typical symptoms of carpal tunnel syndrome: pain, numbness, and tingling in the distribution of the median nerve. Symptoms of more severe cases include hypesthesia, clumsiness, loss of dexterity, and weakness of pinch. In the most severe cases, patients experience marked sensory loss and significant functional impairment with thenar atrophy.

There has been interest in using low-level lasers as a conservative alternative. Low-level lasers are also known as "cold lasers" and non-thermal lasers. Low-level lasers refer to the use of red-beam or near-infrared lasers with a wavelength between 600 and 1000 nm and Watts from 5-500 milliwatts. (In contrast, lasers used in surgery typically use 300 Watts.) When applied to the skin, these lasers produce no sensation and do not burn the skin. Because of the low absorption by human skin, it is hypothesized that the laser light can penetrate deeply into the tissues where it has a photobiostimulative effect. The exact mechanism of its effect on carpal tunnel is unknown: hypotheses have included improved cellular repair and stimulation of the immune, lymphatic, and vascular systems.

One low-level laser device, the MicroLight 830 Laser, has received clearance for marketing from the U.S. Food and Drug Administration (FDA) specifically for the treatment of carpal tunnel syndrome. In the data submitted to the FDA as part of the FDA 510(k) approval process, the treatment consisted of application of the laser over the carpal tunnel three times a week for five weeks. The labeling states that the "MicroLight 830 Laser is indicated for adjunctive use in the temporary relief of hand and wrist pain associated with carpal tunnel syndrome." Other protocols have used low-level laser energy applied to acupuncture points on the fingers and hand. This technique may be referred to as "laser acupuncture."

Policy/Criteria: Low level laser treatment is considered investigational for all indications, including but not limited to carpal tunnel syndrome and other pain disorders, edema, and to enhance wound healing. Given the equivocal or negative outcomes from a significant number of randomized clinical trials, it must be concluded that the body of evidence does not allow conclusions other than that the treatment of most pain syndromes with low level laser therapy provides at best the equivalent of a placebo effect. None of the studies compared LLLT to any of the current accepted conservative treatments for the conditions studied. In addition, data from larger randomized clinical trials comparing LLLT to standard medical and surgical treatment are necessary in order for any differences in outcomes to reach statistical significance so that conclusions can be reached concerning the overall effect of LLT on health outcomes.

Rating: 8b

BlueCross BlueShield. Utilization Management Section - Pain Rehabilitation Programs. Policy No: 5, Effective Date: 06/01/2004

Description
A pain rehabilitation program employs a coordinated multidisciplinary team to deliver an intensive program to modify pain and pain behavior through the treatment of the physiological, psychological and social aspects of chronic pain. Services can be provided on an outpatient or inpatient basis (outpatient is generally preferred). Individualized treatment plans are often administered through group settings. Chronic pain programs may include, but are not limited to, treatment of patients with chronic low back pain, chronic headache, temporal mandibular joint pain, chronic abdominal or pelvic pain.
Pain rehabilitation programs generally consist of three phases:
1. Evaluation/screening
2. Treatment phase
3. Follow-up phase
Components of a chronic pain management program may include physician, psychological, vocational, biofeedback, and nursing services, as well as occupational and physical therapy.
Policy/Criteria
Outpatient pain rehabilitation programs may be considered medically necessary when all of the following criteria are met:
1) The patient's chronic pain is attributable to a physical cause.
2) Previous methods of treating the chronic pain have been unsuccessful and a multidisciplinary program would likely be beneficial.
3) The patient has a significant loss of ability to function independently resulting from the chronic pain.
Integrative summary reports, that include treatment goals, progress assessment and stage of treatment, must be made available upon request and at least on a monthly basis during the course of the treatment program.
Inpatient admissions for pain rehabilitation may be considered medically necessary only if there are significant medical complications meeting medical necessity criteria for acute inpatient hospitalization.

Rating: 8b

BlueCross BlueShield. Surgery Section - Spinal Cord Stimulation for Treatment of Pain. Policy No: 45, Effective Date: 07/06/2004

Spinal cord stimulation has been used in a variety of chronic refractory pain conditions, including pain associated with cancer, failed back syndromes, arachnoiditis and chronic reflex sympathetic dystrophy. There has also been interest in spinal cord stimulation as a treatment of chronic refractory angina

pectoris and treatment of chronic limb ischemia, primarily in patients who are poor candidates for revascularization.
Policy/Criteria: Spinal cord stimulation may be considered medically necessary for the treatment of the following conditions and when patient selection criteria have been met:
1. Severe and chronic pain of the trunk or limbs that is refractory to all other pain therapies
2. Chronic refractory angina pectoris in patients who are not considered candidates for a revascularization procedure.
In addition, all facilities, equipment, professional and support personnel required for the proper diagnosis, treatment and follow-up of the patient are available.
Patient Selection Criteria
Patient selection focuses on determining whether or not the patient is refractory to other types of treatment. The following considerations apply:
1. The treatment is used only as a last resort; other treatment modalities (pharmacological, surgical, psychological, or physical, if applicable) have been tried and failed or are judged to be unsuitable or contraindicated.
2. Pain is neuropathic in nature; i.e. resulting from actual damage to the peripheral nerves. Common indications include, but are not limited to failed back syndrome, complex regional pain syndrome (i.e., reflex sympathetic dystrophy), arachnoiditis, radiculopathies, phantom limb/stump pain, and peripheral neuropathy. Spinal cord stimulation is generally not effective in treating nociceptive pain (resulting from irritation, not damage to the nerves) and central deafferentation pain (related to central nervous system damage from stroke or spinal cord injury).
3. No serious untreated drug habituation exists.
4. Patient was carefully screened, evaluated and diagnosed by a multidisciplinary pain management team prior to application of these therapies.
5. Pain relief from a temporarily implanted electrode has been demonstrated prior to permanent implantation.
Spinal cord stimulation is considered investigational for all other indications including, but not limited to, treatment of critical limb ischemia as a technique to forestall amputation.
The bulk of published literature regarding spinal cord stimulation (SCS) consists of case series. In a systematic literature synthesis of these studies, Turner and colleagues reported that in patients with chronic low back pain, an average of 59% of patients had 50% or greater pain relief with SCS.

Rating: 8b

BlueCross BlueShield. Allied Health - Biofeedback as a Treatment of Chronic Pain. Policy No: 28. Effective Date: 08/03/2004

Treatment for chronic pain is often multimodal, and typically includes a component of behavioral therapy. Behavior techniques vary, but are geared toward reducing muscle tension to break the pain cycle. EMG biofeedback has been used as part of a behavioral treatment program, with the assumption

that the ability to reduce muscle tension will be improved through feedback of data regarding degree of muscle tension to the subject. Other behavioral therapies include a variety of relaxation techniques, such as meditation, mental imagery, and cognitive therapy, which teaches subjects the ability to cope with stressful stimuli by attempting to alter negative thought and dysfunctional attitudes. Relaxation exercises may be part of the coping skills taught with cognitive behavioral therapy.
Biofeedback as a treatment of chronic pain, including but not limited to low back pain, is considered investigational.
Evidence is insufficient to demonstrate the effectiveness of biofeedback for treatment of chronic pain. The available evidence did not clearly show whether biofeedback's effects exceeded nonspecific placebo effects. It was also unclear whether biofeedback added to the effectiveness of relaxation training alone. A variety of randomized, controlled clinical trials have been published that have attempted to isolate the contribution of biofeedback in the treatment of chronic pain. The largest study of biofeedback in the treatment of lower back pain was published by Bush and colleagues who randomized 62 patients to receive either EMG biofeedback, sham biofeedback, or a no treatment control. At the conclusion of the trial, all 3 groups showed significant improvement in multiple measures of pain. There were no significant effects found for treatment type, leading the authors to conclude that biofeedback is not superior to placebo in controlling chronic pain.

Rating: 8b

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BlueCross BlueShield. Medicine Section - Trigger Point Therapy. Policy No: 39. Effective Date: 11/01/2004

Description: A trigger point is a discrete focal tenderness located in a palpable taut band of skeletal muscle, which produces a local twitch in response to stimulus to the band. Myofascial pain syndrome is a regional painful muscle condition with a direct relationship between a specific trigger point and its associated pain region. Modalities used in the treatment of myofascial pain syndrome include trigger point injection with local infiltration of a local anesthetic with or without a steroid, trigger point injection with saline or glucose, intramuscular dry needle stimulation, stretch and spray, massage, ultrasound and TENS. The therapeutic effect of dry needle stimulation relies on mechanical disruption or direct stimulation of trigger points.
Policy/Criteria: Trigger point injections with a local anesthetic with or without steroid may be considered medically necessary for the treatment of chronic low back or neck pain and myofascial pain syndrome when all of the following criteria are met:
1) Trigger points have been identified by palpation
2) Symptoms have persisted for more than three months
3) Medical management therapies such as bed rest, exercises, physical therapy, non-steroidal anti-inflammatory medications (unless contraindicated) and muscle relaxants have failed to control pain.
Up to four trigger point injections per anatomic area are considered medically necessary per year. The frequency of injections should be two months or longer between injection provided that a greater than 50% pain relief is obtained for six weeks. (1, 2)
Dry needle stimulation and trigger point injections with any substance (e.g., saline or glucose) other than local anesthetic with or without steroid are considered investigational.
Scientific Background: The American Society of Interventional Pain Physicians and Medicare medical policy provides the following description of trigger points and trigger point therapy: (2, 3)
Trigger points or trigger zones are self-sustaining, hyper-irritative foci that may occur in any skeletal muscle on the body that are particularly sensitive to touch and when stimulated, become the site of a painful neuralgia. These trigger points produce a referred pain pattern characteristic for that individual muscle and sometimes remote from the point itself and not related to it by anatomically definable

pathways. Usually, the involved muscle is felt as a tight palpable band. Frequently affected sites include the trapezius, supraspinatus, infraspinatus, teres major, lumbar paraspinals (2 sites), gluteus and pectoralis muscles.
There is no laboratory or imaging test for establishing the diagnosis of trigger points. It depends upon the detailed history and a thorough directed examination.
Injections of substances such as anesthetic and/or steroids are done to affect therapy for the pathological condition.
Esenyl et al, randomized 102 patients with chronic trigger point pain of the upper trapezius muscle to: ultrasound and neck stretching exercises (group 1); trigger point injections and neck stretching exercises (group 2); or neck stretching exercises alone (control group). Compared with the control group, patients in group 1 and 2 had a statistically significant reduction in pain intensity, an increase in pressure pain threshold, and an increase in range of motion. There were no statistically significant differences in outcomes between groups 1 and 2. (4)
Karakurum and colleagues randomized 15 patients to dry needle trigger point therapy at 6 trigger point sites or sham dry needle therapy. (5) Mean headache indices improved in both the experimental group and the sham therapy group, however the difference was not statistically significant. In the dry needle trigger point group neck tenderness and neck range-of-motion improved more than in the sham treated group. The number of patients treated was too small for the difference to reach statistical significance. Due to insufficient scientific evidence that dry needling or injection of saline or glucose at trigger point sites affects pain of patients with myofascial pain syndromes or tension headaches, conclusions cannot be reached concerning their effect on health outcomes.
A May 2004 updated search of the literature revealed no new published clinical studies for the investigational indications of dry needling or injection of substances other than local anesthetic and steroids in trigger point therapy.
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Cross References
Prolotherapy, TRG Medical Policy Manual, Medicine, Policy No. 40
Codes Number Description
CPT 20550 Injection tendon sheath, ligament, ganglion cyst
20551 tendon origin/insertion
20552 single or multiple trigger point(s), one or two muscle groups
20553 single or multiple trigger point(s), three or more muscle groups

Rating: 8c

BlueCross BlueShield. Medicine Section - Prolotherapy. Policy No: 40. Effective Date: 07/11/06

Description: Prolotherapy describes a procedure for strengthening lax ligaments by injecting proliferating agents/sclerosing solutions directly into torn or stretched ligaments or into a joint or adjacent structures to create scar tissue in an effort to stabilize a joint. Agents used with prolotherapy have included zinc sulfate, psyllium seed oil, combinations of dextrose, glycerine and phenol, or dextrose alone. "Proliferatives" act to promote tissue repair or growth by prompting release of growth factors, such as cytokines, or increasing the effectiveness of existing circulating growth factors. Prolotherapy may involve a single injection or a series of injections, often diluted with a local anesthetic.
Policy/Criteria: Prolotherapy is considered investigational as a treatment of any condition, including but not limited to musculoskeletal pain.
Scientific Background: Prolotherapy has been investigated as a treatment of various etiologies of pain, including arthritis, degenerative disc disease, fibromyalgia, tendinitis, and plantar fasciitis. As with any therapy for pain, a placebo effect is anticipated, thus randomized placebo-controlled trials are necessary to investigate the extent of the placebo effect and to determine whether any improvement with prolotherapy exceeds that associated with a placebo. Although there is extensive literature regarding prolotherapy, a literature search through April 28, 2004 revealed only five randomized placebo-controlled trials.
Two early trials focused on the use of injections of dextrose, glycerin, and phenol as a treatment of low back pain. In 1987, Ongley and colleagues reported on a trial of 81 patients with low back pain who were randomized to receive spinal manipulation plus prolotherapy compared to a control group that received less forceful spinal manipulation, less local anesthesia, and placebo injections of saline. (2) Although improved responses were reported for the treatment group, it is not possible to isolate the possible contribution of the prolotherapy compared to the impact of the different types of spinal manipulation. In 1993, Klein and colleagues reported on a trial that randomized 79 patients with low back pain to receive a series of six weekly injections, using either saline or a proliferant solution of dextrose, glycerine, and phenol. (3) Thirty of the 39 patients assigned to the proliferant group achieved a 50% or greater diminution in pain compared to 21 of the 40 in the placebo group. While the incremental benefit in the treatment group was statistically significant (p=0.04), blinding of the treatment groups was not maintained, since those assigned to the proliferant group experienced a clinically recognizable local inflammatory response. It is significant to note that this study also fails to isolate the treatment effect of the dextrose-glycerine-phenol injections because both the experimental and control groups received instructions to perform 30 standing forward flexion exercises followed by 20 standing extension exercises 4 times each day during the treatment and follow-up periods. Patients were also encouraged to walk briskly for at least 1 mile five times per week and to continue to pursue normal activities during the study.
In 2000, Reeves and Hassanein reported on two trials that used dextrose alone as a proliferant, thus eliminating the inflammatory response. (4,5) The first trial randomized 68 patients with 111 osteoarthritic knees to receive either 3 bimonthly injections of dextrose or placebo. (4) The patients were

evaluated with a visual analogue scale for pain and swelling, frequency of leg buckling, goniometrically measured flexion, and radiographic measures of joint narrowing. As the data are presented, it is clear that there is a significant improvement in both the placebo and treatment groups, but it is difficult to determine the comparative magnitude of improvement between the two groups. For example, for the various outcome measures of pain, it appears that there are probably no clinically significant incremental effects of prolotherapy compared to the placebo group. However, for other non-pain outcomes, e.g., swelling, buckling and flexion range, prolotherapy may be associated with a significant incremental improvement. The various outcome measures were combined as assessed using a Hotelling multivariate analysis. With this statistical measurement, prolotherapy demonstrated a statistically superior overall effect (p=0.015) compared to the control group. It should be recognized that the statistical significance of this measure is most likely due to the improvements in the non-pain symptoms. In summary, it is not known whether the incremental improvement in the non-pain related outcomes of the prolotherapy group compared to the control group is clinically significant.

In a similarly designed study, the same investigators studied the effectiveness of prolotherapy as a treatment of osteoarthritic thumb and finger joints. (5) A total of 27 patients with 150 osteoarthritic joints were randomized to receive three bimonthly injections of either dextrose or water. Patients were evaluated with both visual analogue scale (VAS) for pain and goniometric assessment of joint movement. Since patients had a variable number of joints injected (ranging from 1 to 22), the VAS score for every symptomatic joint for each patient was added together for a total and divided by the number of symptomatic joints to provide an average joint pain score for each patient. There were improvements in pain scores in both the placebo and treatment groups, but the incremental improvement in the treatment group compared to the placebo group did not reach statistical significance. In terms of flexion, the treatment group reported a statistically significant improvement (p=0.043), while the placebo group reported a greater, statistically significant, decrease (p=0.011). Therefore, the statistically significant difference in flexion between the two groups (p=.003) was primarily related to the decrease in the control group, with a smaller contribution related to the positive response in the treatment group. In summary, the clinical significance of an isolated finding of improved flexion without a corresponding significant improvement in pain is uncertain.

Dechow and colleagues published one additional randomized, double-blind, placebo-controlled trial in which 74 patients with chronic low back pain of more than 6 months' duration received once weekly injections of dextrose-glycerine-phenol with lignocaine vs saline plus lignocaine. (6) The objective of the study was to determine the clinical efficacy of sclerosing injections in patients with chronic low back pain. All patient assessments were performed blind by an experienced physiotherapist. The injections to the ligaments of the L4-5 and L5-S1 lumbar motion segments were given by an orthopaedic physician experienced in the technique, blinded to the nature of the injection solution. There were no statistically significant differences in patient characteristics between the placebo and treatment groups at baseline or for any measure at follow-up. The authors conclude, "In summary, following three, weekly sclerosant injections to the lumbar spinal ligaments we have been unable to demonstrate improvement in pain, self-reported function, somatization, depression or spinal flexion in patients with undifferentiated chronic back pain. The results may be explained in terms of differences in patient selection, underlying pathology, social circumstances, additional treatment modalities or insufficient power of the study.

Further research is needed to identify which components of the regimens are most effective and whether there are subgroups of patients who are more likely to respond to these safe treatments."
Finally, Yelland and colleagues reported on a randomized, partially blinded, controlled trial involving prolotherapy injections, saline injections, and exercises for chronic low back pain in 110 subjects. (7) While decreases in pain and disability were noted in all study groups, there were no significant differences found between treatment groups at 12 and 24 months. Therefore, the effects of prolotherapy did not significantly exceed placebo effects.
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Codes Number Description
CPT 20550 Injection(s); single tendon sheath, or ligament, aponeurosis (e.g., plantar "fascia")

Rating: 8b

BlueCross BlueShield. Radiology Section - Thermography. Policy No: 17. Effective Date: 04/05/2005

Description: Thermography is a non-invasive imaging technique, which is intended to measure temperature distribution of various organs and tissues. The infrared radiation from the tissue reveals temperature variations by producing brightly colored patterns on a liquid crystal display. Interpretation of the color patterns is thought to assist in the diagnosis of many disorders such as breast cancer, Raynaud's phenomenon, digital artery vasospasm in hand-arm vibration syndrome, impaired spermatogenesis in infertile men, degree of burns, deep vein thrombosis, gastric cancer, tear-film layer stability in dry-eye syndrome, Frey's syndrome, headaches, low-back pain, reflex sympathetic dystrophy, and vertebral subluxation.

The American Chiropractic Association suggests that high-resolution infrared imaging is of value in the diagnostic evaluation of patients when the clinical history suggests the presence of one of the following situations:

- Early diagnosis and monitoring of reflex sympathetic dystrophy syndromes
- Evaluation of spinal nerve root fiber irritation and distal peripheral nerve fiber pathology for detection of sensory/autonomic dysfunction
- Evaluation and monitoring of soft tissue injuries, including segmental dysfunction/subluxation, sprain and myofascial conditions (strains and myofascial pain syndromes) not responding to clinical treatment
- Evaluation for the physiological significance of equivocal or minor anatomical findings seen on myelogram, computed tomography (CT) and/or magnetic resonance imaging (MRI)
- Evaluation of feigned disorders

Policy/Criteria: Thermography is considered investigational for all indications.
There is insufficient evidence in the peer-reviewed published literature to reach conclusions concerning the effects of thermography on health outcomes for any indication. The scientific literature is inadequate to validate the clinical role of thermography; no published studies demonstrate how the results of thermography can be used to enhance patient management and improve patient health outcomes.

Rating: 8b

BlueCross. Pulsed Radiofrequency (PRF) Treatment for Chronic Pain Syndromes. Policy #: MED.00071. Current Effective Date: 09/22/2005

Description/Scope. Pulsed radiofrequency treatment (PRF) has been investigated as a potentially less harmful alternative to radiofrequency (RF) thermal neurolytic destruction (thermocoagulation) in the management of certain chronic pain syndromes such as facet joint pain and trigeminal neuralgia.
Policy Statement. Investigational/Not Medically Necessary: Pulsed radiofrequency treatment is considered investigational/not medically necessary for the treatment of chronic pain syndromes.
Rationale. The published literature regarding pulsed radiofrequency treatment for chronic pain syndromes currently is insufficient to assess the efficacy of this procedure and permit scientific conclusions. Mikeladze and colleagues reported on the treatment of lumbar or cervical spine facet joint pathology by application of PRF to the medial branches of the dorsal rami at the appropriate spinal level. This retrospective study included 114 patients at a pain management clinic with clinical signs of facet joint involvement and a favorable response to a diagnostic medial branch block using local anesthetic. Mean duration of pain was 7.52 ± 5.26 years. The result was regarded as successful if pain reduction was more than 50% on a visual analog scale and the duration of effect was more than 1.5 months. Of 114 patients who had a positive response to diagnostic block, 46 patients did not respond favorably to PRF application (pain reduction less than 50%). In 68 patients, the procedure was successful and lasted on average 3.93 ± 1.86 months. Eighteen patients had the procedure repeated with the same duration of pain relief that was achieved initially. The authors concluded that the application of pulsed RF to medial

branches of the dorsal rami in patients with chronic facet joint arthropathy provided temporary pain relief in 68 of 118 patients. However, the authors note that, because of the relatively short duration of effect and the higher success rate with longer duration of thermal RF, pulsed RF appears less effective than the established entity. In a "State of the Art" review, RF, Van Zundert et al. comment that, even though the use of PRF is increasing, "well designed trials should be conducted to establish the real value of this treatment option."

Background/Overview. Pulsed radiofrequency treatment (PRF) has been investigated as a potentially less harmful alternative to radiofrequency (RF) thermal neurolytic destruction (thermocoagulation) in the management of certain chronic pain syndromes such as facet joint pain and trigeminal neuralgia. Thermal radiofrequency (RF) is said to carry the potential risk of neuritis, and histological studies reveal indiscriminate destruction of both small and large fibers following RF treatment. PRF treatment for chronic pain syndromes is thought to be a non destructive alternative to thermal RF in that it applies RF energy with a pulsed time cycle that delivers short bursts of RF current instead of a continuous RF flow. By pulsing the electrical current, the needle remains relatively cool (up to 42 degrees C compared to temperatures in the 60s C with continuous RF) so that the tissue cools slightly between each burst, reducing the risk of destroying nearby tissue and preventing any long-term damage to the nerve. It is postulated this disrupts the transmission of impulses across small unmyelinated fibers without destroying them while larger fibers remain protected by the myelin sheath.

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3. Van Zundert J, Brabant S, Van de Kelft E, et al. Pulsed Radiofrequency Treatment of the Gasserian Ganglion in Patients with Idiopathic Trigeminal Neuralgia. Pain. 2003 Aug;104(3):449-52.
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Rating: 8c

BlueCross of California. Implantable Infusion Pumps. Policy #: SURG.00068. Current Effective Date: 07/14/2005

Description/Scope

An implantable infusion pump is intended to provide long-term, continuous or intermittent drug infusion. This policy addresses the use of implantable infusion pumps.

Policy Statement

Medically Necessary:

Implantable infusion pumps are considered medically necessary when used to deliver drugs for the treatment of:

- Primary liver cancer (intrahepatic artery injection of chemotherapeutic agents);
- Metastatic colorectal cancer where metastases are limited to the liver (intrahepatic artery injection of chemotherapeutic agents);
- Head/neck cancers (intra-arterial injection of chemotherapeutic agents);
- Severe, refractory spasticity of cerebral or spinal cord origin in patients who are unresponsive to or cannot tolerate oral baclofen (Lioresal®) therapy (intrathecal injection of baclofen)

Permanently implanted intrathecal (intraspinal) infusion pumps for the administration of opiates or non-opiate analgesics, in the treatment of chronic intractable pain, are considered medically necessary when:

- Used for the treatment of malignant (cancerous) pain and all of the following criteria are met:

1. Strong opioids or other analgesics in adequate doses, with fixed schedule (not PRN) dosing, have failed to relieve pain or intolerable side effects to systemic opioids or other analgesics have developed; and
2. Life expectancy is greater than 3 months (less invasive techniques such as external infusion pumps provide comparable pain relief in the short term and are consistent with standard of care); and
3. Tumor encroachment on the thecal sac has been ruled out by appropriate testing; and
4. No contraindications to implantation exist such as sepsis or coagulopathy; and
5. A temporary trial of spinal (epidural or intrathecal) opiates has been successful prior to permanent implantation as defined by a 50% reduction in pain. A temporary trial of intrathecal (intraspinal) infusion pumps is considered medically necessary only when criteria 1-4 above are met.

- Used for the treatment of non-malignant (non-cancerous) pain with a duration of greater than 6 months and all of the following criteria are met:

1. Documentation, in the medical record, of the failure of 6 months of other conservative treatment modalities (pharmacologic, surgical, psychologic or physical), if appropriate and not contraindicated; and
2. Intractable pain secondary to a disease state with objective documentation of pathology in the medical record; and
3. Further surgical intervention is not indicated; and
4. Psychological evaluation has been obtained and evaluation unequivocally states that the pain is not psychologic in origin and that benefit would occur with implantation; and
5. No contraindications to implantation exist such as sepsis or coagulopathy; and
6. A temporary trial of spinal (epidural or intrathecal) opiates has been successful prior to permanent implantation as defined by a 50% reduction in pain and documentation in the medical record of improved function. A temporary trial of intrathecal (intraspinal) infusion pumps is considered medically necessary only when criteria 1-5 above are met.

Note: When an implantable/intrathecal infusion pump is determined to be medically necessary, the supplies necessary for the proper use of the pump are considered medically necessary.

Investigational/Not Medically Necessary:

Implantable infusion pumps are considered investigational/not medically necessary for the infusion of heparins for thromboembolic disease or antibiotics for osteomyelitis.

All other uses of implantable infusion pumps, including fully implantable insulin pumps, are considered investigational/not medically necessary.

Rationale

The role of opioid therapy in treatment of pain is well established in the medical literature. Individuals who have proven unresponsive to less invasive medical therapy and who require large doses of opioids may be candidates for an implantable delivery system that permits intrathecal administration. This system delivers the opioid directly to the receptors in the spinal cord, allowing smaller doses to be used and thereby minimizing side effects. This position is supported by multiple case control studies. The use of continuous chemotherapy infusion treatment has been studied for patients with certain types of cancers, including, but not limited to, primary hepatic cancer, metastatic colorectal cancer to the liver, and various head and neck cancers. This method of chemotherapy infusion has been found to improve medical outcomes in select individuals where continuous chemotherapy is believed to be appropriate. The evidence supporting this conclusion includes multiple randomized controlled trials. Prospective randomized trials of individuals with unresectable liver disease have shown that compared to conventional systemic therapy, hepatic artery infusion is associated with an increased tumor response rate.

Implantable pumps for delivery of medication to the intrathecal space have been developed as an alternative to chronic systemic administration for the treatment of spasticity of cerebral or spinal origin. These pumps have been demonstrated in numerous randomized controlled trials to reduce adverse effects such as tolerance, dependency, and neurotoxicity.

The use of implantable pumps for infusion of antithrombotic medications for thromboembolic disease, or for the infusion of antibiotics for osteomyelitis, has not been demonstrated to provide any additional improvement in net health outcomes above standard care with bolus or subcutaneous drug administrations. This therapy does not prevent the occurrence of complications or morbidity nor does it significantly relieve pain over other less invasive treatment methods. The risks involved in the implantation and maintenance of implantable infusion pumps for these conditions is not outweighed by any potential benefits. The evidence supporting this conclusion includes multiple case series studies.

Fully implantable insulin pumps are designed to deliver insulin via intraperitoneal or intravenous routes in a programmed and controlled manner to diabetic patients. However, these pumps have been associated with a high incidence of device malfunction related to catheter obstruction, among other malfunctions. Newer devices are under development that are expected to drastically reduce the problem of catheter obstruction. With additional refinements underway, implantable insulin pumps may eventually prove beneficial in the treatment of insulin dependent diabetic patients. To show benefit, however, additional long-term randomized prospective studies are needed.

Background/Overview

Implantable Infusion Pumps

Implantable infusion pump use for the delivery of intrathecal (intraspinal) opiates is based on the existence of opioid (narcotic) receptors on the spinal cord to achieve "selective spinal analgesia" (pain relief). Pumps provide for the long-term delivery of opioid (narcotic) medication in the management of malignant (cancer) pain and nonmalignant (non-cancer) pain. Examples of appropriate nonmalignant pain syndromes which may be treated with implantable pumps include "failed back surgery", chronic arachnoiditis, visceral pain syndromes, post herpetic neuralgia, phantom limb pain, spinal cord injuries, peripheral neuropathies and reflex sympathetic dystrophy. A successful temporary trial of spinal opiates

is required both to evaluate analgesic responsiveness and to increase the long-term success of the procedure. Individuals must be closely monitored as conversion from high dose oral or systemic opioids to spinally administered opioids will sometimes result in withdrawal symptoms.

Treatment with this therapy should remain a last resort, used only after all other appropriate therapies have failed. A permanently implantable drug-infusion system is not usually appropriate when life expectancy is three months or less; for such patients, external drug infusion systems can appropriately provide spinal analgesia and comparable pain relief.

The implantable infusion pump (IIP) is a drug delivery system that provides continuous infusion of an agent at a constant and precise rate. The purpose of an IIP is to deliver therapeutic levels of a drug directly to a target organ or compartment. It is frequently used to deliver chemotherapy directly to the hepatic artery or superior vena cava.

An IIP is surgically placed in a subcutaneous pocket under the infraclavicular fossa or in the abdominal wall and a catheter is threaded into the desired position. A drug is infused over an extended period of time. The drug reservoir may be refilled as needed by an external needle injection through a self-sealing septum in the IIP. Bacteriostatic water or physiological saline is often used to dilute therapeutic drugs. A heparinized saline solution may also be used during an interruption of drug therapy to maintain catheter patency.

There is a range of totally implanted catheters with implanted reservoirs and manual pumps as well as totally implanted catheters with implanted infusion pumps. Implantable infusion pumps are available in either programmable or non-programmable models, depending on the type of medication delivery required. Programmable pumps are for flexible medication delivery as dose titration and regulation will vary due to the dynamic nature of the patient. Programmable designs facilitate flexible dosing options and precise dose titration over time.

An example of a flexible medication delivery pump is the SynchroMed® electronic pump, manufactured by Medtronic Inc. (Minneapolis, MN, USA). This pump contains a collapsible reservoir that can be filled with 10 to 18ml of liquid medication and a peristaltic pump that pushes the medication through a bacteriostatic filter and catheter into the spinal canal.

Non-programmable pumps are for fixed rate medication delivery when the dosage is expected to be stable. Possible routes of administration include intravenous, intrahepatic, intra-arterial, subcutaneous, intraperitoneal, intrathecal, epidural, and intraventricular.

An example of a fixed rate pump is the Infusaid Implantable Infusion Pump, manufactured by Arrow International (Reading, PA, USA). One chamber holds the medication and the other, a charging fluid. Once inserted into the abdomen, the pump regulates to the temperature of the body, leading to the expansion of the charging fluid, which pressurizes the medication chamber to push the drug through the catheter.

Fully Implantable Insulin Pumps

At the time of this writing, no implantable insulin pumps have received FDA approval for marketing. The MiniMed® 2000 and MiniMed® 2001 implantable insulin pumps have been granted investigational status and are currently being evaluated in clinical trials.

Intrathecal Infusion Pumps

The intrathecal (IT) catheter is inserted through a needle into the intraspinal space, usually at the lumbar or thoracic level. The other end of the catheter is connected to the pump and then filled with medication. The choice of IT pump depends on the indications for intraspinal therapy, the need for bolus versus continuous infusion, the available support services, cost to the patient, and the patient's general medical condition, ambulatory status and life expectancy.

External programming is used to set the dosage, rate and timing via telemetry to the pump. The pump needs to be refilled every four to eight weeks by percutaneous injection, depending on flow rate, and trained medical, nursing or technical staff must perform the refilling process.

Definitions

- Bacteriostatic: an agent that inhibits the growth or multiplication of bacteria
- Bolus: a dose of a drug given intravenously; specifically a large dose given for the purpose of rapidly achieving the needed therapeutic concentration in the bloodstream
- Hepatic colorectal metastases: cancer that has spread from its site of origin to another part of the body
- Infraclavicular fossa: a triangular depression bounded by the clavicle and the adjacent borders of the deltoid and pectoralis major muscles
- Intrathecal space: the space between the spinal cord and the surrounding membrane (dura mater), which is filled with cerebrospinal fluid
- Primary liver cancer: a cancer that originates within liver cells, as opposed to having spread from other organs
- Parenteral: by injection as in subcutaneous, intramuscular, or intravenous
- Osteomyelitis: a condition characterized by inflammation of bone caused by infection; inflammation may remain localized or may spread through the bone to involve the marrow, cortex, cancellous tissue and periosteum

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Rating: 8a

Blue Cross/Blue Shield. Opioid Antagonists Under Heavy Sedation or General Anesthesia as a Technique of Opioid Detoxification. Date of Origin: Section: Mental Health Policy No: 14. Approved Date: 10/03/2006.

Opioid antagonists under heavy sedation or general anesthesia (i.e., ultra-rapid detoxification) are considered investigational as a technique for opioid detoxification.

Rating: 8b

Blum K, Chen TJ, Martinez-Pons M, Dinubile NA, Waite RL, Schoolfield J, Blum SH, Mengucci J, Downs BW, Meshkin B. The H-Wave small muscle fiber stimulator, a nonpharmacologic alternative for the treatment of chronic soft-tissue injury and neuropathic pain: an extended population observational study. Adv Ther. 2006 Sep-Oct;23(5):739-49.

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In a previous study, the H-Wave small-muscle fiber stimulator significantly reduced chronic pain and restored physical function among patients with pain in the lower and upper extremities and spine. In this extended population observational study, a cross-sectional,computer-administered 10-item survey was administered to 6774 patients (3367 men [49.7%], 3406 women [50.3%], and 1 sex not reported [<1%]; mean+/-SD age, 45.28+/-10.08 y; range, 18-65 y) with chronic soft-tissue injury or neuropathic pain to assess their therapeutic response. The mean+/-SE duration of self-administered H-Wave treatment before the survey was completed was 87.35+/-1.39 d. Sixty-five percent of study participants reported a reduced or eliminated need for pain medication; 79% reported improved functional capacity or activity; and 78% reported 25% or greater reduction of pain. This cross-sectional evaluation represents the largest

outcome study on the benefits of the H-Wave device in patients with chronic soft-tissue injury or neuropathic pain. The results suggest that this nonpharmacologic approach may provide an important alternative to standard pharmacologic treatment.

PMID: 17142209

Rating: 4c

Patient Selection Criteria from the study: All enrolled patients had a previous physician-documented diagnosis of chronic soft-tissue injury or neuropathic pain in an upper or lower extremity or the spine that was unresponsive to conventional therapy, such as physical therapy, medications, and transcutaneous electrical nerve stimulation (TENS), and other analgesic electrical stimulator modalities.

Blum K, DiNubile NA, Tekten T, Chen TJ, Waite RL, Schoolfield J, Martinez-Pons M, Callahan MF, Smith TL, Mengucci J, Blum SH, Meshkin B. H-Wave, a nonpharmacologic alternative for the treatment of patients with chronic soft tissue inflammation and neuropathic pain: a preliminary statistical outcome study. Adv Ther. 2006 May-Jun;23(3):446-55.

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The burden of chronic soft tissue inflammation and neuropathic pain on individuals and society is substantial. This study was conducted to evaluate the H-wave device--an innovative form of treatment for chronic pain and inflammation--in patients with persistent pain associated with injuries or conditions affecting the upper or lower extremities or the back. Patients with at least moderate pain despite conventional therapy were included in a systematic survey after they had been given 2 to 6 wk of treatment with the H-wave device. Measures of improvement involved the proportion of patients with diminished medication requirements, improved function, or pain relief greater than 25%. More than 60% of patients with pain in the lower extremities, upper extremities, or back experienced pain relief exceeding 25%. The proportion of patients whose function improved and who were able to perform a new activity was consistently greater than 50% across the 3 anatomic subgroups. More than 40% of patients in each group were able to reduce or completely eliminate the use of pain medications. These benefits of treatment were independent of the type of pain therapy administered previously. In each anatomic subgroup, the proportion of patients who reported improvement on more than 1 of the 3 endpoints was significantly higher than the expected response to placebo therapy (P<.001). Results suggest that the H-wave device provided important benefits to patients with chronic soft tissue inflammation and neuropathic pain.

PMID: 16912027

Rating: 4c

Blum K, Chen AL, Chen TJ, Prihoda TJ, Schoolfield J, Dinubile N, Waite RL, Arcuri V, Kerner M, Braverman ER, Rhoades P, Tung H. The H-Wave(R) device is an effective and safe non-pharmacological analgesic for chronic pain: a meta-analysis. Adv Ther. 2008 Jul;25(7):644-57.

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INTRODUCTION: This meta-analysis was conducted to systematically review the efficacy and safety of the H-Wave(R) (Electronic Waveform Lab, Inc, Huntington Beach, CA, USA) device and programme as a non-pharmacological analgesic treatment in chronic soft tissue inflammation and neuropathic pain. METHODS: Five studies related to pain relief, reduction in pain medication and increased functionality obtained with the H-Wave device were included in the analysis. Data were analysed using the random effects model, including adjustment to evaluate variability, size of study and bias in effect size. A total of 6535 participants were included in the meta-analysis; there were 8065 participants' outcomes measured due to multiple measurements per participant. RESULTS: The H-Wave device decreased pain ratings across various chronic soft tissue inflammation and neuropathic pain conditions. The mean weighted effect size was 0.59, and the estimated effect size variance was 0.00003 (95% confidence intervals [CI]: 0.580, 0.600). The H-Wave device also decreased the intake of pain medication in patients with various chronic soft tissue inflammation and neuropathic pain conditions. The mean weighted effect size was 0.56, and the estimated effect size variance was 0.000013 (95% CI: 0.553, 0.567). Patient functionality was also improved with use of the H-Wave device. The mean weighted effect size was 0.70, and the estimated effect size variance was 0.00002 (95% CI: 0.691, 0.709). A chi-square test for homogeneous effect sizes found highly significant ($P<0.00001$) variability, indicating a robust significant effect size for increased functionality relative to both pain relief and reduction in pain medication. There was little to no evidence of any adverse effects associated with the use of the H-Wave device. CONCLUSION: The findings indicate a moderate to strong effect of the H-Wave device in providing pain relief, reducing the requirement for pain medication and increasing functionality. The most robust effect was observed for improved functionality, suggesting that the H-Wave device may facilitate a quicker return to work and other related daily activities.

PMID: 186362

Rating: 1c

Note: The low quality rating for this "meta-analysis" is primarily because the numbers were dominated by results from studies that were not prospective randomized controlled trials. For reported results concerning "Reduction in pain medication" and "Increased functionality," the meta-analysis relied 100% on the Blum 2006 studies. For reported results concerning "Reduction in pain," there were 4 studies,

with 3 small prospective studies that looked only at diabetic neuropathy, plus the Blum 2006 study, but the Blum study accounted for 92% of the effect size sample for this measurement. The study also says, "RCTs were found to have a signifcantly lower effect size." The Blum 2006 studies that dominate this meta-analysis were retrospective observational studies using a patient survey, the H-Wave Customer Service Questionnaire, without a prospective control group. According to this meta-analysis, "double-blinded studies of the H-Wave device are currently underway and results will be awaited with interest." The study author is an outside independent consultant of Electronic Waveform Lab, Inc.

Blumenfeld AM, Schim JD, Chippendale TJ. Botulinum toxin type A and divalproex sodium for prophylactic treatment of episodic or chronic migraine. Headache. 2008 Feb;48(2):210-20. Epub 2007 Nov 28.

The Neurology Center, Encinitas, CA 92024, USA.

DESIGN/METHODS: This was a randomized, double-blind, single-center prospective study. Fifty-nine patients. CONCLUSIONS: Both BoNTA and DVPX significantly reduced disability associated with migraine; BoNTA had a favorable tolerability profile compared with DVPX.

PMID: 18047502

Rating: 2b

Bocanegra TS, Weaver AL, Tindall EA, Sikes DH, Ball JA, Wallemark CB, Geis GS, Fort JG. Diclofenac/misoprostol compared with diclofenac in the treatment of osteoarthritis of the knee or hip: a randomized, placebo controlled trial. Arthrotec Osteoarthritis Study Group. J Rheumatol. 1998;25:1602-11.

Arthritis Center of Nebraska, Lincoln, USA.

OBJECTIVE: Gastric (GU) and duodenal ulcers (DU) are common adverse effects of nonsteroidal anti-inflammatory drugs (NSAID). Endoscopically diagnosed upper gastrointestinal (GI) ulceration occurs in about 24% of long-term NSAID users. Co-administration of misoprostol with the NSAID reduces the incidence of NSAID induced GU and DU and their complications. However, compliance is limited by the different dosing regimens of misoprostol and NSAID and GI symptoms associated with misoprostol at its recommended q.i.d. dose. We compared the efficacy, safety, and incidence of endoscopic upper GI ulceration associated with the administration of 2 combinations of diclofenac (50 or 75 mg) and misoprostol 200 microg (D50/M200 t.i.d., D75/M200 b.i.d.), diclofenac 75 mg b.i.d., and placebo in a 6 week, randomized, double blind study in patients with osteoarthritis (OA) of the knee or hip. METHODS: A total of 572 patients with symptomatic OA of the knee or hip and history of GU, DU. or 10 or more erosions were randomized to receive D50/M200 t.i.d., D75/M200 b.i.d., diclofenac 75 mg b.i.d., or placebo for 6 weeks. Arthritis assessments were performed at baseline, 2, and 6 weeks, and

upper GI endoscopies at baseline and end of treatment. RESULTS: All active treatment groups were significantly better than placebo, at all visits, in improving OA symptoms. There were no significant differences in arthritis efficacy between the diclofenac/ misoprostol combinations and diclofenac. However, endoscopically diagnosed GU and/or DU were significantly less frequent in patients receiving D50/M200 t.i.d. (8%), D75/M200 b.i.d. (7%), and placebo (4%) compared to diclofenac 75 mg b.i.d. (17%). Adverse events were not different between the active treatment groups, except for higher incidences of flatulence with D75/M200 and diarrhea with D50/M200. CONCLUSION: Diclofenac 50 mg/misoprostol 200 microg t.i.d. and diclofenac 75 mg/misoprostol 200 microg b.i.d. are as efficacious as diclofenac 75 mg b.i.d. in the treatment of OA, but are associated with a significantly lower incidence of gastric and/or duodenal ulcers.

PMID: 9712107

Rating: 2a

Bolona ER, Uraga MV, Haddad RM, Tracz MJ, Sideras K, Kennedy CC, Caples SM, Erwin PJ, Montori VM. Testosterone use in men with sexual dysfunction: a systematic review and meta-analysis of randomized placebo-controlled trials. Mayo Clin Proc. 2007;82:20-8.

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OBJECTIVE: To conduct a systematic review and meta-analysis of randomized placebo-controlled trials to measure the effect of testosterone use on sexual function in men with sexual dysfunction and varying testosterone levels. METHODS: Librarian-designed search strategies were used to search the MEDLINE (1966 to October 2004), EMBASE (1988 to October 2004), and Cochrane CENTRAL (inception to October 2004) databases. The MEDLINE search was rerun in March 2005. We also reviewed reference lists from included studies and content expert files. We selected randomized placebo-controlled trials of testosterone vs placebo that enrolled men with sexual dysfunction and measured satisfaction with erectile function and libido and overall sexual satisfaction. RESULTS: We included 17 trials (N = 862 participants) in this review. Trials that enrolled participants with low testosterone levels showed (1) a moderate nonsignificant and inconsistent effect of testosterone use on satisfaction with erectile function (random-effects pooled effect size, 0.80; 95% confidence interval [CI], -0.10 to 1.60), (2) a large effect on libido (pooled effect size, 1.31; 95% CI, 0.40 to 2.25), and (3) no significant effect on overall sexual satisfaction. Trials that enrolled patients with low-normal and normal testosterone levels at baseline showed testosterone that caused (1) a small effect on satisfaction with erectile function (pooled effect size, 0.34; 95% CI, 0.03 to 0.65), (2) moderate nonsignificant effect on libido (pooled effect size, 0.41; 95% CI, -0.01 to 0.83), and (3) no significant effect on overall sexual satisfaction. CONCLUSION: Testosterone use in men is associated with small improvements in satisfaction with erectile function and moderate improvements in libido. Unexplained inconsistent results across trials, wide CIs, and possible reporting bias weaken these inferences.

PMID: 17285782

Rating: 1a

Boothby LA, Doering PL, Halton RC. Carisoprodol: A marginally effective skeletal muscle relaxant with serious abuse potential. Hospital Pharmacy. 2003;38:337-45.

This reference is not listed in PubMed.

The review examined literature on the efficacy and abuse of carisoprodol and made recommendations for use. This was a literature review. There was little evidence to support the use of carisoprodol in pain control. Patients with a previous history of substance abuse were more likely to abuse this drug. It was suggested that the medication be rescheduled as a schedule IV controlled substance in all states were this had not already happened. A weaning protocol with phenobarbital was described.

Rating: 9b

Borg-Stein J, Simons DG. Focused review: myofascial pain. Arch Phys Med Rehabil. 2002 Mar;83(3 Suppl 1):S40-7, S48-9.

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Myofascial pain is defined as pain that originates from myofascial trigger points in skeletal muscle. It is prevalent in regional musculoskeletal pain syndromes, either alone or in combination with other pain generators. The appropriate evaluation and management of myofascial pain is an important part of musculoskeletal rehabilitation of regional axial and limb pain syndromes. This article reviews the current hypotheses regarding the pathophysiology of myofascial trigger points and muscle pain. A critical evidence-based review of the pharmacologic, nonpharmacologic, alternative medicine, and exercise treatments of myofascial pain is provided, as well as future research directions. OVERALL LEARNING OBJECTIVE: To review critically the state of the art knowledge of myofascial pain, including pathophysiology and comprehensive management. Areas of future research are identified. Copyright 2002 by the American Academy of Physical Medicine and Rehabilitation

Publication Types:
Review

PMID: 11973695

Rating: 5a

Borsook D, Becerra LR. Breaking down the barriers: fMRI applications in pain, analgesia and analgesics. Mol Pain. 2006 Sep 18;2:30.

P.A.I.N. Group, Brain Imaging Center, Department of Psychiatry, McLean Hospital, Belmont, MA, USA. dborsook@mclean.harvard.edu

This review summarizes functional magnetic resonance imaging (fMRI) findings that have informed our current understanding of pain, analgesia and related phenomena, and discusses the potential role of fMRI in improved therapeutic approaches to pain. It is divided into 3 main sections: (1) fMRI studies of acute and chronic pain. Physiological studies of pain have found numerous regions of the brain to be involved in the interpretation of the 'pain experience'; studies in chronic pain conditions have identified a significant CNS component; and fMRI studies of surrogate models of chronic pain are also being used to further this understanding. (2) fMRI studies of endogenous pain processing including placebo, empathy, attention or cognitive modulation of pain. (3) The use of fMRI to evaluate the effects of analgesics on brain function in acute and chronic pain. fMRI has already provided novel insights into the neurobiology of pain. These insights should significantly advance therapeutic approaches to chronic pain.
PMID: 16982005

Rating: 5b

Borsook, D., et al. Neuroimaging revolutionizes therapeutic approaches to chronic pain. Molecular Pain. 2000; Volume 3, Number 25.

Rating: 5c

Quality: N/A. Total Rating: N/A. Comment: Does not meet inclusion criteria for evidence-based review. [CA DWC]

Boseman J, Disability management. Application of a nurse based model in a large corporation, AAOHN J 2001 Apr;49(4):176-86

Global Occupational Health Services, IBM Corporation, San Jose, CA, USA.

1. Minimizing the impact of injury, disability, and disease on employees is important not only to enhance the employee's quality of life, but also to maintain worker performance. Key to the disability management plan is early, aggressive, and safe return to work programs, which minimize personal and corporate costs. 2. The challenge is to improve the delivery of various disability programs (including

short term disability, long term disability, and workers' compensation), and minimize escalating costs. 3. Program development provides the foundation for a disability management system. Implementation is key to achieving success. To successfully market case management, the occupational health nurse must articulate the cost benefit, as well as other concepts behind case management. 4. Disability management can be operationally defined as an active process for minimizing the impact of an impairment (resulting from injury, illness, or disease) on the individual's capacity to participate competitively in the work environment.

PMID: 11760522

Rating: 5b

Boswell MV, Shah RV, Everett CR, Sehgal N, Mckenzie-Brown AM, Abdi S, Bowman RC, Deer TR, Datta S, Colson JD, Spillane WF, Smith HS, Lucas LF, Burton AW, Chopra P, Staats PS, Wasserman RA, Manchikanti L. Interventional Techniques in The Management of Chronic Spinal Pain: Evidence-Based Practice Guidelines. Pain Physician. 2005;8:1-47

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[Note: Much of the evidence used in this practice guideline for pain physicians is based on studies published in Pain Physician, a journal not included in Medline's list of indexed journals evaluated for quality that offer the credibility of an independent peer-review process. These studies were not part of the evidence base for ODG Treatment or the ACOEM Guidelines.]
Results: The accuracy of facet joint nerve blocks was strong in the diagnosis of lumbar and cervical facet joint pain, whereas, it was moderate in the diagnosis of thoracic facet joint pain. The evidence was strong for lumbar discography, whereas, the evidence was limited for cervical and thoracic discography. The evidence was moderate for transforaminal epidural injections or selective nerve root blocks in the preoperative evaluation of patients with negative or inconclusive imaging studies. The evidence was moderate for sacroiliac joint injections in the diagnosis of sacroiliac joint pain. The evidence for therapeutic lumbar intraarticular facet injections of local anesthetics and steroids was moderate for short-term improvement and limited for long-term improvement, whereas, it was negative for cervical facet joint injections. The evidence for lumbar and cervical medial branch blocks was moderate. The evidence for medial branch neurotomy was moderate to strong for relief of chronic low back and neck pain. The evidence for caudal epidural steroid injections was strong for short-term relief and moderate for long-term relief in managing chronic low back and radicular pain, and limited in managing pain of postlumbar laminectomy syndrome. The evidence for interlaminar epidural steroid injections was strong for short-term relief and limited for long-term relief in managing lumbar radiculopathy, whereas, for cervical radiculopathy the evidence was moderate. The evidence for transforaminal epidural steroid injections was strong for short-term and moderate for long-term improvement in managing lumbar nerve

root pain, whereas, it was moderate for cervical nerve root pain and limited for lumbar post laminectomy syndrome and spinal stenosis. The evidence for percutaneous epidural adhesiolysis was strong. For spinal endoscopic adhesiolysis, the evidence was strong for short-term relief and moderate for longterm relief. For sacroiliac intraarticular injections, the evidence was moderate for short-term relief and limited for long-term relief. The evidence for radiofrequency neurotomy for sacroiliac joint pain was indeterminate. The evidence for intradiscal electrothermal therapy was strong for short-term relief and moderate for long-term relief in managing chronic discogenic low back pain, whereas, for nucleoplasty, the evidence was limited. The evidence for spinal cord stimulation in failed back surgery syndrome and complex regional pain syndrome was strong for shortterm relief and moderate for long-term relief. The evidence for implantable intrathecal infusion systems was moderate to strong. Conclusion: These guidelines included the evaluation of evidence for diagnostic and therapeutic procedures in managing chronic spinal pain and recommendations for managing spinal pain. These guidelines do not represent a "standard of care."

Rating: 6c

Boswell MV, Trescot AM, Datta S, Schultz DM, Hansen HC, Abdi S, Sehgal N, Shah RV, Singh V, Benyamin RM, Patel VB, Buenaventura RM, Colson JD, Cordner HJ, Epter RS, Jasper JF, Dunbar EE, Atluri SL, Bowman RC, Deer TR, Swicegood JR, Staats PS, Smith HS, Burton AW, Kloth DS, Giordano J, Manchikanti L. Interventional Techniques: Evidence-based Practice Guidelines in the Management of Chronic Spinal Pain. Pain Physician. 2007;10:7-111.

See also http://www.asipp.org/documents/guidelines2007.pdf

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Background: The evidence-based practice guidelines for the management of chronic spinal pain with interventional techniques were developed to provide recommendations to clinicians in the United States.
Objective: To develop evidence-based clinical practice guidelines for interventional techniques in the diagnosis and treatment of chronic spinal pain, utilizing all types of evidence and to apply an evidence-based approach, with broad representation by specialists from academic and clinical practices.
Design: Study design consisted of formulation of essentials of guidelines and a series of potential evidence linkages representing conclusions and statements about relationships between clinical interventions and outcomes.
Methods: The elements of the guideline preparation process included literature searches, literature synthesis, systematic review, consensus evaluation, open forum presentation, and blinded peer review. Methodologic quality evaluation criteria utilized included the Agency for Healthcare Research and Quality (AHRQ) criteria, Quality Assessment of Diagnostic Accuracy Studies (QUADAS) criteria, and Cochrane review criteria. The designation of levels of evidence was from Level I (conclusive), Level II (strong), Level III (moderate), Level IV (limited), to Level V (indeterminate).

Results: Among the diagnostic interventions, the accuracy of facet joint nerve blocks is strong in the diagnosis of lumbar and cervical facet joint pain, whereas, it is moderate in the diagnosis of thoracic facet joint pain. The evidence is strong for lumbar discography, whereas, the evidence is limited for cervical and thoracic discography. The evidence for transforaminal epidural injections or selective nerve root blocks in the preoperative evaluation of patients with negative or inconclusive imaging studies is moderate. The evidence for diagnostic sacroiliac joint injections is moderate. The evidence for therapeutic lumbar intraarticular facet injections is moderate for short-term and long-term improvement, whereas, it is limited for cervical facet joint injections. The evidence for lumbar and cervical medial branch blocks is moderate. The evidence for medial branch neurotomy is moderate. The evidence for caudal epidural steroid injections is strong for short-term relief and moderate for long-term relief in managing chronic low back and radicular pain, and limited in managing pain of postlumbar laminectomy syndrome. The evidence for interlaminar epidural steroid injections is strong for short-term relief and limited for long-term relief in managing lumbar radiculopathy, whereas, for cervical radiculopathy the evidence is moderate. The evidence for transforaminal epidural steroid injections is strong for short-term and moderate for long-term improvement in managing lumbar nerve root pain, whereas, it is moderate for cervical nerve root pain and limited in managing pain secondary to lumbar post laminectomy syndrome and spinal stenosis.
The evidence for percutaneous epidural adhesiolysis is strong. For spinal endoscopic adhesiolysis, the evidence is strong for short-term relief and moderate for long-term relief. For sacroiliac intraarticular injections, the evidence is moderate for short-term relief and limited for long-term relief. The evidence for radiofrequency neurotomy for sacroiliac joint pain is limited. The evidence for intradiscal electrothermal therapy is moderate in managing chronic discogenic low back pain, whereas for annuloplasty the evidence is limited. Among the various techniques utilized for percutaneous disc decompression, the evidence is moderate for short-term and limited for long-term relief for automated percutaneous lumbar discectomy, and percutaneous laser discectomy, whereas it is limited for nucleoplasty and for DeKompressor technology. For vertebral augmentation procedures, the evidence is moderate for both vertebroplasty and kyphoplasty. The evidence for spinal cord stimulation in failed back surgery syndrome and complex regional pain syndrome is strong for short-term relief and moderate for long-term relief. The evidence for implantable intrathecal infusion systems is strong for short-term relief and moderate for long-term relief.
Conclusion: These guidelines include the evaluation of evidence for diagnostic and therapeutic procedures in managing chronic spinal pain and recommendations for managing spinal pain. However, these guidelines do not constitute inflexible treatment recommendations. These guidelines also do not represent a "standard of care."

Rating: 6b

Braham R, Dawson B, Goodman C, The effect of glucosamine supplementation on people experiencing regular knee pain, Br J Sports Med. 2003 Feb;37(1):45-9; discussion 49

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OBJECTIVE: The purpose of this study was to examine the effects of oral glucosamine supplementation on the functional ability and degree of pain felt by individuals who had regular knee pain, most likely due to previous articular cartilage damage, and possibly osteoarthritis. METHODS: Subjects were randomly supplemented with either glucosamine (G) (n=24) or placebo (P) (lactose) (n=22) for 12 weeks at a dose of 2,000 mg per day. Over this period, four testing sessions were conducted, with changes in knee pain and function assessed by clinical and functional tests, (joint line palpation, a 3 metre "duck walk" and a repeated, walking stair climb), two questionnaires (the Knee Injury and Osteoarthritis Outcome Score (KOOS) and the Knee Pain Scale (KPS)) and participant subjective evaluations. RESULTS: The clinical and functional test scores improved with time (main effects: $p<0.05$, $p<0.01$) but there were no significant differences between the two groups. The questionnaire results also recorded a significant main effect for time ($p<0.05$), but the glucosamine group was found to have significantly better KOOS quality of life scores at week eight and 12 ($p<0.05$), and lower KPS scores ($p<0.05$) at week eight than the placebo group. On self report evaluations of changes across the 12 week supplementation period, 88% (n=21) of the glucosamine group reported some degree of improvement in their knee pain versus only 17% (n=3) in the placebo group. CONCLUSIONS: These results suggest that glucosamine supplementation can provide some degree of pain relief and improved function in persons who experience regular knee pain, which may be caused by prior cartilage injury and/or osteoarthritis. The trends in the results also suggest that, at a dosage of 2,000 mg per day, the majority of improvements are present after eight weeks.

PMID: 12547742

Rating: 2b

Bramness JG, Skurtveit S, Mørland J, Engeland A. The risk of traffic accidents after prescriptions of carisoprodol. Accid Anal Prev. 2007;39:1050-5.

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Having a prescription for carisoprodol dispensed increased the standardized incidence ratio for being involved in an accident with person injury to 3.7 (95% CI 2.9-4.8) the first week after the date of dispensing. This was similar to diazepam (2.8; 2.2-3.6).

PMID: 17854578

Rating: 3a

Bramness JG, Skurtveit S, Mørland J. Impairment due to intake of carisoprodol. Drug Alcohol Depend. 2004;74:311-8.

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BACKGROUND: It is unclear whether therapeutic intake of carisoprodol leads to impairment, and the effect of supratherapeutic doses has not been investigated. Possible impairment could further be a product of the parent drug and/or the metabolite meprobamate. The present study aimed to investigate if carisoprodol had an impairing effect by it self. CONCLUSION: Carisoprodol probably has an impairing effect by itself, at least at blood concentration levels above which can be seen after therapeutic intake of the drug.

PMID: 15194209

Rating: 4b

Breit R, Van der Wall H. Transcutaneous electrical nerve stimulation for postoperative pain relief after total knee arthroplasty. J Arthroplasty. 2004 Jan;19(1):45-8.

Department of Orthopedic Surgery, Concord Hospital, Sydney, Australia.

Transcutaneous electrical nerve stimulation (TENS) has been used to treat chronic pain syndromes and has been reported to be of some utility in the treatment of postsurgical pain. A randomized, blinded, placebo-controlled trial was designed to evaluate the utility of TENS after total knee arthroplasty. Patients were randomly enrolled into patient-controlled anesthesia (PCA) alone, PCA plus TENS, or PCA plus sham TENS. The cumulative dose of morphine by PCA for each group was used as the end-point of the study. There was no significant reduction in the requirement for patient-controlled analgesia with or without TENS. We conclude that there is no utility for TENS in the postoperative management of pain after knee arthroplasty.

PMID: 14716650

Rating 2c

Brekke M; Hjortdahl P; Kvien TK. Severity of musculoskeletal pain: relations to socioeconomic inequality. Social Science and Medicine. 01-Jan-2002; 54(2): 221-8.
Abstract:
The main aim of the study was to investigate possible associations between severity of non-inflammatory musculoskeletal pain and residential areas of contrasting socioeconomic status. A 4-page questionnaire inquiring about musculoskeletal pain, and also physical disability, mental health, life

satisfaction and use of health services was sent to 10,000 randomly selected adults in Oslo, Norway. For the purpose of this study, we analysed data from respondents living in two socioeconomically contrasting areas of the city. Measures of pain (intensity, duration, localisation), physical disability (MHAQ), mental distress (SCL-5, sleep disturbances), life satisfaction and use of health services (general practitioner, rheumatologist, medication, involvement in and satisfaction with own care) were compared between respondents living in the two areas (n = 870 and n = 892 respondents, respectively) of whom 493 in each area reported non-inflammatory musculoskeletal pain. Multiple regression analyses adjusting for age revealed that living in the less affluent area was associated with strong and widespread pain, with high levels of physical disability and mental distress and with low life satisfaction. Living in the less affluent area was also associated with frequent use of analgesics and with low level of involvement in own health care, after adjustment for age, pain intensity and levels of physical disability and mental distress. Non-inflammatory musculoskeletal pain seems to be a more serious condition in a population living in a less affluent residential area compared with a more affluent one, even in an egalitarian society like Norway. Increased disease severity may thus amplify the impact of greater chronic morbidity in the disadvantaged part of the population. This should have implications for health care provision if the goal is treatment according to needs.
Major Subjects:

- Health Services / * utilization
- Musculoskeletal Diseases / complications / * epidemiology
- Pain / * epidemiology / etiology
- Severity of Illness Index
- Socioeconomic Factors

Publication Type: Case Control Study, 10,000 cases

Brinkhaus B, Witt CM, Jena S, Linde K, Streng A, Wagenpfeil S, Irnich D, Walther HU, Melchart D, Willich SN. Acupuncture in patients with chronic low back pain: a randomized controlled trial. Arch Intern Med. 2006 Feb 27;166(4):450-7.

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BACKGROUND: Acupuncture is widely used by patients with low back pain, although its effectiveness is unclear. We investigated the efficacy of acupuncture compared with minimal acupuncture and with no acupuncture in patients with chronic low back pain. METHODS: Patients were randomized to treatment with acupuncture, minimal acupuncture (superficial needling at nonacupuncture points), or a waiting list control. Acupuncture and minimal acupuncture were administered by specialized acupuncture physicians in 30 outpatient centers, and consisted of 12 sessions per patient over 8 weeks. Patients completed standardized questionnaires at baseline and at 8, 26, and 52 weeks after randomization. The primary outcome variable was the change in low back pain intensity from baseline to the end of week 8, as determined on a visual analog scale (range, 0-100 mm). RESULTS: A total of 298 patients (67.8% female; mean +/- SD age, 59 +/- 9 years) were included. Between baseline and week 8, pain intensity

decreased by a mean +/- SD of 28.7 +/- 30.3 mm in the acupuncture group, 23.6 +/- 31.0 mm in the minimal acupuncture group, and 6.9 +/- 22.0 mm in the waiting list group. The difference for the acupuncture vs minimal acupuncture group was 5.1 mm (95% confidence interval, -3.7 to 13.9 mm; P = .26), and the difference for the acupuncture vs waiting list group was 21.7 mm (95% confidence interval, 13.9-30.0 mm; P<.001). Also, at 26 (P=.96) and 52 (P=.61) weeks, pain did not differ significantly between the acupuncture and the minimal acupuncture groups. CONCLUSION: Acupuncture was more effective in improving pain than no acupuncture treatment in patients with chronic low back pain, whereas there were no significant differences between acupuncture and minimal acupuncture.

Publication Types:
Randomized Controlled Trial

PMID: 16505266

Rating: 2a

Brosseau L, Welch V, Wells G, DeBie R, Gam A, Harman K, Morin M, Shea B, Tugwell P, Low level laser therapy (Classes I, II and III) for treating osteoarthritis, Cochrane Database Syst Rev. 2004;(3):CD002046

School of Rehabilitation Sciences, University of Ottawa, 451 Smyth Road, Ottawa, Ontario, CANADA, K1H 8M5.

BACKGROUND: Osteoarthritis (OA) affects a large proportion of the population. Low Level Laser Therapy (LLLT) is a light source that generates extremely pure light, of a single wavelength. The effect is not thermal, but rather related to photochemical reactions in the cells. LLLT was introduced as an alternative non-invasive treatment for OA about 20 years ago, but its effectiveness is still controversial. OBJECTIVES: To assess the effectiveness of LLLT in the treatment of OA. SEARCH STRATEGY: We searched MEDLINE, EMBASE, the Cochrane Musculoskeletal registry, the registry of the Rehabilitation and Related Therapies field and the Cochrane Controlled Trials Register up to January 30, 2004. SELECTION CRITERIA: Following an a priori protocol, only controlled clinical trials of LLLT for the treatment of patients with a clinical diagnosis of OA were eligible. Abstracts were excluded unless further data could be obtained from the authors. DATA COLLECTION AND ANALYSIS: Two reviewers independently selected trials and abstracted data using predetermined forms. Heterogeneity was tested with Cochran's Q test. A fixed effects model was used throughout for continuous variables, except where heterogeneity existed, in which case, a random effects model was used. Results were analyzed as weighted mean differences (WMD) with 95% confidence intervals (CI), where the difference between the treated and control groups was weighted by the inverse of the variance. Standardized mean differences (SMD) were calculated by dividing the difference between treated and control by the baseline variance. SMD were used when different scales were used to measure the same concept (e.g. pain). Dichotomous outcomes were analyzed with odds ratios. MAIN RESULTS:

Seven trials were included, with 184 patients randomized to laser, 161 patients to placebo laser. Treatment duration ranged from 4 to 12 weeks. Pain was assessed by four trials. The pooled estimate (random effects) of three trials showed no effect on pain measured using a scale (SMD: -0.2, 95% CI: -1.0, +0.6), but there was statistically significant heterogeneity (p>0,05). Three of the trials showed no effect and two demonstrated very beneficial effects with laser. In another trial, with no scale-based pain outcome, significantly more patients reported pain relief (yes/no) with laser with an odds ratio of 0.05, (95% CI: 0.0 to 1.56). Only one study found significant results for increased knee range of motion (WMD: -10.62 degrees, 95% CI: -14.07,-7.17). Other outcomes of joint tenderness and strength were not significant. Lower dosage of LLLT was found as effective than higher dosage for reducing pain and improving knee range of motion. REVIEWERS' CONCLUSIONS: For OA, the results are conflicting in different studies and may depend on the method of application and other features of the LLLT application. Clinicians and researchers should consistently report the characteristics of the LLLT device and the application techniques used. New trials on LLLT should make use of standardized, validated outcomes. Despite some positive findings, this meta-analysis lacked data on how LLLT effectiveness is affected by four important factors: wavelength, treatment duration of LLLT, dosage and site of application over nerves instead of joints. There is clearly a need to investigate the effects of these factors on LLLT effectiveness for OA in randomized controlled clinical trials.

PMID: 15266461

Rating: 1b

Brown RL, Rounds LA. Conjoint screening questionnaires for alcohol and other drug abuse: criterion validity in a primary care practice. Wis Med J. 1995;94(3):135-40.

Department of Family Medicine, University of Wisconsin Medical School, Madison 53715, USA.

The US Preventive Services Task Force recommended that physicians use the CAGE questions to screen patients for alcohol abuse. A similarly brief screening instrument for abuse of other drugs is needed. Two conjoint screening questionnaires for alcohol and other drug abuse were adapted from the CAGE questions and the Short Michigan Alcoholism Screening Test (SMAST). For 124 patients of an academic, community family practice, the conjoint questionnaires and their forerunners were compared with DSM-III-R diagnoses of substance use disorders as measured by the Diagnostic Interview Schedule-Revised (DIS-R). The SMAST and its conjoint analog exhibited low sensitivity. The CAGE Adapted to Include Drugs (CAGE-AID) was more sensitive but less specific for substance abuse than the CAGE, especially when a reduced criterion score was employed. The CAGE-AID was more sensitive than the CAGE for subjects of varying sex, income, and level of education, as well as most patterns of substance use disorders. The diminished specificity of the CAGE-AID may have been, at least in part, artifactual. The CAGE-AID holds promise for identifying primary care patients with alcohol and drug disorders.

PMID: 7778330

Rating: 4a

Browning R, Jackson JL, O'Malley PG, Cyclobenzaprine and back pain: a meta-analysis, Arch Intern Med. 2001 Jul 9;161(13):1613-20.

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BACKGROUND: Back pain is a common problem for which cyclobenzaprine hydrochloride is frequently prescribed. OBJECTIVE: To perform a systematic review of cyclobenzaprine's effectiveness in the treatment of back pain. METHODS: We searched MEDLINE, PsycLIT, CINAHL, EMBASE, AIDSLINE, HEALTHSTAR, CANCERLIT, the Cochrane Library, Micromedex, Federal Research in Progress, and the references of reviewed articles, and contacted Merck, Sharpe and Dohme for English-language, randomized, placebo-controlled trials of cyclobenzaprine in adults with back pain. Outcomes included global improvement and 5 specific domains of back pain (local pain, muscle spasm, range of motion, tenderness to palpation, and activities of daily living). Study quality was assessed using the methods of Jadad. Summary outcomes were obtained using a random-effects model. RESULTS: Patients treated with cyclobenzaprine were nearly 5 times (odds ratio, 4.7; 95% confidence interval, 2.7-8.1) as likely to report symptom improvement by day 14 as were those treated with placebo. Slightly fewer than 3 individuals (2.7; 95% confidence interval, 2.0-4.2) needed treatment for 1 to improve. The magnitude of this improvement was modest, with an effect size of 0.38 to 0.58 in all 5 outcomes (local pain, muscle spasm, tenderness to palpation, range of motion, and activities of daily living). Treatment efficacy for these 5 outcomes was greatest early, in the first few days of treatment, declining after the first week. Patients receiving cyclobenzaprine also experienced more adverse effects, the most common being drowsiness. CONCLUSIONS: Cyclobenzaprine is more effective than placebo in the management of back pain; the effect is modest and comes at the price of greater adverse effects. The effect is greatest in the first 4 days of treatment, suggesting that shorter courses may be better. Studies comparing the relative value of acetaminophen, nonsteroidal anti-inflammatory drugs, and cyclobenzaprine individually and in combination in the treatment of back pain are needed.

PMID: 11434793

Rating: 1a

Bruce B, Fries J, Lubeck D. Aerobic exercise and its impact on musculoskeletal pain in older adults: a 14 year prospective, longitudinal study. Arthritis Res Ther 2005 Sept 19; R1263-R1270

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Abstract
We studied the long term impact of running and other aerobic exercise on musculoskeletal pain in a cohort of healthy aging male and female seniors who had been followed for 14 years. We conducted a prospective, longitudinal study in 866 Runners' Association members (n = 492) and community controls (n = 374). Subjects were also categorized as Ever-Runners (n = 565) and Never-Runners (n = 301) to include runners who had stopped running. Pain was the primary outcome measure and was assessed in annual surveys on a double-anchored visual analogue scale (0 to 100; 0 = no pain). Baseline differences between Runners' Association members and community controls and between Ever-Runners versus Never-Runners were compared using chi-square and t-tests. Statistical adjustments for age, body mass index (BMI), gender, health behaviors, history of arthritis and comorbid conditions were performed using generalized estimating equations. Runner's Association members were younger (62 versus 65 years, $p < 0.05$), had a lower BMI (22.9 versus 24.2, $p < 0.05$), and less arthritis (35% versus 41%, $p > 0.05$) than community controls. Runners' Association members averaged far more exercise minutes per week (314 versus 123, $p < 0.05$) and miles run per week (26 versus 2, $p < 0.05$) and tended to report more fractures (53% versus 47%, $p > 0.05$) than controls. Ever-Runners were younger (62 versus 66 years, $p < 0.05$), had lower BMI (23.0 versus 24.3, $p < 0.05$), and less arthritis (35% versus 43%, $p < 0.05$) than Never-Runners. Ever-Runners averaged more exercise minutes per week (291 versus 120, $p < 0.05$) and miles run per week (23 versus 1, $p < 0.05$) and reported a few more fractures (52% versus 48%, $p > 0.05$) than Never-Runners. Exercise was associated with significantly lower pain scores over time in the Runners' Association group after adjusting for gender, baseline BMI, and study attrition ($p < 0.01$). Similar differences were observed for Ever-Runners versus Never-Runners. Consistent exercise patterns over the long term in physically active seniors are associated with about 25% less musculoskeletal pain than reported by more sedentary controls, either by calendar year or by cumulative area-under-the-curve pain over average ages of 62 to 76 years.

Introduction
The prevalence of older adults in the United States is growing at a substantial rate. By 2030, nearly one-fifth of Americans will be in their sixties or older, which will have a considerable impact on public health. Numerous epidemiological and clinical studies have established that older adults who participate in regular physical activity are healthier and have a better quality of life than those who are inactive. Regular exercise has also been shown to reduce pain in patients with knee osteoarthritis and to help prevent mechanical low back pain. In contrast, inactivity has been associated with greater pain with injury and has been associated with lower bone density and muscle tone . On the other hand, some aerobic activities, such as running, have been found to result in increased risk for stress or other fractures. Recurring trauma to soft tissue resulting from excessive physical activity conceivably could increase pain and disability. Few studies have addressed the relationship between aerobic exercise and the perception of pain with advancing age. To study the effect of exercise on disability and pain, our group had investigated the relationship of running and its impact on musculoskeletal pain and disability in cohorts of Runners' Association members and community controls and Ever-Runners and Never-Runners who were followed prospectively for six years. In that study, no increase in joint pain or stiffness with age was observed in subjects who exercised often and intensely compared with their more

sedentary counterparts. Pain was reduced, however, at all time points by about 25% in the exercising group. In fact, there was a slight decrease in pain for women who exercised over time. In this investigation, we have extended that research in those cohorts. We have evaluated the association of vigorous physical activity with pain with advancing age after 14 years of follow-up. We hypothesized that those who regularly participated in running or other aerobic activity would report less musculoskeletal pain rather than more over the long term than did their inactive counterparts.

Rating: 3a

Bruehl S, Harden RN, Galer BS, Saltz S, Bertram M, Backonja M, Gayles R, Rudin N, Bhugra MK, Stanton-Hicks M. External validation of IASP diagnostic criteria for Complex Regional Pain Syndrome and proposed research diagnostic criteria. International Association for the Study of Pain. Pain. 1999 May;81(1-2):147-54.

Center for Pain Studies, Rehabilitation Institute of Chicago, IL 60611, USA.

Recent work in our research consortium has raised internal validity concerns regarding the current IASP criteria for Complex Regional Pain Syndrome (CRPS), suggesting problems with inadequate sensitivity and specificity. The current study explored the external validity of these IASP criteria for CRPS. A standardized evaluation of signs and symptoms of CRPS was conducted by study physicians in 117 patients meeting IASP criteria for CRPS, and 43 patients experiencing neuropathic pain with established non-CRPS etiology (e.g. diabetic neuropathy, post-herpetic neuralgia). Multiple discriminant function analyses were used to test the ability of the IASP diagnostic criteria and decision rules, as well as proposed research modifications of these criteria, to discriminate between CRPS patients and those experiencing non-CRPS neuropathic pain. Current IASP criteria and decision rules (e.g. signs or symptoms of edema, or color changes or sweating changes satisfy criterion 3) discriminated significantly between groups ($P < 0.001$). However, although sensitivity was quite high (0.98), specificity was poor (0.36), and a positive diagnosis of CRPS was likely to be correct in as few as 40% of cases. Empirically-based research modifications to the criteria, which are more comprehensive and require presence of signs and symptoms, were also tested. These modified criteria were also able to discriminate significantly, between the CRPS and non-CRPS groups ($P < 0.001$). A decision rule, requiring at least two sign categories and four symptom categories to be positive optimized diagnostic efficiency, with a diagnosis of CRPS likely to be accurate in up to 84% of cases, and a diagnosis of non-CRPS neuropathic pain likely to be accurate in up to 88% of cases. These results indicate that the current IASP criteria for CRPS have inadequate specificity and are likely to lead to overdiagnosis. Proposed modifications to these criteria substantially improve their external validity and merit further evaluation.

Publication Types:
Guideline
Practice Guideline

PMID: 10353502

Rating: 4b

Bruns D. Colorado Division of Workers' Compensation, Comprehensive Psychological Testing: Psychological Tests Commonly Used in the Assessment of Chronic Pain Patients. 2001

This comprehensive review shows test name; test characteristics; strengths and weaknesses; plus length, scoring options & test taking time. The following 26 tests are described and evaluated:

1) BHI™ 2 (Battery for Health Improvement – 2nd edition)
2) MBHI™ (Millon Behavioral Health Inventory) [Has been superceded by the MBMD. The updated version of the test, the MBMD, should be administered instead.]
3) MBMD™ (Millon Behavioral Medical Diagnostic)
4) PAB (Pain Assessment Battery)
5) MCMI-111™ (Millon Clinical Multiaxial Inventory, 3rd edition)
6) MMPI-2™ (Minnesota Inventory- 2nd edition ™)
7) PAI™ (Personality Assessment Inventory)
8) BBHI™ 2 (Brief Battery for Health Improvement – 2nd edition)
9) MPI (Multidimensional Pain Inventory)
10) P-3™ (Pain Patient Profile)
11) Pain Presentation Inventory
12) PRIME-MD (Primary Care Evaluation for Mental Disorders)
13) PHQ (Patient Health Questionnaire)
14) SF 36 ™
15) (SIP) Sickness Impact Profile
16) BSI® (Brief Symptom Inventory)
17) BSI® 18 (Brief Symptom Inventory-18)
18) SCL-90-R® (Symptom Checklist –90 Revised)
19) BDI ®–II (Beck Depression Inventory-2nd edition)
20) CES-D (Center for Epidemiological Studies Depression Scale)
21) PDS™ (Post Traumatic Stress Diagnostic Scale)
22) Zung Depression Inventory
23) MPQ (McGill Pain Questionnaire)
24) MPQ-SF (McGill Pain Questionnaire – Short Form)
25) Oswestry Disability Questionnaire
26) Visual Analogue Pain Scale (VAS)

All tests were judged to have acceptable evidence of validity and reliability except as noted. Tests published by major publishers are generally better standardized, and have manuals describing their psychometric characteristics and use. Published tests are also generally more difficult to fake, as access to test materials is restricted to qualified professionals. Third party review (by journal peer review or Buros Institute) supports the credibility of the test. Test norms provide a benchmark to which an individual's score can be compared. Tests with patient norms detect patients who are having unusual psychological reactions, but may overlook psychological conditions common to patients. Community norms are often more sensitive to detecting psychological conditions common to patients, but are also more prone to false positives. Double normed tests (with both patient and community norms) combine the advantages of both methods. Preference should be given to psychological tests designed and normed for the population you need to assess. Psychological tests designed for medical patients often assess syndromes unique to medical patients, and seek to avoid common pitfalls in the psychological assessment of medical patients. Psychological tests designed for psychiatric patients are generally more difficult to interpret when administered to medical patients, as they tend to assume that all physical symptoms present are psychogenic in nature (i.e. numbness and tingling may be assumed to be a sign of somatization). This increases the risk of false positive psychological findings. Tests sometimes undergo revision and features may change. When a test is updated, the use of the newer version of the test is strongly encouraged. Document developed by Daniel Bruns, PsyD and accepted after review and revisions by the Chronic Pain Task Force, June 2001. Dr. Bruns is the coauthor of the BHI 2 and BBHI 2 tests.

Rating: 7a

Burch F, Fishman R, Messina N, Corser B, Radulescu F, Sarbu A, Craciun-Nicodin MM, Chiriac R, Beaulieu A, Rodrigues J, Beignot-Devalmont P, Duplan A, Robertson S, Fortier L, Bouchard S. A comparison of the analgesic efficacy of Tramadol Contramid OAD versus placebo in patients with pain due to osteoarthritis. J Pain Symptom Manage. 2007;34:328-38.

Radiant Research, San Antonio, Texas, USA.

One thousand twenty-eight (1,028) patients with pain due to osteoarthritis (OA) of the knee were enrolled in this multicenter, randomized, double-blind, parallel study designed to assess the analgesic efficacy and safety of Tramadol Contramid OAD compared to placebo. An open-label phase was followed by a double-blind phase, in which a total of 646 patients were randomized to double-blind treatment with placebo or Tramadol Contramid OAD. Patients were titrated to their optimal dose (200mg or 300 mg), which was maintained for 12 weeks. An absolute mean reduction of 3.0+/-2.1 on a Pain Intensity Numerical Rating Scale (PI-NRS) was noted in the Tramadol Contramid OAD treatment group. The difference between active and placebo groups regarding this absolute mean reduction was statistically significant (P<0.001) throughout the study. The responder analysis demonstrated that a significantly greater percentage of patients in the active treatment arm achieved a reduction of >or=1 and >or=2 points on the PI-NRS score by the end of the study (P=0.035). A significantly greater

percentage of respondents in the Tramadol Contramid OAD group indicated improvement on both the Patient and Physician Global Impressions of Change (P=0.0002). Both the 200mg and 300 mg doses contributed to the overall superiority of Tramadol Contramid OAD. The most frequent adverse events were consistent with the known side effects of tramadol and were generally mild to moderate in intensity. These results confirm that Tramadol Contramid OAD given once daily is an efficacious and safe treatment for pain due to OA.

PMID: 17583466

Rating: 2c

Burton AW, Interventional Therapies. In: Complex Regional Pain Syndrome: Treatment Guidelines. Ed. Harden N. Reflex Sympathetic Dystrophy Syndrome Association. 2006. Retrieved July 2008. Available at: http://www.rsds.org/3/clinical_guidelines/index.html.

No abstract available. A discussion of the role of interventional therapy for CRPS.

Rating: 5a

Buchner M, Zahlten-Hinguranage A, Schiltenwolf M, Neubauer E. Therapy outcome after multidisciplinary treatment for chronic neck and chronic low back pain: a prospective clinical study in 365 patients. Scand J Rheumatol. 2006 Sep-Oct;35(5):363-7.

Department of Orthopaedic Surgery, University of Heidelberg, Germany. Matthias.Buchner@ok.uni-heidelberg.de

OBJECTIVES: This prospective longitudinal clinical study analyses the therapy outcome of 365 patients with either chronic neck (n = 134) or low back (n = 231) pain treated with a multidisciplinary biopsychosocial therapy approach. METHODS: Patients with chronic neck pain (NP) or low back pain (LBP) for 3 months or longer, corresponding sick leave for longer than 6 weeks, and clearly defined inclusion and exclusion criteria underwent a 3-week standardized inpatient multidisciplinary biopsychosocial therapy. Baseline sociodemographic, occupational, functional, and psychological data at entry into the study (T0) were comparable in both groups. At the 6-month follow-up (T1), five different therapy outcomes were analysed in both groups: back-to-work status, generic health status (the 36-item Short Form Health Survey, SF-36), pain intensity (visual analogue scale), functional capacity (Hannover back capacity score), and satisfaction with the therapy. RESULTS: Both treatment groups improved significantly in all outcome criteria between T0 and T1. In the total group, the back-to-work rate was 67.4%. At the final follow-up there were no significant differences between the group with chronic NP and the group with chronic LBP in the outcome criteria back-to-work status, improvement of health status and functional capacity, satisfaction with therapy, and reduction of pain. CONCLUSION: Evaluation of the main results of this study suggests that patients with chronic NP also derive significant

benefit from a multidisciplinary treatment strategy, demonstrated in the literature so far mainly for patients with chronic LBP.

PMID: 17062436

Rating: 3a

Buchner M, Neubauer E, Zahlten-Hinguranage A, Schiltenwolf M. The influence of the grade of chronicity on the outcome of multidisciplinary therapy for chronic low back pain. Spine. 2007 Dec 15;32(26):3060-6.

Department of Orthopaedic Surgery, University of Heidelberg, Heidelberg, Germany. Matthias.Buchner@t-online.de

STUDY DESIGN: Prospective longitudinal clinical study. OBJECTIVE: The objective of the study was to analyze the outcome of different stages of chronicity in patients with chronic low back pain treated with a multidisciplinary therapy. SUMMARY OF BACKGROUND DATA: Results of studies comparing different grades of chronicity in therapy for chronic low back pain have not been published so far. METHODS: A total of 387 patients with chronic low back pain for 3 months or longer and a corresponding sick leave for longer than 6 weeks underwent a 3-week standardized multidisciplinary therapy. At baseline (T0), patients were assigned into 3 groups of chronicity grades according to the classification of von Korff et al (Group A, Grades I and II; Group B, Grade III; Group C, Grade IV) and were prospectively followed. At the 6-month follow-up (T1), 5 different therapy outcomes were analyzed and compared in the 3 groups: back-to-work status, generic health status (SF-36), pain intensity (visual analogue scale), functional capacity (Hannover back capacity score), and satisfaction with the therapy. RESULTS: At T0, patients in Group C had a higher pain level, a longer history of pain, and more general and more psychosomatic comorbidities than patients with lower levels of chronicity. All 3 treatment groups improved significantly in all outcome criteria between T0 and T1. In the total group, the back-to-work rate was 67.4%. At the final follow-up, there were significantly better results in terms of functional capacity and pain level in patients with lower grades of chronicity but mostly due also to worse initial baseline values. Back-to-work rate, satisfaction with therapy, and the Mental Component Summary of the SF-36 did not show a significant difference at T1 between the groups analyzed. CONCLUSION: According to the results of this study, patients with chronic low back pain also derive significant benefit from a multidisciplinary treatment strategy in higher stages of chronicity. Therefore, therapy should not be limited to the patients in lower stages of chronicity.

PMID: 18091502

Rating: 3a

December 27, 2007 — Multidisciplinary treatment strategies are effective for patients with chronic low back pain (CLBP) in all stages of chronicity and should not only be given to those with lower grades of CLBP, according to the results of a prospective longitudinal clinical study reported in the December 15 issue of Spine. "The treatment of choice for patients with CLBP seems to be a multidisciplinary therapy incorporating multiple treatment components, such as intensive physical exercises and biopsychosocial and behavioral interventions," write Matthias Buchner, MD, PhD, from the University of Heidelberg in Germany, and colleagues. "This prospective clinical study with a 6 months' duration is, to the authors' knowledge, the first to evaluate separately the prognostic value of the chronicity stage in the therapy outcome of patients with CLBP treated with a multidisciplinary biopsychosocial therapy approach."

Burleson AM. American Academy of Pain Medicine 24th Annual Meeting (Orlando, FL): Abstract 105. February 15, 2008.

Amy M. Burleson, PsyD, from the Cleveland Clinic Foundation, Ohio

Physical conditioning in chronic pain patients can have immediate and long-term benefits, according to a new study presented at the American Academy of Pain Medicine 24th Annual Meeting. A frequent comorbid condition of chronic pain is profound physical deconditioning, which results from inactivity. "People with chronic pain don't want to exercise — the main reason is that they are in so much pain," the study's lead investigator, Amy M. Burleson, PsyD, from the Cleveland Clinic Foundation, in Ohio, told Medscape Neurology & Neurosurgery here. "We were hoping this [study] would show people how important exercise is."
Effects of Brief Exercise: Objective assessment of physical conditioning in patients with chronic pain has been impeded by several factors that this study attempted to overcome, the authors write. "Of primary importance is verifying the efficacy of a physical reconditioning program." Decreases in pain, depression, and anxiety following treatment in a pain rehabilitation program have been well documented, they add, but to date, no study has determined the immediate effects of brief exercise on these factors. The review aimed to determine the effect of a 3-week aerobic training program on physical conditioning and to assess the acute effects of a brief, 10-minute exercise protocol on pain, mood, and perceived exertion. The final sample of 28 patients — lowered from 54 due to factors such as lack of motivation to exercise and fear of exercise — had an immediate perception change about exercise upon starting the program. Measures of heart rate, mood, pain, and perceived exertion were obtained. On average, patients received 5 hours of conditioning per week, in addition to routine daily activities. Results demonstrated significant short- and long-term benefits of exercise. Patients showed a statistically significant reduction in exercise-induced cardiac acceleration from admission to 3 weeks. The brief exercise protocol also produced significant immediate antidepressant and anxiolytic effects. The research suggests that relatively modest exercise leads to improved mood and physical capacity, which has further implications for mortality risk. The review also suggests that brief exercise is a safe, cost-free, nonpharmacologic strategy for immediately reducing depression and anxiety. "I think a lot of people think you can treat chronic pain with 1 specialty," Burleson said. "I think what this study shows

is that the interdisciplinary team is so important. We feel like the entire team makes a difference in the chronic pain of the patient."

Rating: 10b

Buscemi N, Vandermeer B, Friesen C et al. Manifestations and Management of Chronic Insomnia in Adults. Summary,Evidence Report/Technology Assessment No. 125. (Prepared by the University of Alberta Evidence-based Practice Center, under Contract No. C400000021.) AHRQ Publication No.05-E021-1. Rockville, MD: Agency for Healthcare Research and Quality. June 2005.

Rating 1 a

Buscemi N, Vandermeer B, Friesen C, Bialy L, Tubman M, Ospina M, Klassen TP, Witmans M. The efficacy and safety of drug treatments for chronic insomnia in adults: a meta-analysis of RCTs. J Gen Intern Med. 2007;22:1335-50.

University of Alberta/Capital Health Evidence-Based Practice Centre, Department of Pediatrics, University of Alberta, Alberta, Canada.

BACKGROUND: Hypnotics have a role in the management of acute insomnia; however, the efficacy and safety of pharmacological interventions in the management of chronic insomnia is unclear. OBJECTIVE: The objective of this paper is to conduct a systematic review of the efficacy and safety of drug treatments for chronic insomnia in adults. DATA SOURCES: Twenty-one electronic databases were searched, up to July 2006. STUDY SELECTION: Randomized double-blind, placebo-controlled trials were eligible. Quality was assessed using the Jadad scale. Data were pooled using the random effects model. DATA SYNTHESIS: One hundred and five studies were included in the review. Sleep onset latency, as measured by polysomnography, was significantly decreased for benzodiazepines (BDZ), (weighted mean difference: -10.0 minutes; 95% CI: -16.6, -3.4), non-benzodiazepines (non-BDZ) (-12.8 minutes; 95% CI: -16.9, -8.8) and antidepressants (ADP) (-7.0 minutes; 95% CI: -10.7, -3.3). Sleep onset latency assessed by sleep diaries was also improved (BDZ: -19.6 minutes; 95% CI: -23.9, -15.3; non-BDZ: -17.0 minutes; 95% CI: -20.0, -14.0; ADP: -12.2 minutes; 95% CI: -22.3, -2.2). Indirect comparisons between drug categories suggest BDZ and non-BDZ have a similar effect. All drug groups had a statistically significant higher risk of harm compared to placebo (BDZ: risk difference [RD]: 0.15; non-BDZ RD: 0.07; and ADP RD: 0.09), although the most commonly reported adverse events were minor. Indirect comparisons suggest that non-BDZ are safer than BDZ. CONCLUSIONS: Benzodiazepines and non-benzodiazepines are effective treatments in the management of chronic insomnia, although they pose a risk of harm. There is also some evidence that antidepressants are effective and that they pose a risk of harm.

Rating: 1a

Bush C, Ditto B, Feuerstein M. A controlled evaluation of paraspinal EMG biofeedback in the treatment of chronic low back pain. Health Psychol. 1985;4(4):307-21.

Sixty-six chronic low back pain sufferers were randomly divided into three groups. Following individual assessments consisting of psychological questionnaires, pain monitoring, and measurement of paraspinal electromyogram (EMG), one group received paraspinal EMG biofeedback and another a placebo treatment. The third group received no intervention. Two further assessments were carried out on all groups immediately after treatment and at a 3-month follow-up. All groups showed significant reduction in pain, anxiety, depression, and paraspinal EMG following treatment and at follow-up, but there were no differences between groups. A regression analysis failed to identify subjects' characteristics that predicted positive outcome in the biofeedback group. However, high scores on the Evaluative scale of the McGill Pain Questionnaire and high hypnotizability were significant predictors of positive outcome for the placebo group. It is concluded that paraspinal EMG biofeedback is not a specific treatment for chronic low back pain in a nonhospitalized population.

PMID: 2932330

Rating: 2b

Buvanendran A, Kroin JS. Useful adjuvants for postoperative pain management. Best Pract Res Clin Anaesthesiol. 2007 Mar;21(1):31-49.

Department of Anesthesiology, 1653 W Congress Parkway, # 739, Rush University Medical Center, Chicago, IL 60612, USA. asokumar@aol.com

Adjuvants are compounds which by themselves have undesirable side-effects or low potency but in combination with opioids allow a reduction of narcotic dosing for postoperative pain control. Adjuvants are needed for postoperative pain management due to side-effects of opioid analgesics, which hinder recovery, especially in the increasingly utilized ambulatory surgical procedures. NMDA antagonists have psychomimetic side-effects at high doses, but at moderate doses do not cause stereotypic behavior but allow reduction in opioid dose to obtain better pain control. Alpha-2 adrenergic agonists cause sedation, hypotension and bradycardia at moderate doses, but at low doses can be opioid sparing especially in spinal administration. Gabapentin-like compounds have low potency against acute pain, but in combination with opioids allow a reduction in opioid dose with improved analgesia. Corticosteroids may have only a limited role as adjuvants while acetylcholine esterase inhibitors may have too many side-effects. Newer adjuvants will be needed to reduce opioid dose and concomitant side-effects, even more as same day surgeries become more routine.

PMID: 17489218

Rating: 5b

California Technology Assessment Forum. Interferential stimulation for the treatment of musculoskeletal pain. 2005.

Interferential stimulation: Does Not Meet CTAF Criteria
This topic was reviewed by the California Technology Assessment Forum on October 19, 2005. It was recommended that interferential stimulation for the treatment of musculoskeletal pain does not meet CTAF Technology Assessment Criteria 2 through 5 for safety, effectiveness, and improvement in health outcomes

Note: Click on link above to go to a description of each individual study.

Hou CR, Tsai LC, Cheng KF, Chung KC, Hong CZ. Immediate effects of various physical therapeutic modalities on cervical myofascial pain and trigger-point sensitivity. Arch Phys Med Rehabil. Oct 2002;83(10):1406-1414.
Hurley DA, McDonough SM, Dempster M, Moore AP, Baxter GD. A randomized clinical trial of manipulative therapy and interferential therapy for acute low back pain. Spine. Oct 15 2004;29(20):2207-2216.
Hurley DA, Minder PM, McDonough SM, Walsh DM, Moore AP, Baxter DG. Interferential therapy electrode placement technique in acute low back pain: a preliminary investigation. Arch Phys Med Rehabil. Apr 2001;82(4):485-493.
Jarit GJ, Mohr KJ, Waller R, Glousman RE. The effects of home interferential therapy on post-operative pain, edema, and range of motion of the knee. Clin J Sport Med. Jan 2003;13(1):16-20.
Werners R, Pynsent PB, Bulstrode CJ. Randomized trial comparing interferential therapy with motorized lumbar traction and massage in the management of low back pain in a primary care setting. Spine. Aug 1 1999;24(15):1579-1584.

Rating: 8b

California. Division of Workers' Compensation. Functional Improvement Report. October 2007.

§ 9792.27. DWC Form FIR "Functional Improvement Report"

ASSESSMENTS (May substitute discipline specific assessments): Since there are numerous instruments, measures, rating scales, or tools available, it is up to the provider to choose an assessment suitable for the injury condition being treated. The importance of an assessment is to have a measure that can be used repeatedly over the course of treatment to demonstrate improvement. Therefore, it is important to report progress over time by recording the dates of the measurements. Furthermore it is important to state the desired outcome or goal to be achieved. There are several different categories of assessments. Test and measures with established validity and sensitivity for the diagnosis are preferred. The progress report must document the pertinent progress made and functional levels obtained at the end

of the billing period compared to the levels shown in the initial assessment. Date progress when function can be consistently performed or when meaningful functional improvement is made. Completion of data in each column is important to provide clear documentation of the patient progress over time. The "Goal" column on the right should have quantitative goals for each test or measure (e.g. selfreport score, ROM in degrees, amount of weight to lift, etc.) These goals may be updated over the course of care. Provide dates for when goals are set as well as when they are achieved.
Work Functions and/or Activities of Daily Living, Self Report of Disability (e.g., walking, driving, keyboard or lifting tolerance, Oswestry, pain scales, etc): Objective measures of the patient's functional performance in the clinic (e.g., able to lift 10 lbs floor to waist x 5 repetitions) are preferred, but this may include self-report of functional tolerance and can document the patient self-assessment of functional status through the use of questionnaires, pain scales, etc (Oswestry, DASH, VAS, etc.)
Physical Impairments (e.g., joint ROM, muscle flexibility, strength, or endurance deficits): Include objective measures of clinical exam findings. ROM should be in documented in degrees.
Approach to Self-Care and Education/Reduced Reliance on Other Treatments, Modalities, or Medications: This includes the provider's assessment of the patient compliance with a home program and motivation. The provider should also indicate a progression of care with increased active interventions (vs. passive interventions) and reduction in frequency of treatment over course of care.
ICF Code (optional): The International Classification of Functioning, Disability and Health (ICF) is published by the World Health Organization (WHO) to standardize descriptions of health and disability. This is an emerging system to codify function and disability. While, it is included here as an optional data element, providers are strongly encouraged to indicate the ICF Code.

Rating: 7a

Carr DB and Goudas LC. Acute Pain. Lancet 1999;353:2051-58.
Publication Type: Review

Carroll D, Moore RA, McQuay HJ, Fairman F, Tramer M, Leijon G, Transcutaneous electrical nerve stimulation (TENS) for chronic pain, Cochrane Database Syst Rev. 2001;(3):CD003222.

IPC 814, Pfizer Ltd, Sandwich, Kent, UK, CT13 9NJ. dawn.carroll@pfizer.com

BACKGROUND: Transcutaneous electrical nerve stimulation (TENS) is used in a variety of different clinical settings to treat a range of different acute and chronic pain conditions and has become popular with both patients and health professionals. OBJECTIVES: To evaluate the effectiveness of TENS in chronic pain. SEARCH STRATEGY: The Cochrane Library, Embase, Medline, CINAHL and The Oxford Pain Database were searched. Reference lists from retrieved reports and reviews were examined. Date of the most recent search: March 1999. SELECTION CRITERIA: RCTs were eligible if they included the following treatment comparisons: active TENS versus sham TENS controls active TENS versus no treatment controls active TENS versus active TENS controls (for instance High Frequency

TENS vs Low Frequency TENS) Studies of patients suffering chronic pain for three months or more which included subjective outcome measures for pain intensity, or pain relief were eligible for evaluation in this review. No restrictions were made to language or sample size. Data from abstracts, letters, or unpublished studies, and studies of TENS in angina, headache and migraine, and dysmenorrhoea were not included. DATA COLLECTION AND ANALYSIS: Data were extracted and summarised on the following items: patients and details of pain condition, study treatments, study duration, design, methods, subjective pain outcome measures, methodological quality, results for pain outcome measures and adverse effects, and the conclusions made by the authors of the original studies. Extracted data and methodological quality of each report was confirmed by at least three of the reviewers. MAIN RESULTS: Of 107 reports identified from the searches, 88 were excluded as they did not fulfil the pre-defined entry criteria. Nineteen RCTs (from 18 reports) were evaluated. The included trials varied in terms of design, analgesic outcomes, chronic pain conditions, TENS treatments and overall methodological quality. Studies included single and multiple dose treatment comparisons of TENS. The studies were small. The reporting of the methods used and results for the analgesic outcomes were generally poor. TENS treatments and controls were often poorly defined. Few studies evaluated the long-term analgesic effectiveness of TENS and single dose evaluations of TENS are unhelpful in making clinical decisions of the long-term effectiveness of TENS in the management of chronic pain. Meta-analysis was not possible. Overall in 10 of 15 inactive control studies there was a positive analgesic outcome in favour of the active TENS treatments. For the multiple dose treatment comparison studies only three of seven were considered to be in favour of the active TENS treatments. For the active controlled studies, seven studies made direct comparisons between HFTENS and LFTENS. Five of seven studies could find no difference in terms of analgesic efficacy between HFTENS and LFTENS at any time point. REVIEWER'S CONCLUSIONS: The results of this review are inconclusive; the published trials do not provide information on the stimulation parameters which are most likely to provide optimum pain relief, nor do they answer questions about long-term effectiveness. Large multi-centre randomised controlled trials of TENS in chronic pain are urgently needed.

Rating: 1a

PMID: 11687055

Casimiro L, Barnsley L, Brosseau L, Milne S, Robinson V, Tugwell P, Wells G, Casimiro L. Acupuncture and electroacupuncture for the treatment of rheumatoid arthritis. Cochrane Database Syst Rev. 2005 Oct 19;(4):CD003788.

BACKGROUND: Acupuncture has been used by rehabilitation specialists as an adjunct therapy for the symptomatic treatment of rheumatoid arthritis (RA). Acupuncture is a traditional Chinese medicine where thin needles are inserted in specific documented points believed to represent concentration of body energies. In some cases a small electrical impulse is added to the needles. Once the needles are inserted in some of the appropriate points, endorphins, morphine-like substances, have been shown to be

released in the patient's system, thus inducing local or generalised analgesia (pain relief). This review is an update of the original review published in July 2002. OBJECTIVES: To evaluate the effects of acupuncture or electroacupuncture on the objective and subjective measures of disease activity in patients with RA. SEARCH STRATEGY: A comprehensive search of MEDLINE, EMBASE, PEDro, Current Contents , Sports Discus and CINAHL, initially done in September 2001, was updated in May 2005.The Cochrane Field of Rehabilitation and Related Therapies and the Cochrane Musculoskeletal Review Group were also contacted for a search of their specialized registries. Handsearching was conducted on all retrieved papers and content experts were contacted to identify additional studies. SELECTION CRITERIA: Comparative controlled studies, such as randomized controlled trials and controlled clinical trials in patients with RA were eligible. Trials published in languages other than French and English were not analyzed. Abstracts were excluded unless further data could be obtained from the authors. DATA COLLECTION AND ANALYSIS: Two independent reviewers identified potential articles from the literature search and extracted data using pre-defined extraction forms. Consensus was reached on all the extracted data. Quality was assessed by two reviewers using a five point validated tool that measured the quality of randomization, double-blinding and description of withdrawals. MAIN RESULTS: After the updated searches were conducted, five further potential articles were identified; however, these did not meet the inclusion criteria. Two studies involving a total of 84 people were included. One study used acupuncture while the other used electroacupuncture. In the acupuncture study, no statistically significant difference was found between groups for erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), visual analogue scale for patient's global assessment (VAS G), number of swollen joints and tender joints, general health questionnaire (GHQ), modified disease activity scale (DAS) or for the decrease in analgesic intake. Although not statistically significant, pain in the treatment group improved by 4 points on a 0-100mm visual analogue scale versus no improvement in the placebo group. In the second study, using electroacupuncture, a significant decrease in knee pain was reported in the experimental group, 24 hours post treatment, when compared to the placebo group (WMD: -2.0 with 95% CI -3.6,-4.0). A significant decrease was found also at four months post-treatment (WMD -0.2, 95% CI: -0.36, -0.04) AUTHORS' CONCLUSIONS: Although the results of the study on electroacupuncture show that electroacupuncture may be beneficial to reduce symptomatic knee pain in patients with RA 24 hours and 4 months post treatment, the reviewers concluded that the poor quality of the trial, including the small sample size preclude its recommendation. The reviewers further conclude that acupuncture has no effect on ESR, CRP, pain, patient's global assessment, number of swollen joints, number of tender joints, general health, disease activity and reduction of analgesics. These conclusions are limited by methodological considerations such as the type of acupuncture (acupuncture vs electroacupuncture), the site of intervention, the low number of clinical trials and the small sample size of the included studies.

PMID: 16235342

Rating: 1b

Cepeda M, Carr D, Lau J. Local anesthetic sympathetic blockade for complex regional pain syndrome. Cochrane Database Syst Rev. 2005 Oct 19;4:CD004598.

BACKGROUND: Local anesthetic blockade of the sympathetic chain is widely used to treat reflex sympathetic dystrophy (RSD) and causalgia. These two pain syndromes are now conceptualized as variants of a single entity: complex regional pain syndrome (CRPS). A recent meta-analysis of the topic has been published. However, this study only evaluated studies in English language and therefore it could have overlooked some randomized controlled trials. OBJECTIVES: This systematic review had three objectives: to determine the likelihood of pain alleviation after sympathetic blockade with local anesthetics in the patient with CRPS; to assess how long any benefit persists; and to evaluate the incidence of adverse effects of the procedure. SEARCH STRATEGY: We searched the Cochrane Pain, Palliative and Supportive Care Register, the Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE, LILACS, and conference abstracts of the World Congresses of the International Association for the Study of Pain. Bibliographies from retrieved articles were also searched for additional studies. SELECTION CRITERIA: We considered for inclusion randomized controlled trials that evaluated the effect of sympathetic blockade with local anesthetics in children or in adult patients to treat RSD, causalgia, or CRPS. DATA COLLECTION AND ANALYSIS: The outcomes of interest were the number of patients who obtained at least 50% of pain relief shortly after sympathetic blockade (30 minutes to 2 hours) and 48 hours or later. We also assessed the presence of adverse effects in each treatment arm. A random effects model was used to combine the studies. MAIN RESULTS: Two small randomized double blind cross over studies that evaluated 23 subjects were found. The combined effect of the two trials produced a relative risk (RR) to achieve at least 50% of pain relief 30 minutes to 2 hours after the sympathetic blockade of 1.17 (95% CI 0.80-1.72). It was not possible to determine the effect of sympathetic blockade on long-term pain relief because the authors of the two studies evaluated different outcomes. AUTHORS' CONCLUSIONS: This systematic review revealed the scarcity of published evidence to support the use of local anesthetic sympathetic blockade as the 'gold standard' treatment for CRPS. The two randomized studies that met inclusion criteria had very small sample sizes, therefore, no conclusion concerning the effectiveness of this procedure could be drawn. There is a need to conduct randomized controlled trials to address the value of sympathetic blockade with local anesthetic for the treatment of CRPS.

PMID: 16235369

Rating: 1c

Cepeda MS, Camargo F, Zea C, Valencia L. Tramadol for osteoarthritis. Cochrane Database Syst Rev. 2006 ;19;3:CD005522.

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BACKGROUND: Tramadol is increasingly used for the treatment of osteoarthritis because, in contrast to nonsteroidal anti-inflammatory drugs (NSAIDs), tramadol does not produce gastrointestinal bleeding or renal problems, and does not affect articular cartilage. OBJECTIVES: We sought to determine the analgesic effectiveness, the effect on physical function, the duration of benefit and the safety of oral tramadol in people with osteoarthritis. SEARCH STRATEGY: We searched the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE and LILACS databases up to August 2005. SELECTION CRITERIA: We included randomized controlled trials (RCTs) that evaluated the effect of tramadol or tramadol plus paracetamol on pain levels and/or physical function in people with osteoarthritis. No language restriction was applied. DATA COLLECTION AND ANALYSIS: We analyzed separately placebo-controlled and active-controlled studies. We used fixed-effect models for the meta-analyses as the results across studies were similar. MAIN RESULTS: We included eleven RCTs with a total of 1019 participants who received tramadol or tramadol/paracetamol and 920 participants who received placebo or active-control.The placebo-controlled studies indicated that participants who received tramadol had less pain (-8.5 units on a 0 to 100 scale; 95% confidence interval (CI) -12.0 to -5.0) than patients who received placebo. This represents a 12% relative decrease in pain intensity from baseline. Participants who received tramadol had a 37% increase (95% CI 1.2 to 1.5) in the likelihood of reporting moderate improvement (number needed to treat to benefit = 6; 95% CI 4 to 9). Participants who received tramadol had 2.27 times the risk of developing minor adverse events and 2.6 times the risk of developing major adverse events, compared to participants who received placebo. Of every eight people who receive tramadol or tramadol/paracetamol, one will stop taking the medication because of adverse events, number needed to treat to harm (NNTH)= 8 (95% CI 7 to 12) for major adverse events.No conclusion could be drawn on how tramadol or tramadol/paracetamol compared with available pharmacological treatments because of the limited number of studies that evaluated such therapies. AUTHORS' CONCLUSIONS: Tramadol or tramadol/paracetamol decreases pain intensity, produces symptom relief and improves function, but these benefits are small. Adverse events, although reversible and not life threatening, often cause participants to stop taking the medication and could limit tramadol or tramadol plus paracetamol usefulness.

PMID: 16856101

Rating: 1a

Cepeda MS, Lau J, Carr DB. Defining the therapeutic role of local anesthetic sympathetic blockade in complex regional pain syndrome: a narrative and systematic review. Clin J Pain. 2002;18:216-33.

Department of Anesthesia, San Ignacio Hospital, and Javeriana University School of Medicine, Bogota, Colombia.

OBJECTIVE: There is growing controversy on the value of blocking the sympathetic nervous system for the treatment of complex regional pain syndromes (CRPS). The authors sought to evaluate the efficacy of sympathetic blockade with local anesthetic in these syndromes. In addition, they performed a

comprehensive review of the pathophysiology and other treatments for CRPS. DESIGN: Systematic review of the literature was performed. MEDLINE was searched from 1966 through 1999. The authors identified only three randomized controlled trials (RCTs) that evaluated sympathetic blockade with local anesthetic, but because of differences in study design they were unable to pool the study data. The authors therefore included nonrandomized studies and case series. INTERVENTIONS: Studies were included if local anesthetic sympathetic blockade was used in at least 10 patients. Studies were excluded if continuous infusion techniques, somatic nerve blocks, or combined sympatholytic therapies were evaluated. OUTCOME MEASURES: Pain relief was classified as full, partial, or absent. The lack of a comparison group in the studies allowed only the calculation of distribution of the response categories, and the sum of the pooled rates does not equal 100%. RESULTS: Twenty-nine studies were included that evaluated 1,144 patients. Nineteen studies were retrospective, 5 prospective case series, 3 RCTs, and 2 nonrandomized controlled studies. The quality of the publications was generally poor. Twenty-nine percent of patients had full response, 41% had partial response, and 32% had absent response. It was not possible to estimate the duration of pain relief. CONCLUSIONS: This review raises questions as to the efficacy of local anesthetic sympathetic blockade as treatment of CRPS. Its efficacy is based mainly on case series. Less than one third of patients obtained full pain relief. The absence of control groups in case series leads to an overestimation of the treatment response that can explain the findings. PMID: 12131063

Rating: 1c

CFSAN/Office of Nutritional Products, Labeling, and Dietary Supplements. Guidance for Industry: Frequently Asked Questions About Medical Foods. Center for Food and Safety and Applied Nutrition, FDA. Available at: http://www.cfsan.fda.gov/~dms/medfguid.html. Accessed: July 2008

Rating: 8b

Chabal C, Erjavec MK, Jacobson L, Mariano A, Chaney E. Prescription opiate abuse in chronic pain patients: clinical criteria, incidence, and predictors. Clin J Pain. 1997 Jun;13(2):150-5.

Anesthesiology Department, University of Washington, Seattle, USA.

OBJECTIVES: Opiates are commonly used to treat patients with chronic nonmalignant pain. There is much controversy over the definition, incidence, and risk factors of prescription opiate abuse in chronic pain treatment. The present study, done at the Seattle VA Medical Center, was designed to create opiate abuse criteria, test inter-rater reliability of the criteria, apply the criteria to a group of chronic pain patients, and correlate the risk of opiate abuse with the results of alcohol and drug testing. DESIGN/OUTCOME MEASURES: A committee of experienced pain providers designed a five-point prescription opiate abuse checklist based on DSM-III-R parameters. The criteria were then applied to patients enrolled in the pain clinic. The reliability of the criteria were determined using two providers who were familiar with every patient in the clinic. Drug, alcohol, and psychosocial testing were

correlated with the risk of opiate abuse. RESULTS: A total of 19% (76/403) of all pain clinic patients were using chronic opiates. Thirty-four percent (26/76) met one, and 27.6% (21/76) met three or more of the abuse criteria. The criteria had an inter-rater reliability of > 0.9. There were no differences between chronic opiate users (n = 76) and opiate abusers (n = 21) for a history of drug or alcohol abuse or on psychosocial testing. CONCLUSIONS: Prescription opiate abuse criteria for use in patients with chronic nonmalignant pain were designed. The criteria had good reliability and can be applied during normal clinic interactions. The percentage of chronic opiate users who become opiate abusers in pain treatment is within the range reported by others. Past opiate or alcohol abuse or psychosocial testing on clinic admission failed to predict who would become an opiate abuser. The criteria can be used to identify patients who will subsequently require more intensive treatment or intervention or can be used as an outcome to measure to test the effectiveness of treatment strategies.

PMID: 9186022

Rating: 4a

Chan AT, Manson JE, Albert CM, Chae CU, Rexrode KM, Curhan GC, Rimm EB, Willett WC, Fuchs CS. Nonsteroidal antiinflammatory drugs, acetaminophen, and the risk of cardiovascular events. Circulation. 2006;113:1578-87.

Gastrointestinal Unit, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA. achan@partners.org RESULTS: We examined the influence of NSAIDs and acetaminophen on the risk of major cardiovascular events (nonfatal myocardial infarction, fatal coronary heart disease, nonfatal and fatal stroke) in a prospective cohort of 70,971 women. Women who reported occasional (1 to 21 d/mo) use of NSAIDs or acetaminophen did not experience a significant increase in the risk of cardiovascular events. CONCLUSIONS: Use of NSAIDs or acetaminophen at high frequency or dose is associated with a significantly increased risk for major cardiovascular events, although more moderate use did not confer substantial risk.

PMID: 16534006

Rating: 3a

Chan FK, Graham DY. Review article: prevention of non-steroidal anti-inflammatory drug gastrointestinal complications--review and recommendations based on risk assessment. Aliment Pharmacol Ther. 2004;19:1051-61.

Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Hong Kong, China.

The incidence of non-steroidal anti-inflammatory drug-related ulcer complications remains high despite the availability of potent anti-ulcer drugs and selective cyclo-oxygenase-2 inhibitors. Non-steroidal anti-

inflammatory drug-related ulcer complications can be minimized by prospective assessment of patients' baseline risk, rational choice and use of non-steroidal anti-inflammatory drugs, and selective use of co-therapy strategies with gastroprotectives. Current recommendations regarding strategies using anti-ulcer drugs and cyclo-oxygenase-2 inhibitors for prevention of clinical non-steroidal anti-inflammatory drug upper gastrointestinal events are largely derived from studies using surrogates such as endoscopic ulcers, erosions, and symptoms in low- to average-risk patients. Conclusions based on surrogate and potentially manipulatable end-points are increasingly suspect with regard to applicability to clinical situations. This article reviews the risks associated with non-steroidal anti-inflammatory drugs including aspirin and includes the effect of the patients' baseline risk, and the confounding effects of Helicobacter pylori infection. In addition, uncertainties regarding the clinical efficacy of anti-ulcer drugs and cyclo-oxygenase-2 inhibitors against non-steroidal anti-inflammatory drug-related ulcer complications are put into perspective. We propose management strategies based on the risk category: low risk (absence of risk factors) (least ulcerogenic non-steroidal anti-inflammatory drug at lowest effective dose), moderate risk (one to two risk factors) (as above, plus an antisecretory agent or misoprostol or a cyclo-oxygenase-2 inhibitor), high risk (multiple risk factors or patients using concomitant low-dose aspirin, steroids, or anticoagulants) (cyclo-oxygenase-2 inhibitor alone with steroids, plus misoprostol with warfarin, or plus a proton pump inhibitors or misoprostol with aspirin), and very high risk (history of ulcer complications) (avoid all non-steroidal anti-inflammatory drugs, if possible or a cyclo-oxygenase-2 plus a proton pump inhibitors and/or misoprostol). The presence of H. pylori infection increases the risk of upper gastrointestinal complications in non-steroidal anti-inflammatory drug users by two- to fourfold suggesting that all patients requiring regular non-steroidal anti-inflammatory drug therapy be tested for H. pylori.

PMID: 15142194

Rating: 5b

Chang G, Chen L, Mao J. Opioid tolerance and hyperalgesia. Med Clin North Am. 2007;91:199-211.

Massachusetts General Hospital Pain Center, Division of Pain Medicine, Department of Anesthesia and Critical Care, Massachusetts General Hospital, Harvard Medical School, Boston, MA 02114, USA.

Opioids have been successfully used for the management of acute and cancer-related pain. Concerns regarding side effects, tolerance, dependence, addiction, and hyperalgesia have limited the use of opioids for the management of chronic nonmalignant pain. This article will review updated information from both clinical and preclinical studies regarding opioid-induced hyperalgesia, tolerance, and dependence. The implications of these issues in clinical opioid therapy also will be discussed.

PMID: 17321281

Rating: 5a

Chelminski PR, Ives TJ, Felix KM, Prakken SD, Miller TM, Perhac JS, Malone RM, Bryant ME, DeWalt DA, Pignone MP. A primary care, multi-disciplinary disease management program for opioid-treated patients with chronic non-cancer pain and a high burden of psychiatric comorbidity. BMC Health Serv Res. 2005 Jan 13;5(1):3.

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BACKGROUND: Chronic non-cancer pain is a common problem that is often accompanied by psychiatric comorbidity and disability. The effectiveness of a multi-disciplinary pain management program was tested in a 3 month before and after trial. METHODS: Providers in an academic general medicine clinic referred patients with chronic non-cancer pain for participation in a program that combined the skills of internists, clinical pharmacists, and a psychiatrist. Patients were either receiving opioids or being considered for opioid therapy. The intervention consisted of structured clinical assessments, monthly follow-up, pain contracts, medication titration, and psychiatric consultation. Pain, mood, and function were assessed at baseline and 3 months using the Brief Pain Inventory (BPI), the Center for Epidemiological Studies-Depression Scale scale (CESD) and the Pain Disability Index (PDI). Patients were monitored for substance misuse. RESULTS: Eighty-five patients were enrolled. Mean age was 51 years, 60% were male, 78% were Caucasian, and 93% were receiving opioids. Baseline average pain was 6.5 on an 11 point scale. The average CESD score was 24.0, and the mean PDI score was 47.0. Sixty-three patients (73%) completed 3 month follow-up. Fifteen withdrew from the program after identification of substance misuse. Among those completing 3 month follow-up, the average pain score improved to 5.5 ($p = 0.003$). The mean PDI score improved to 39.3 ($p < 0.001$). Mean CESD score was reduced to 18.0 ($p < 0.001$), and the proportion of depressed patients fell from 79% to 54% ($p = 0.003$). Substance misuse was identified in 27 patients (32%). CONCLUSIONS: A primary care disease management program improved pain, depression, and disability scores over three months in a cohort of opioid-treated patients with chronic non-cancer pain. Substance misuse and depression were common, and many patients who had substance misuse identified left the program when they were no longer prescribed opioids. Effective care of patients with chronic pain should include rigorous assessment and treatment of these comorbid disorders and intensive efforts to insure follow up.

PMID: 15649331

Rating: 4b

Chen YF, Jobanputra P, Barton P, Bryan S, Fry-Smith A, Harris G, Taylor RS. Cyclooxygenase-2 selective non-steroidal anti-inflammatory drugs (etodolac, meloxicam, celecoxib, rofecoxib, etoricoxib, valdecoxib and lumiracoxib) for osteoarthritis and rheumatoid arthritis: a systematic review and economic evaluation. Health Technol Assess. 2008 Apr;12(11):1-178.

Department of Public Health and Epidemiology, University of Birmingham, UK.

OBJECTIVES: To review the clinical effectiveness and cost-effectiveness of cyclooxygenase-2 (COX-2) selective non-steroidal anti-inflammatory drugs (NSAIDs) (etodolac, meloxicam, celecoxib, rofecoxib, etoricoxib, valdecoxib and lumiracoxib) for osteoarthritis (OA) and rheumatoid arthritis (RA). DATA SOURCES: Electronic databases were searched up to November 2003. Industry submissions to the National Institute for Health and Clinical Excellence (NICE) in 2003 were also reviewed. REVIEW METHODS: Systematic reviews of randomised controlled trials (RCTs) and a model-based economic evaluation were undertaken. Meta-analyses were undertaken for each COX-2 selective NSAID compared with placebo and non-selective NSAIDs. The model was designed to run in two forms: the 'full Assessment Group Model (AGM)', which includes an initial drug switching cycle, and the 'simpler AGM', where there is no initial cycle and no opportunity for the patient to switch NSAID. RESULTS: Compared with non-selective NSAIDs, the COX-2 selective NSAIDs were found to be equally as efficacious as the non-selective NSAIDs (although meloxicam was found to be of inferior or equivalent efficacy) and also to be associated with significantly fewer clinical upper gastrointestinal (UGI) events (although relatively small numbers of clinical gastrointestinal (GI) and myocardial infarction (MI) events were reported across trials). Subgroup analyses of clinical and complicated UGI events and MI events in relation to aspirin use, steroid use, prior GI history and Helicobacter pylori status were based on relatively small numbers and were inconclusive. In the RCTs that included direct COX-2 comparisons, the drugs were equally tolerated and of equal efficacy. Trials were of insufficient size and duration to allow comparison of risk of clinical UGI events, complicated UGI events and MIs. One RCT compared COX-2 (celecoxib) with a non-selective NSAID combined with a gastroprotective agent (diclofenac combined with omeprazole); this included arthritis patients who had recently suffered a GI haemorrhage. Although no significant difference in clinical GI events was reported, the number of events was small and more such studies, where patients genuinely need NSAIDs, are required to confirm these data. A second trial showed that rofecoxib was associated with fewer diarrhoea events than a combination of diclofenac and misoprostol (Arthrotec). Previously published cost-effectiveness analyses indicated a wide of range of possible incremental cost per quality-adjusted life-year (QALY) gained estimates. Using the simpler AGM, with ibuprofen or diclofenac alone as the comparator, all of the COX-2 products are associated with higher costs (i.e. positive incremental costs) and small increases in effectiveness (i.e. positive incremental effectiveness), measured in terms of QALYs. The magnitude of the incremental costs and the incremental effects, and therefore the incremental cost-effectiveness ratios, vary considerably across all COX-2 selective NSAIDs. The base-case incremental cost per QALY results for COX-2 selective NSAIDs compared with diclofenac for the simpler model are: celecoxib (low dose) 68,400 pounds; celecoxib (high dose) 151,000 pounds; etodolac (branded) 42,400 pounds; etodolac (generic) 17,700 pounds; etoricoxib 31,300 pounds; lumiracoxib 70,400 pounds; meloxicam (low dose) 10,300 pounds; meloxicam (high dose) 17,800 pounds; rofecoxib 97,400 pounds; and valdecoxib 35,500 pounds. When the simpler AGM was run using ibuprofen or diclofenac combined with proton pump inhibitor (PPI) as the comparator, the results change substantially, with the COX-2 selective NSAIDs looking generally unattractive from a cost-effectiveness point of view (COX-2 selective NSAIDs were dominated by ibuprofen or diclofenac

combined with PPI in most cases). This applies both to 'standard' and 'high-risk' arthritis patients defined in terms of previous GI ulcers. The full AGM produced results broadly in line with the simpler model. CONCLUSIONS: The COX-2 selective NSAIDs examined were found to be similar to non-selective NSAIDs for the symptomatic relief of RA and OA and to provide superior GI tolerability (the majority of evidence is in patients with OA). Although COX-2 selective NSAIDs offer protection against serious GI events, the amount of evidence for this protective effect varied considerably across individual drugs. The volume of trial evidence with regard to cardiovascular safety also varied substantially between COX-2 selective NSAIDs. Increased risk of MI compared to non-selective NSAIDs was observed among those drugs with greater volume of evidence in terms of exposure in patient-years. Economic modelling shows a wide range of possible costs per QALY gained in patients with OA and RA. Costs per QALY also varied if individual drugs were used in 'standard' or 'high'-risk patients, the choice of non-selective NSAID comparator and whether that NSAID was combined with a PPI. With reduced costs of PPIs, future primary research needs to compare the effectiveness and cost-effectiveness of COX-2 selective NSAIDs relative to non-selective NSAIDs with a PPI. Direct comparisons of different COX-2 selective NSAIDs, using equivalent doses, that compare GI and MI risk are needed. Pragmatic studies that include a wider range of people, including the older age groups with a greater burden of arthritis, are also necessary to inform clinical practice.

PMID: 18405470

Rating: 1b

Cherry DA, Eldredge K. A 'leaking' Synchromed pump. Pain. 1997;71:109.

Pain Management Unit, Flinders Medical Centre, Bedford Park, Australia.

PMID: 9200180

A case report of a patient who was diverting morphine from her intrathecal pump resivoir.

Rating: 11

Cheshire WP, Abashian SW, Mann JD. Botulinum toxin in the treatment of myofascial pain syndrome. Pain 1994;59:65-9.

Abstract:

Six patients with chronic myofascial pain syndrome involving cervical paraspinal and shoulder girdle muscles received trigger point injections of botulinum toxin type A (Botox) or saline in a randomized, double-blind, placebo-controlled study. Four patients experienced reduction in pain of at least 30% following Botox, but not saline, injections, as measured by visual analog scales, verbal descriptors for

pain intensity and unpleasantness, palpable muscle firmness, and pressure pain thresholds. Results were statistically significant. Botox, which inhibits muscle contraction by blocking the release of acetylcholine from peripheral nerves, appears to be an effective treatment for focal myofascial pain disorders.

Conclusion:
Local blockade of neuromuscular transmission with Botox is effective in some patients with myofascial pain of shoulder girdle/neck.

Publication Type: RCT, 6 cases

Chessick CA, Allen MH, Thase M, Batista Miralha da Cunha AB, Kapczinski FF, de Lima MS, dos Santos Souza JJ. Azapirones for generalized anxiety disorder. Cochrane Database Syst Rev. 2006; 3: CD006115.

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BACKGROUND: Azapirones are a group of drugs that work at the 5-HT1A receptor and are used to treat patients suffering from generalized anxiety disorder (GAD). However, several studies have shown conflicting results. Whether azapirones are useful as first line treatment in general anxiety disorders still needs to be answered. OBJECTIVES: To assess the efficacy and the acceptability of azapirones for the treatment of GAD. SEARCH STRATEGY: Initially the Cochrane Collaboration Depression, Anxiety and Neurosis Controlled Trials Register (CCDANCTR) and The Cochrane Central Register of Controlled Trials (CENTRAL) were searched, incorporating results of group searches of MEDLINE (1966 to June 2005), EMBASE (1980 to June 2005), CINAHL (1982 to June 2005), PsycLIT (1974 to June 2005), PSYNDEX (1977 to June 2005), and LILACS (1982 to June 2005). Subsequently the revised Cochrane Collaboration Depression, Anxiety and Neurosis Controlled Trials Registers (CCDANCTR-Studies and CCDANCTR-References) were searched on 21-10-2005. Reference lists of relevant papers and major text books of anxiety disorder were examined. Authors, other experts in the field and pharmaceutical companies were contacted for knowledge of suitable trials, published or unpublished. Specialist journals concerning azapirones were handsearched. SELECTION CRITERIA: Randomized controlled trials of azapirones, including buspirone versus placebo and/or other medication and/or psychological treatment, were included. Participants were males and females of all ages with a diagnosis of generalized anxiety disorder. DATA COLLECTION AND ANALYSIS: Data were extracted from the original reports independently by CC, MA and MT. The main outcomes studied were related to the objectives stated above. Data were analysed for generalized anxiety disorder versus placebo, versus other medication and versus psychological treatment separately. Data were analysed using Review Manager Version 4.2.7. MAIN RESULTS: Thirty six trials were included in the review, reporting on 5908 participants randomly allocated to azapirones and/or placebo, benzodiazepines, antidepressants, psychotherapy or kava kava. Azapirones, including buspirone, were superior to placebo

in treating GAD. The calculated number needed to treat for azapirones using the Clinical Global Impression scale was 4.4 (95% confidence interval (CI) 2.16 to 15.4). Azapirones may be less effective than benzodiazepines and we were unable to conclude if azapirones were superior to antidepressants, kava kava or psychotherapy. Azapirones appeared to be well tolerated. Fewer participants stopped taking benzodiazepines compared to azapirones. The length of studies ranged from four to nine weeks, with one study lasting 14 weeks. AUTHORS' CONCLUSIONS: Azapirones appeared to be useful in the treatment of GAD, particularly for those participants who had not been on a benzodiazepine. Azapirones may not be superior to benzodiazepines and do not appear as acceptable as benzodiazepines. Side effects appeared mild and non serious in the azapirone treated group. Longer term studies are needed to show that azapirones are effective in treating GAD, which is a chronic long-term illness.

PMID: 16856115

Rating: 1c

Choi HK, Seeger JD, Kuntz KM, Effects of rofecoxib and naproxen on life expectancy among patients with rheumatoid arthritis: a decision analysis, Am J Med. 2004 May 1;116(9):621-9.

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BACKGROUND: The VIOXX Gastrointestinal Outcomes Research (VIGOR) trial showed a 53% decrease in the risk of upper gastrointestinal toxicity and a fivefold increase in the risk of myocardial infarction for rofecoxib (a selective cyclooxygenase-2 inhibitor) compared with naproxen. We examined the effects of these competing adverse events on life expectancy in patients with rheumatoid arthritis. METHODS: We used decision analysis to compare the life expectancy of a cohort of rheumatoid arthritis patients taking naproxen versus a similar cohort taking rofecoxib, using data from the VIGOR trial. We incorporated the competing risks of upper gastrointestinal toxicity and myocardial infarction, as well as their long-term health consequences, on the basis of population-based studies. RESULTS: For 58-year-old women with rheumatoid arthritis (i.e., typical of participants in the VIGOR trial), naproxen was associated with a longer life expectancy than was rofecoxib (difference = 4.4 months). This difference was larger among 58-year-old men (7.8 months). The probability that naproxen is associated with a longer life expectancy than rofecoxib among 58-year-old patients was 92% for women and 98% for men. Life expectancy became the same between the two treatments when the risk of upper gastrointestinal toxicity was 70% higher or the risk of myocardial infarction was 40% lower than that of the base case among women, and when the risk of upper gastrointestinal toxicity was 4.4-fold higher or the risk of myocardial infarction was 70% lower among men. CONCLUSION: Our analysis suggests that the competing risks of upper gastrointestinal toxicity and myocardial infarction shown in the VIGOR trial would project a longer life expectancy with naproxen than rofecoxib among patients with rheumatoid arthritis, except in those at low risk of myocardial infarction or at high risk of upper gastrointestinal toxicity.

PMID: 15093759
Rating: 1b

Chong MS, Bajwa ZH. Diagnosis and treatment of neuropathic pain. J Pain Symptom Manage. 2003 May;25(5 Suppl):S4-S11.

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Currently, no consensus on the optimal management of neuropathic pain exists and practices vary greatly worldwide. Possible explanations for this include difficulties in developing agreed diagnostic protocols and the coexistence of neuropathic, nociceptive and, occasionally, idiopathic pain in the same patient. Also, neuropathic pain has historically been classified according to its etiology (e.g., painful diabetic neuropathy, trigeminal neuralgia, spinal cord injury) without regard for the presumed mechanism(s) underlying the specific symptoms. A combined etiologic/mechanistic classification might improve neuropathic pain management. The treatment of neuropathic pain is largely empirical, often relying heavily on data from small, generally poorly-designed clinical trials or anecdotal evidence. Consequently, diverse treatments are used, including non-invasive drug therapies (antidepressants, antiepileptic drugs and membrane stabilizing drugs), invasive therapies (nerve blocks, ablative surgery), and alternative therapies (e.g., acupuncture). This article reviews the current and historical practices in the diagnosis and treatment of neuropathic pain, and focuses on the USA, Europe and Japan.

PMID: 12694987

Rating: 5c

Chou R, Helfand M, Peterson K, Dana T, Roberts C. Comparative Effectiveness and Safety of Analgesics for Osteoarthritis. Comparative Effectiveness Review No. 4. (Prepared by the Oregon Evidence-based Practice Center under Contract No. 290-02-0024.) Rockville, MD: Agency for Healthcare Research and Quality. September 2006.

AHRQ released new consumer and clinician guides that summarize findings of an AHRQ comparative effectiveness review on osteoarthritis pain medications. The guides, which are the first ancillary products from the Effective Health Care program, are written in plain language and draw on a review of 360 published studies. The consumer guide, titled Choosing Pain Medication for Osteoarthritis, summarizes the evidence on both prescription and over-the-counter drugs. It includes information on effectiveness, cost, and potential side effects for non-steroidal anti-inflammatory drugs (NSAIDs), COX-2 inhibitors, Tylenol, and others. The guide for clinicians, Choosing Non-Opioid Analgesics for Osteoarthritis, provides similar information while evaluating the scientific evidence that applies to the drugs' benefits and risks. Each of the analgesics evaluated in this report was associated with a unique set

of benefits and risks. Each was also associated with gaps in the evidence necessary to determine the true balance of benefits vs. harms. The role of selective and nonselective oral NSAIDs and alternative agents will continue to evolve as additional information emerges. At this time, although the amount and quality of evidence vary, no currently available analgesic reviewed in this report was identified as offering a clear overall advantage compared with the others. This is not surprising, given the complex tradeoffs between the many benefits (pain relief, improved function, improved tolerability, and others) and harms (CV, renal, GI, and others) involved. Individuals are likely to differ in how they prioritize the importance of the various benefits and harms of treatment. Adequate pain relief at the expense of an increase in CV risk, for example, could be an acceptable tradeoff for some patients. Others may consider even a marginal increase in CV risk unacceptable. Factors that should be considered when weighing the potential effects of an analgesic include age (older age being associated with increased risks for bleeding and CV events), comorbid conditions, and concomitant medication use (such as aspirin and anticoagulation medications). As in other medical decisions, choosing the optimal analgesic for an individual with osteoarthritis should always involve careful consideration and thorough discussion of the relevant tradeoffs.

Rating: 1a

Chou R, Huffman LH; American Pain Society; American College of Physicians. Medications for acute and chronic low back pain: a review of the evidence for an American Pain Society/American College of Physicians clinical practice guideline. Ann Intern Med. 2007;147:505-14.

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BACKGROUND: Medications are the most frequently prescribed therapy for low back pain. A challenge in choosing pharmacologic therapy is that each class of medication is associated with a unique balance of risks and benefits. PURPOSE: To assess benefits and harms of acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs), antidepressants, benzodiazepines, antiepileptic drugs, skeletal muscle relaxants, opioid analgesics, tramadol, and systemic corticosteroids for acute or chronic low back pain (with or without leg pain). DATA SOURCES: English-language studies were identified through searches of MEDLINE (through November 2006) and the Cochrane Database of Systematic Reviews (2006, Issue 4). These electronic searches were supplemented by hand searching reference lists and additional citations suggested by experts. STUDY SELECTION: Systematic reviews and randomized trials of dual therapy or monotherapy with 1 or more of the preceding medications for acute or chronic low back pain that reported pain outcomes, back-specific function, general health status, work disability, or patient satisfaction. DATA EXTRACTION: We abstracted information about study design, population characteristics, interventions, outcomes, and adverse events. To grade methodological quality, we used the Oxman criteria for systematic reviews and the Cochrane Back Review Group criteria for individual trials. DATA SYNTHESIS: We found good evidence that NSAIDs,

acetaminophen, skeletal muscle relaxants (for acute low back pain), and tricyclic antidepressants (for chronic low back pain) are effective for pain relief. The magnitude of benefit was moderate (effect size of 0.5 to 0.8, improvement of 10 to 20 points on a 100-point visual analogue pain scale, or relative risk of 1.25 to 2.00 for the proportion of patients experiencing clinically significant pain relief), except in the case of tricyclic antidepressants (for which the benefit was small to moderate). We also found fair evidence that opioids, tramadol, benzodiazepines, and gabapentin (for radiculopathy) are effective for pain relief. We found good evidence that systemic corticosteroids are ineffective. Adverse events, such as sedation, varied by medication, although reliable data on serious and long-term harms are sparse. Most trials were short term (< or =4 weeks). Few data address efficacy of dual-medication therapy compared with monotherapy, or beneficial effects on functional outcomes. LIMITATIONS: Our primary source of data was systematic reviews. We included non-English-language trials only if they were included in English-language systematic reviews. CONCLUSIONS: Medications with good evidence of short-term effectiveness for low back pain are NSAIDs, acetaminophen, skeletal muscle relaxants (for acute low back pain), and tricyclic antidepressants (for chronic low back pain). Evidence is insufficient to identify one medication as offering a clear overall net advantage because of complex tradeoffs between benefits and harms. Individual patients are likely to differ in how they weigh potential benefits, harms, and costs of various medications.

PMID: 17909211

Rating: 1b

Chou R, Peterson K, Helfand M. Comparative efficacy and safety of skeletal muscle relaxants for spasticity and musculoskeletal conditions: a systematic review. J Pain Symptom Manage. 2004;28:140-75.

Department of Medicine, Oregon Health & Science University, Portland, Oregon, USA.

Skeletal muscle relaxants are a heterogeneous group of medications used to treat two different types of underlying conditions: spasticity from upper motor neuron syndromes and muscular pain or spasms from peripheral musculoskeletal conditions. Although widely used for these indications, there appear to be gaps in our understanding of the comparative efficacy and safety of different skeletal muscle relaxants. This systematic review summarizes and assesses the evidence for the comparative efficacy and safety of skeletal muscle relaxants for spasticity and musculoskeletal conditions. Randomized trials (for comparative efficacy and adverse events) and observational studies (for adverse events only) that included oral medications classified as skeletal muscle relaxants by the FDA were sought using electronic databases, reference lists, and pharmaceutical company submissions. Searches were performed through January 2003. The validity of each included study was assessed using a data abstraction form and predefined criteria. An overall grade was allocated for the body of evidence for each key question. A total of 101 randomized trials were included in this review. No randomized trial was rated good quality, and there was little evidence of rigorous adverse event assessment in included

trials or observational studies. There is fair evidence that baclofen, tizanidine, and dantrolene are effective compared to placebo in patients with spasticity (primarily multiple sclerosis). There is fair evidence that baclofen and tizanidine are roughly equivalent for efficacy in patients with spasticity, but insufficient evidence to determine the efficacy of dantrolene compared to baclofen or tizanidine. There is fair evidence that although the overall rate of adverse effects between tizanidine and baclofen is similar, tizanidine is associated with more dry mouth and baclofen with more weakness. There is fair evidence that cyclobenzaprine, carisoprodol, orphenadrine, and tizanidine are effective compared to placebo in patients with musculoskeletal conditions (primarily acute back or neck pain). Cyclobenzaprine has been evaluated in the most clinical trials and has consistently been found to be effective. There is very limited or inconsistent data regarding the effectiveness of metaxalone, methocarbamol, chlorzoxazone, baclofen, or dantrolene compared to placebo in patients with musculoskeletal conditions. There is insufficient evidence to determine the relative efficacy or safety of cyclobenzaprine, carisoprodol, orphenadrine, tizanidine, metaxalone, methocarbamol, and chlorzoxazone. Dantrolene, and to a lesser degree chlorzoxazone, have been associated with rare serious hepatotoxicity. Copyright 2004 U.S. Cancer Pain Relief Committee

PMID: 15276195

Rating: 1a

Ciccone DS, Just N, Bandilla MA et al. Psychological Correlates of Opiod Use in Patients with Chronic Nonmalignant Pain: A Preliminary Test of the Downhill Spiral Hypothesis. Journal of Pain and Symptom Management 2000;20:180-92.
Abstract:
There is still controversy surrounding the use of opioid medication for patients with chronic nonmalignant pain. Schofferman has argued that long-term opioid use leads to a "downhill spiral" associated with loss of functional capacity and a corresponding increase in depressed mood. The present study was a retrospective comparison of opioid users vs. non-users to determine whether: (a) users have higher levels of disability, medical visitation, depression, and pain; (b) the behavioral problems associated with opioid use persist after controlling for the influence of other medication; (c) opioid use is in fact a predictor of illness behavior; and (d) higher levels of opioid consumption are associated with higher levels of disability and depression. A consecutive series of 243 patients with nonmalignant pain about to enroll at a tertiary clinic were retrospectively assigned to either an Opioid User (n = 87) or Non-User (n = 156) group. Compared to Non-Users, Opioid Users were more likely to be physically disabled ($P < 0.05$) and depressed ($P < 0.05$), as well as more likely to report pain at higher levels ($P < 0.001$) and in more locations ($P < 0.05$). Despite the appearance of a downhill spiral, we were unable to demonstrate an association between opioid use and any measure of illness behavior after controlling for benzodiazepine use (with the possible exception of domestic disability). Instead, we found that

benzodiazepine use was significantly associated with activity level (P<0.05), medical visitation (P<0.01), domestic disability (P<0.01), depression (P <0.01), and to a lesser degree, disability days (P<0.1). Using somatization as a reference variable, we found that opioid use failed to explain a comparable amount of variance in illness behavior. Finally, there was no evidence that higher levels of opioid use were associated with higher levels of disability or depression.
Publication Type: Case Control, 243 cases

CIGNA HealthCare. Coverage Position: Ultra-Rapid Detoxification. Coverage Position Number 0384. 7/15/2006

Coverage Position
CIGNA HealthCare does not cover opioid antagonist agent detoxification under sedation or general anesthesia (e.g., ultra-rapid detoxification) as a method for opioid detoxification because it is considered experimental, investigational or unproven.
Summary
The data supporting the safety and effectiveness of ultra-rapid detoxification is limited. Adequate safety has not been established. The patient population seeking treatment is inconsistent. Comparisons to traditional approaches to detoxification are lacking. Studies are needed that compare the duration and severity of symptoms associated with ultra-rapid detoxification and other detoxification methods. Additional research is needed to address the short- and long-term post-procedure abstinence rate. Response to ultra-rapid detoxification may vary according to the duration of dependence or prior attempts at traditional detoxification. In view of the lack of evidence from well-designed, randomized controlled clinical trials to evaluate the safety and efficacy of this treatment compared with other established methods of detoxification, the role of ultra-rapid detoxification as a method for opioid detoxification has not been established.

Rating: 8b

Cleland LG, James MJ, Proudman SM, The role of fish oils in the treatment of rheumatoid arthritis, Drugs. 2003;63(9):845-53.

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Fish oils are a rich source of omega-3 long chain polyunsaturated fatty acids (n-3 LC PUFA). The specific fatty acids, eicosapentaenoic acid and docosahexaenoic acid, are homologues of the n-6 fatty acid, arachidonic acid (AA). This chemistry provides for antagonism by n-3 LC PUFA of AA metabolism to pro-inflammatory and pro-thrombotic n-6 eicosanoids, as well as production of less active n-3 eicosanoids. In addition, n-3 LC PUFA can suppress production of pro-inflammatory cytokines and cartilage degradative enzymes. In accordance with the biochemical effects, beneficial anti-inflammatory effects of dietary fish oils have been demonstrated in randomised, double-blind, placebo-controlled trials

in rheumatoid arthritis (RA). Also, fish oils have protective clinical effects in occlusive cardiovascular disease, for which patients with RA are at increased risk.Implementation of the clinical use of anti-inflammatory fish oil doses has been poor. Since fish oils do not provide industry with the opportunities for substantial profit associated with patented prescription items, they have not received the marketing inputs that underpin the adoption of usual pharmacotherapies. Accordingly, many prescribers remain ignorant of their biochemistry, therapeutic effects, formulations, principles of application and complementary dietary modifications. Evidence is presented that increased uptake of this approach can be achieved using bulk fish oils. This approach has been used with good compliance in RA patients. In addition, an index of n-3 nutrition can be used to provide helpful feedback messages to patients and to monitor the attainment of target levels.Collectively, these issues highlight the challenges in advancing the use of fish oil amid the complexities of modern management of RA, with its emphasis on combination chemotherapy applied early.

Publication Types:
- Review
- Review, Tutorial

PMID: 12678571

Rating: 5b

Clinical Pharmacology. Gold Standard Inc. Tampa, FL. 2008. http://www.clinicalpharmacology.com

CMS National Coverage Policy, Part B Supplemental Instructions Article (SIA): Epidural Injections: Transforaminal, Indications and Limitations of Coverage and/or Medical Necessity, CMS Coverage Database ID Number A21834. 08/05/2004

Indications And Limitations:
Transforaminal epidural injections are appropriate for the following diagnostic purposes:
- To differentiate the level of radicular nerve root pain;
- To differentiate radicular from non-radicular pain;
- To evaluate a discrepancy between imaging studies and clinical findings;
- To identify the source of pain in the presence of multi-level nerve root compression; and/or
- To identify the level of pathology at a previous operative site.

It might be necessary to perform injections at two (2) different nerve root levels on the same date of service, whether injected unilaterally or bilaterally, if multi-level nerve root compression or stenosis is present on imaging studies and documented in the medical record.
Transforaminal epidural injections are appropriate for the following therapeutic purposes:
- Radicular pain resistant to other therapeutic means or when surgery is contraindicated;
- Post-decompressive radiculitis or post-surgical scarring;

- Monoradicular pain, confirmed by diagnostic blockade, in which a surgically correctable lesion cannot be identified;
- Treatment of acute herpes zoster or post-herpetic neuralgia; and/or
- Reflex sympathetic dystrophy or causalgia/complex regional pain syndrome I and II in lieu of sympathetic block.

For chronic pain, the standard of care for all transforaminal epidural and selective nerve root injections requires that these procedures be performed under fluoroscopic or CT-guided imaging. Therefore, injections for chronic pain performed without imaging guidance will be denied as inappropriate and not reasonable or necessary.

ICD-9 Codes that Support Medical Necessity
337.20 Reflex sympathetic dystrophy unspecified
337.21 Reflex sympathetic dystrophy of the upper limb
337.22 Reflex sympathetic dystrophy of the lower limb
337.29 Reflex sympathetic dystrophy of other specified site
353.2 Cervical root lesions not elsewhere classified
353.3 Thoracic root lesions not elsewhere classified
353.4 Lumbosacral root lesions not elsewhere classified
354.4 Causalgia of upper limb
355.0 Lesion of sciatic nerve
355.71 Causalgia of lower limb
722.0 Displacement of cervical intervertebral disc without myelopathy
722.10 Displacement of lumbar intervertebral disc without myelopathy
722.11 Displacement of thoracic intervertebral disc without myelopathy
722.71 Intervertebral disc disorder with myelopathy cervical region
722.72 Intervertebral disc disorder with myelopathy thoracic region
722.73 Intervertebral disc disorder with myelopathy lumbar region
722.81 Postlaminectomy syndrome of cervical region
722.82 Postlaminectomy syndrome of thoracic region
722.83 Postlaminectomy syndrome of lumbar region
723.0 Spinal stenosis in cervical region
723.4 Brachial neuritis or radiculitis nos
724.01 Spinal stenosis of thoracic region
724.02 Spinal stenosis of lumbar region
724.4 Thoracic or lumbosacral neuritis or radiculitis unspecified

ICD-9 Codes that DO NOT Support Medical Necessity
724.2 Lumbago
724.5 Backache unspecified
729.0 Rheumatism unspecified and fibrositis
729.1 Myalgia and myositis unspecified
729.2 Neuralgia neuritis and radiculitis unspecified
729.5 Pain in limb

729.9 Other and unspecified disorders of soft tissue
Frequency and Number of Injections or Interventions:
In the diagnostic phase, a patient may receive injections at intervals of no sooner than one week or preferably, two weeks, except for blockade in cancer pain. The number of injections in the diagnostic phase should be limited to no more than two times. Once a structure is proven to be negative, no repeat interventions should be directed at that structure unless there is a new clinical presentation with symptoms, signs, and diagnostic studies of known reliability and validity that implicate the structure. The effect of injected corticosteroids may remain for several weeks. The benefit is attributed to a decrease of local inflammation and perhaps some local anesthetic effect. It is usually not necessary to repeat an injection if there has been a satisfactory response to the first injection. Patients who relapse after a satisfactory response may be candidates for another trial after an appropriate interval. Consideration should be given to the cumulative dose injected and limitations made to avoid steroid complications. In the therapeutic phase (after the diagnostic phase is completed), the frequency of interventional techniques should be two months or longer between each injection, provided that at least >50% relief is obtained for six to eight weeks. The therapeutic frequency must remain at least two months or longer for each region.
In the treatment or therapeutic phase, the interventional procedures should be repeated only as medically necessary. No more than four therapeutic injections of any type (interlaminar or caudal epidural, transforaminal epidural, paravertebral facet joint or nerve, and/or sacroiliac joint) per region per patient per year are anticipated for the majority of patients. Under unusual circumstances with a recurrent injury, carcinoma, or reflex sympathetic dystrophy, blocks may be repeated more frequently in the treatment phase after diagnosis/stabilization.

Rating: 8a

Cohen M, Wolfe R, Mai T, Lewis D. A randomized, double blind, placebo controlled trial of a topical cream containing glucosamine sulfate, chondroitin sulfate, and camphor for osteoarthritis of the knee. J Rheumatol. 2003 Mar;30(3):523-8.

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OBJECTIVE: To assess the ability of a topical preparation of glucosamine sulfate and chondroitin sulfate to reduce pain related to osteoarthritis (OA) of the knee. METHODS: Sixty-three patients were randomized to receive either a topical glucosamine and chondroitin preparation or placebo to be used as required over an 8 week period. Efficacy was assessed using a visual analog scale (VAS) for pain as well as the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), and the SF-36 questionnaire. RESULTS: VAS scores indicated a greater mean reduction in pain for the glucosamine/chondroitin preparation group (mean change -3.4 cm, SD 2.6 cm) compared to the placebo group (mean change -1.6 cm, SD 2.7 cm) after 8 weeks. After 4 weeks the difference between active and

placebo groups in their mean reduction from baseline was 1.2 (95% CI 0.1 to 2.4, p = 0.03) and after 8 weeks was 1.8 (95% CI for difference between groups, 0.6 to 2.9 cm; p = 0.002). CONCLUSION: Topical application of glucosamine and chondroitin sulfate is effective in relieving the pain from OA of the knee and improvement is evident within 4 weeks.

Publication Types:
Clinical Trial
Randomized Controlled Trial

PMID: 12610812

Rating: 2b

Collins SL, Moore RA, McQuayHJ, Wiffen P. Antidepressants and anticonvulsants for diabetic neuropathy and postherpetic neuralgia: a quantitative systematic review. J Pain Symptom Manage. 2000 Dec;20(6):449-58.

Pain Research, Nuffield Department of Anaesthetics, University of Oxford, Oxford Radcliffe Hospital, Headington, United Kingdom.

To determine the relative efficacy and adverse effects of antidepressants and anticonvulsants in the treatment of diabetic neuroapathy and postherpetic neuralgia, published reports were identified from a variety of electronic databases, including Medline, EMBASE, the Cochrane Library and the Oxford Pain Relief Database, and from two previously published reviews. Additional studies were identified from the reference lists of retrieved reports. The relative benefit (RB) and number-needed-to-treat (NNT) for one patient to achieve at least 50 % pain relief was calculated from available dichotomous data, as was the relative risk (RR) and number-needed-to-harm (NH) for minor adverse effects and drug related study withdrawal. In diabetic neuropathy, 16 reports compared antidepressants with placebo (491 patient episodes) and three compared anticonvulsants with placebo (321). The NNT for at least 50 % pain relief with antidepressants was 3.4 (95 % confidence interval 2.6-4. 7) and with anticonvulsants 2. 7 (2. 2-3. 8). In postherpetic neuralgia, three reports compared antidepressants with placebo (145 patient episodes) and one compared anticonvulsants with placebo (225), giving an NNT with antidepressants of 2.1 (1. 7-3) and with anticonvulsants 3.2 (2.4-5). There was little difference in the incidence of minor adverse effects with either antidepressants or anticonvulsants compared with placebo, with 1VH (minor) values of about 3. For drug-related study withdrawal, antidepressants had an NNH (major) of 17 (11-43) compared with placebo, whereas with anticonvulsants there was no significant difference from placebo. Antidepressants and anticonvulsants had the same efficacy and incidence of minor adverse effects in these two neuropathic pain conditions. There was no evidence that selective serotonin reuptake inhibitors (SSRIs) were better than older antidepressants, and no evidence that gabapentin was better than older anticonvulsants. In these trials patients were more likely to stop taking antidepressants than anticonvulsants because of adverse effects.

Publication Types:
Review

PMID: 11131263

Rating: 2b

Colombo B, Annovazzi PO, Comi G. Medications for neuropathic pain: current trends. Neurol Sci. 2006 May;27 Suppl 2:s183-9.

Department of Neurology, Headache Center, IRCCS San Raffaele Hospital, Via Olgettina 48, I-20132, Milan, Italy.

Neuropathic pain is by definition a chronic pain condition that occurs and persists in a heterogeneous group of aetiologically different diseases characterised by a primary lesion or dysfunction of the peripheral or central nervous system. Neuropathic pain has an important prevalence in the general population, and a severe impact on quality of life and mood of affected patients. Therapy is based on tricyclic antidepressants and antiepileptic drugs, the most frequently studied drug classes. Opioids and analgesics are a second-line choice. Topical medications could be useful in several pain situations.

PMID: 16688627

Rating: 5b

Compton P, Darakjian J, Miotto K. Screening for addiction in patients with chronic pain and "problematic" substance use: evaluation of a pilot assessment tool. J Pain Symptom Manage. 1998 Dec;16(6):355-63.

UCLA School of Nursing 90095-6918, USA.

Assessing for the presence of addiction in the chronic pain patient receiving chronic opioid analgesia is a challenging clinical task. This paper presents a recently developed screening tool for addictive disease in chronic pain patients, and pilot efficacy data describing its ability to do so. In a small sample of patients (n = 52) referred from a multidisciplinary pain center for "problematic" medication use, responses to the screening questionnaire were compared between patients who met combined diagnostic criteria for a substance use disorder and those who did not, as assessed by a trained addiction medicine specialist. Responses of addicted patients significantly differed from those of nonaddicted patients on multiple screening items, with the two groups easily differentiated by total questionnaire score. Further, three key

screening indicators were identified as excellent predictors for the presence of addictive disease in this sample of chronic pain patients.

PMID: 9879160

Rating: 4b

Condon JE, Borg-Stein J, Revord J et al. A multicenter trial of percutaneous neuromodulation therapy for low back pain patients with a subacute duration of lower extremity pan. Presented at the American Academy of Pain Medicine Annual Meeting. San Francisco, CA, March 1, 2002

From its description, neuromodulation appears to be a variant of PENS, varying in length of the needle and its placement at specific anatomical landmarks, instead of specifically at the site of pain. A literature search identified 1 abstract focusing on neuromodulation. This study was an uncontrolled case series of 83 patients with low back pain. While pain improved at 5-week follow-up, the lack of a control group precludes scientific assessment. Two additional earlier abstracts describe studies examining the importance of electrode placement for effective neuromodulation therapy. These preliminary reports do not offer data on outcomes in pain management.
Rating: 10c

Cook AJ; Chastain DC. The classification of patients with chronic pain: age and sex differences. Pain Research & Management. 2001 Fall; 6(3): 142-51.
Abstract:
OBJECTIVE: To further develop an empirically based classification system for chronic pain patients through the examination of age and sex differences, and incorporation of pain duration in the grouping algorithm. SUBJECTS: Three hundred seventy-four chronic pain patients (300 aged 13 to 59 years; 74 aged 60 to 89 years) assessed at an outpatient, multidisciplinary pain management centre. METHODS: Patients completed measures of demographic and descriptive information, pain intensity (box rating scale), perceived disability (modified Pain Disability Index) and affective distress (Symptom Checklist-90 Revised) before multidisciplinary treatment. Standardized scores from the assessment measures were entered into a series of hierarchical, multivariate cluster analyses to identify underlying patient subgroups. RESULTS: Age-based patient groupings from prior research were partially replicated. Significant differences in clinical presentations were observed across age and sex groups. Pain duration was found to make an important contribution to the patient groupings. 'Good control' (low pain, disability, distress) and variants of 'chronic pain syndrome' (elevated pain, disability, distress) groupings were identified across all analyses. Two variants of a 'stoic' profile were identified among older patients, with low levels of distress relative to pain and perceived disability. One of these profiles was associated with long pain duration and was found only among males. Several unique clinical profiles were identified for female patients. CONCLUSIONS: There are important age and sex differences in the clinical presentations of chronic pain patients. Some older patients present with unique clinical profiles

that may reflect cohort differences, and/or physiological or psychological adjustment processes. There appears to be a greater number of distinct chronic pain presentations among females. Research on the classification of chronic pain patients within homogeneous diagnostic subgroups is needed.
Major Subjects:

- Aging
- Pain / * classification / epidemiology / * physiopathology / psychology
- Patients / * classification / psychology / statistics & numerical data
- Sex Characteristics

Publication Type: Case Control Study, 374 cases

Corbin L. Safety and efficacy of massage therapy for patients with cancer. Cancer Control. 2005 Jul;12(3):158-64.

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BACKGROUND: As the popularity of complementary/alternative medicine (CAM) grows, patients are incorporating more CAM therapies into their conventional cancer care. Massage therapy, a CAM therapy known primarily for its use in relaxation, may also benefit patients with cancer in other ways. Massage can also be associated with risks in the oncology population. Risks can be minimized and benefits maximized when the clinician feels comfortable discussing CAM with his or her patients. This article reviews and summarizes the literature on massage and cancer to help provide the clinician with information to help facilitate discussions with patients. METHODS: MEDLINE and CINAHL databases were searched to identify relevant articles. These were reviewed for content and other pertinent references. RESULTS: Significant information was extracted from these resources to provide this overview of the use of massage for patients with cancer. CONCLUSIONS: Conventional care for patients with cancer can safely incorporate massage therapy, although cancer patients may be at higher risk of rare adverse events. The strongest evidence for benefits of massage is for stress and anxiety reduction, although research for pain control and management of other symptoms common to patients with cancer, including pain, is promising. The oncologist should feel comfortable discussing massage therapy with patients and be able to refer patients to a qualified massage therapist as appropriate.

PMID: 16062163

Rating: 5b

Correll GE, Maleki J, Gracely EJ, Muir JJ, Harbut RE. Subanesthetic ketamine infusion therapy: a retrospective analysis of a novel therapeutic approach to complex regional pain syndrome. Pain Med. 2004 Sep;5(3):263-75.

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Complex Regional Pain Syndrome (CRPS) is a disorder that can be accompanied by severe pain that is often both chronic and resistant to conventional therapy. Harbut and Correll previously reported the successful treatment of a 9-year case of intractable Type I CRPS with an intravenous inpatient infusion of ketamine in an adult female patient. OBJECTIVE: The purpose of this study was to ascertain if indeed the use of subanesthetic inpatient infusions of ketamine provide meaningful improvements in pain scores, and thus, quality of life, in patients suffering from CRPS. To achieve this objective we focused our analysis on the relief of pain obtained by patients undergoing this novel treatment option developed at Mackay Base Hospital, Queensland, Australia. METHODS: Case notes of 33 patients whose CRPS pain was treated by the inpatient administration of a continuous subanesthetic intravenous infusion of ketamine were reviewed. The dose and duration of ketamine therapy and the degree and duration of relief obtained were recorded. Notable side effects were also recorded. The degree of relief obtained (immediately after the infusion) was assessed using pre- and posttreatment numeric pain scores. The duration of relief obtained (throughout the follow-up period) was analyzed using a Kaplan-Meier cumulative survival curve analysis. RESULTS: A total of 33 patients with diagnoses of CRPS who had undergone ketamine treatment at least once were identified. Due to relapse, 12 of 33 patients received a second course of therapy, and two of 33 patients received a third. The degree of relief obtained following the initial course of therapy was impressive (N=33); there was complete pain relief in 25 (76%), partial relief in six (18%), and no relief in two (6%) patients. The degree of relief obtained following repeat therapy (N=12) appeared even better, as all 12 patients who received second courses of treatment experienced complete relief of their CRPS pain. The duration of relief was also impressive, as was the difference between the duration of relief obtained after the first and after the second courses of therapy. In this respect, following the first course of therapy, 54% of 33 individuals remained pain free for >/=3 months and 31% remained pain free for >/=6 months. After the second infusion, 58% of 12 patients experienced relief for >/=1 year, while almost 33% remained pain free for >3 years. The most frequent side effect observed in patients receiving this treatment was a feeling of inebriation. Hallucinations occurred in six patients. Less frequent side effects also included complaints of lightheadedness, dizziness, and nausea. In four patients, an alteration in hepatic enzyme profile was noted; the infusion was terminated and the abnormality resolved thereafter. CONCLUSION: This retrospective review suggests that limited subanesthetic inpatient infusions of ketamine may offer a promising therapeutic option in the treatment of appropriately selected patients with intractable CRPS. More study is needed to further establish the safety and efficacy of this novel approach.

PMID: 15367304

Rating: 4b

Cowan P, Kelly N. Quality Of Life Scale, A Measure Of Function For People With Pain. The American Chronic Pain Association. 2008

The American Chronic Pain Association has developed a Quality of Life Scale. It is a self-assessment of function for people with pain. ACPA members -- and other persons living with pain -- can use it to track how they're doing over time, and also use it to communicate with their doctors. Pain is a highly personal experience. The degree to which pain interferes with the quality of a person's life is also highly personal. The American Chronic Pain Association Quality of Life Scale looks at ability to function, rather than at pain alone. It can help people with pain and their health care team to evaluate and communicate the impact of pain on the basic activities of daily life. This information can provide a basis for more effective treatment and help to measure progress over time. The scale is meant to help individuals measure activity levels. We recognize that homemakers, parents and retirees often don't work outside the home, but activity can still be measured in the amount of time one is able to "work" at fulfilling daily responsibilities be that in a paid job, as a volunteer, or within the home. With a combination of sound medical treatment, good coping skills, and peer support, people with pain can lead more productive, satisfying lives. The American Chronic Pain Association can help.
0 Non-functioning; Stay in bed all day; feel hopeless and helpless about life
1 Stay in bed at least half the day; Have no contact with outside world
2 Get out of bed but don't get dressed; Stay at home all day.
3 Get dressed in the morning; Minimal activities at home; Contact with friends via phone, email
4 Do simple chores around the house; Minimal activities outside of home two days a week
5 Struggel but fulfill daily home responsibilities; No outside activity; Not able to work / volunteer
6 Work/volunteer limited hours; Take part in limited social activities on weekends
7 Work/volunteer for a few hours daily; Can be active at least 5 hours/day; Can make plans to do simple activities on weekends
8 Work/volunteer for at least 6 hours daily; Have energy to make plans for one evening social activity during the week; Active on weekends
9 Work/volunteer/be active eight hours daily; Take part in family life; Outside social activities limited
10 Normal quality of life; Go to work/volunteer each day; Normal daily activities each day; Have a social life outside of work; Take an active part in family life.

Rating: 8b

Croce RV. The effects of EMG biofeedback on strength acquisition. Biofeedback Self Regul. 1986 Dec;11(4):299-310.

This study investigated the effectiveness of electromyographic (EMG) biofeedback in maximizing strength gains and integrated electromyographic (IEMG) levels of the quadriceps muscle group resulting from an isokinetic exercise program. Twenty-one male volunteers recruited from physical education classes at a large southwestern university were randomly assigned to one of the following three treatment groups: (1) a biofeedback (BF) trained group, (2) a deception (DEC) trained group, and (3) a nonfeedback (NF) trained group. Subjects were trained and tested for strength by extension on a Cybex Isokinetic Exercise Machine at a speed of 30 degrees per second. Training sessions were performed

three times per week for five weeks; pretest and posttest data were based on the best score of three trials of a 1-RM maximum effort. A pretraining to posttraining comparison indicated significant increases in strength (p less than .001) and IEMG levels (p less than .001) for all treatment groups when a paired t test was applied to the data. A multivariate analysis of covariance (MANCOVA) revealed that the BF trained group showed significantly greater peak torque values than DEC and NF trained groups (p less than .01) and produced significantly greater IEMG levels than the NF trained group (p less than .05). Overall, these results were taken as supporting the hypothesis that a training program of combined isokinetics and EMG biofeedback produces significant gains in maximal force and IEMG activity of leg-extensor muscles.

PMID: 3607096

Rating: 2c

Crofford LJ, Rowbotham MC, Mease PJ, Russell IJ, Dworkin RH, Corbin AE, Young JP Jr, LaMoreaux LK, Martin SA, Sharma U; Pregabalin 1008-105 Study Group. Pregabalin for the treatment of fibromyalgia syndrome: results of a randomized, double-blind, placebo-controlled trial. Arthritis Rheum. 2005;52:1264-73.

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OBJECTIVE: Fibromyalgia syndrome (FMS) is characterized by widespread musculoskeletal pain and lowered pain threshold. Other prominent symptoms include disordered sleep and fatigue. FMS affects an estimated 2% of the population, predominantly women. This trial was designed to evaluate the efficacy and safety of pregabalin, a novel alpha(2)-delta ligand, for treatment of symptoms associated with FMS. METHODS: This multicenter, double-blind, 8-week, randomized clinical trial compared the effects of placebo with those of 150, 300, and 450 mg/day pregabalin on pain, sleep, fatigue, and health-related quality of life in 529 patients with FMS. The primary outcome variable was the comparison of end point mean pain scores, derived from daily diary ratings of pain intensity, between each of the pregabalin treatment groups and the placebo group. RESULTS: Pregabalin at 450 mg/day significantly reduced the average severity of pain in the primary analysis compared with placebo (-0.93 on a 0-10 scale) (P </= 0.001), and significantly more patients in this group had >/=50% improvement in pain at the end point (29%, versus 13% in the placebo group; P = 0.003). Pregabalin at 300 and 450 mg/day was associated with significant improvements in sleep quality, fatigue, and global measures of change. Pregabalin at 450 mg/day improved several domains of health-related quality of life. Dizziness and somnolence were the most frequent adverse events. Rates of discontinuation due to adverse events were similar across all 4 treatment groups. CONCLUSION: Pregabalin at 450 mg/day was efficacious for the treatment of FMS, reducing symptoms of pain, disturbed sleep, and fatigue compared with placebo. Pregabalin was well tolerated and improved global measures and health-related quality of life.
PMID: 15818684

Rating: 2b

Cruccu G, Aziz TZ, Garcia-Larrea L, Hansson P, Jensen TS, Lefaucheur JP, Simpson BA, Taylor RS. EFNS guidelines on neurostimulation therapy for neuropathic pain. Eur J Neurol. 2007 Sep;14(9):952-70.

EFNS Panel on Neuropathic Pain, Vienna, Austria. cruccu@uniroma1.it

Pharmacological relief of neuropathic pain is often insufficient. Electrical neurostimulation is efficacious in chronic neuropathic pain and other neurological diseases. European Federation of Neurological Societies (EFNS) launched a Task Force to evaluate the evidence for these techniques and to produce relevant recommendations. We searched the literature from 1968 to 2006, looking for neurostimulation in neuropathic pain conditions, and classified the trials according to the EFNS scheme of evidence for therapeutic interventions. Spinal cord stimulation (SCS) is efficacious in failed back surgery syndrome (FBSS) and complex regional pain syndrome (CRPS) type I (level B recommendation). High-frequency transcutaneous electrical nerve stimulation (TENS) may be better than placebo (level C) although worse than electro-acupuncture (level B). One kind of repetitive transcranial magnetic stimulation (rTMS) has transient efficacy in central and peripheral neuropathic pains (level B). Motor cortex stimulation (MCS) is efficacious in central post-stroke and facial pain (level C). Deep brain stimulation (DBS) should only be performed in experienced centres. Evidence for implanted peripheral stimulations is inadequate. TENS and r-TMS are non-invasive and suitable as preliminary or add-on therapies. Further controlled trials are warranted for SCS in conditions other than failed back surgery syndrome and CRPS and for MCS and DBS in general. These chronically implanted techniques provide satisfactory pain relief in many patients, including those resistant to medication or other means.

PMID: 17718686

Rating: 8b

Curtis CL, Harwood JL, Dent CM, Caterson B, Biological basis for the benefit of nutraceutical supplementation in arthritis, Drug Discov Today. 2004 Feb 15;9(4):165-72.

Cardiff School of Biosciences, Cardiff University, Cardiff CF10 3US, UK.

Arthritis is a common disease in which the end-point results in joint replacement surgery. This article reviews the use of nutraceuticals as alternative treatments for pathological manifestations of arthritic disease. The efficacy of fish oils (e.g. cod liver oil) in the diet has been demonstrated in several clinical trials, animal feeding experiments and in vitro models that mimic cartilage destruction in arthritic disease. In addition, there is some evidence for beneficial effects of other nutraceuticals, such as green

tea, herbal extracts, chondroitin sulphate and glucosamine. However, in most cases, there is little scientific evidence at the cellular and molecular levels to explain their mechanisms of action.

Publication Types:
- Review
- Review, Multicase

PMID: 14960396
Rating: 5b

Cyr MG, Wartman SA. The effectiveness of routine screening questions in the detection of alcoholism. JAMA. 1988 Jan 1;259(1):51-4.

Division of General Internal Medicine, Rhode Island Hospital, Providence 02902.

According to the abstract: 'To assess the prevalence of alcoholism in an ambulatory medical clinic and to determine the effectiveness of screening questions for alcoholism, 232 new patients in a medical primary care unit were interviewed using a questionnaire that included the Michigan Alcoholism Screening Test (MAST). Based on MAST scores, 47 of 232 subjects were designated as alcoholics, yielding a prevalence of alcoholism of 20.3%. Sensitivities and specificities for alcohol-use questions were calculated using the MAST diagnosis of alcoholism. The questions "How much do you drink?" and "How often do you drink?" yielded low sensitivities of 34.0% and 46.8%, respectively. The question "Have you ever had a drinking problem?" considered alone had a high sensitivity of 70.2%; when combined with "When was your last drink?" this question had a sensitivity of 91.5%. We recommend the routine incorporation of these last two questions into the medical history in light of the high prevalence of alcoholism in this outpatient population.'

PMID: 3334771

Rating: 4a

Daniell HW, Lentz R, Mazer NA. Open-label pilot study of testosterone patch therapy in men with opioid-induced androgen deficiency. J Pain. 2006;7:200-10.

Department of Family Practice, University of California Davis Medical School, Redding, California, USA.

We conducted a 24-week open-label pilot study of testosterone (T) patch therapy in 23 men with opioid-induced androgen deficiency (OPIAD). The T dosage was 5 mg/day for the first 12 weeks and 7.5 mg/day for the second 12 weeks. Seven subjects discontinued prematurely: 4 for noncompliance, 2 for skin irritation and 1 for hepatitis C treatment. In the "completers" population (n = 16), mean (SD) free T

levels (normal range 52 to 280 pg/mL) were 28.5 (18.6) pg/mL at baseline, 72.8 (29.6) pg/mL on 5 mg/day (P < .001 vs. baseline), and 120.2 (69.5) pg/mL on 7.5 mg/day (P < .001 vs. baseline and P < .01 vs. 5 mg/day). Total T, dihydrotestosterone, and estradiol showed parallel changes. Sex hormone-binding globulin levels were elevated at baseline and decreased modestly with treatment (P < .05 vs. baseline at 5 mg/day; P < .01 vs. baseline at 7.5 mg/day). Luteinizing hormone levels were in the low-normal range at baseline and suppressed markedly with treatment (P < .001 vs. baseline at both doses). Androgen deficiency symptoms (ADSQ), sexual function (Watts SFQ), mood (PGWB), depression (BDI-II), and hematocrit levels showed improvement during treatment, generally more so at the 7.5 mg/day dosage (P < .001 vs. baseline for most parameters). Pain scores (BPI-SF) decreased slightly on 7.5 mg/day (interference score: P < .05 vs. baseline and 5 mg/day); the use of opioids did not change appreciably. The testosterone patches were generally well tolerated. PERSPECTIVE: Long-acting opioid preparations suppress the hypothalamic-pituitary-gonadal axis in men and produce a symptomatic state of opioid-induced androgen deficiency (OPIAD). Testosterone patch therapy at a dose of 7.5 mg/day normalizes hormone levels and appears to improve a number of quality of life parameters (eg, sexual function, well-being, mood) in men with OPIAD.

PMID: 16516826Finch PM,

Rating: 4c

Dart RC, Bailey E. Does therapeutic use of acetaminophen cause acute liver failure? Pharmacotherapy. 2007;27:1219-30.

Rocky Mountain Poison and Drug Center, Denver Health and Hospital Authority, Denver, Colorado 80204, USA. rdart@rmpdc.org

CONCLUSION: Prospective studies indicated that repeated use of a true therapeutic acetaminophen dosage may slightly increase the level of serum aminotransferase activity, but hepatic failure or death was not reported. Retrospective reports indicated a higher rate of increased serum aminotransferase levels, and several reported associated liver injury and death. The differing results and presence of evidence indicating inaccurate acetaminophen dosage information in some case reports suggests that these cases may be inadvertent overdoses, rather than true therapeutic dosages.

PMID: 17723075

Rating: 1b

Davies RA, Maher CG, Hancock MJ. A systematic review of paracetamol for non-specific low back pain. Eur Spine J. 2008 Sep 17. [Epub ahead of print]

Back Pain Research Group, University of Sydney, Sydney, Australia.

The objective of this study was to assess the efficacy of paracetamol (acetaminophen) in the treatment of pain and disability in patients with non-specific low back pain. No trial reported a statistically significant difference in favor of paracetamol. There is insufficient evidence to assess the efficacy of paracetamol in patients with low back pain.

PMID: 18797937

Rating: 1c

Day M. Sympathetic blocks: the evidence. Pain Pract. 2008. 8:98-109

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The sympathetic nervous system has been implicated in numerous pain syndromes ranging from neuropathic pain to vascular pain to visceral pain. In light of this, sympathetic ganglia have been the target of local anesthetic blockade to determine the sympathetic role in the transmission of pain. If analgesia is afforded with local anesthetic blockade, chemical or thermal neurolysis have been utilized to attempt to provide long-term relief. Despite frequent use of minimally invasive sympathetic blocks and neurolysis by pain practitioners, their efficacy for providing analgesia has been sparsely reported in the literature. Many case reports and case series have been published, but few placebo-controlled, blinded studies exist. This manuscript will review the literature on sympathetic blocks and summarize existing studies for each of the sympathetic blocks. The goal is to provide past, current, and future pain physicians with evidence that they can use to provide appropriate care for their patients.
PMID: 18366465

Rating: 1c

DEA (Drug Enforcement Administration). Policy Statement: Dispensing Controlled Substances for the Treatment of Pain. 2006

SUMMARY: On January 18, 2005, DEA published in the Federal Register a solicitation of comments on the subject of dispensing controlled substances for the treatment of pain. Many of the comments that DEA received asked the agency to elaborate on the legal requirements and agency policy relating to this subject. This document provides such information.

Rating: 6a

De Benedittis G, Massei R. Serotonin precursors in chronic primary headache. A double-blind cross-over study with L-5-hydroxytryptophan vs. placebo. J Neurosurg Sci. 1985 Jul-Sep;29(3):239-48.

A double-blind cross-over study has been carried out in 31 patients. We conclude that L-5-HTP is a medication of moderate efficacy and remarkable safety, providing us with another alternative approach to CPH prophylaxis.

PMID: 3913752

Rating: 2c

Deer TR. Current and future trends in spinal cord stimulation for chronic pain. Curr Pain Headache Rep. 2001 Dec;5(6):503-9.

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Spinal cord stimulation (SCS) is a reversible treatment for chronic pain that is gaining favor as a first-line therapy for many disease states. Because there are no addictive issues and no side effects systemically, the treatment is moving up the treatment continuum ladder. First used clinically in 1967, the procedure was used exclusively for failed back surgery syndrome. Over the past 30 years selection criteria, psychologic screening, and technology have improved. These advances have broadened the treatment options for many patients in pain. This review focuses on the selection, indications, techniques, new advances, complications, and outcomes involved with SCS. A review is provided for the treatment of radiculitis, failed back surgery syndrome, complex regional pain syndrome, peripheral neuropathies, pelvic pain, occipital neuralgia, angina, ischemic extremity pain, and spasticity. Technologic advances such as multi-lead and multi-electrode arrays are also discussed in regard to the impact these developments have on the clinical application of the therapy.

Publication Types:
- Review
- Review, Tutorial

PMID: 11676884
Rating: 5b

Deer T, Chapple I, Classen A, et al. Intrathecal Drug Delivery for Treatment of Chronic Low Back Pain: Report From the National Outcomes Registry for Low Back Pain. Pain Med 2004;5:6-13.

Background. Low back pain is one of the most common and costly musculoskeletal problems in the United States, affecting 60% to 80% of adults and becoming a chronic problem in 5% to 10% of patients. For 2 decades, implantable drug-delivery systems (IDDSs) have been in use for the

management of intractable pain. An IDDS consists of an infusion pump that is placed in a subcutaneous pocket of the abdomen and a catheter that is inserted into the intrathecal space of the spine and tunneled under the skin to connect to the pump. Potential benefits of intrathecal drug delivery include reductions in drug dose due to direct administration, less need for oral medication, and improved ability to perform activities of daily living. To date, there has been a paucity of information on long-term patient outcomes with IDDS. The National Outcomes Registry of Low Back Pain was created to collect prospective data on patients with chronic low back pain who underwent a screening or trial for an IDDS.
Results. Centers that participated in this study were clinically experienced in the use of IDDS and completed data collection at trial registration and 6- and 12-month follow-up periods. Thirty-six physicians enrolled 166 patients for trialing (ie, evaluation with a temporary intraspinal analgesic for adequacy of pain relief and acceptable side effects) with IDDS. Patients who were trialed for IDDS had chronic low back pain with or without leg pain, but with greater back pain than leg pain. A total of 154 patients (93%) succeeded in qualifying and 136 (82%) patients were implanted. At 12 months, numeric back-pain ratings for these patients decreased by 48% and leg-pain ratings declined by 32% (Table). The overall pain reduction was 58% at 6 months and 62% at 12 months. Oswestry low back pain disability scores showed that by 6 and 12 months, the percentages in the minimal-to-moderate disability range had increased to 65% and 73%, respectively, whereas the percentages of patients with severe disability had declined to 30% and 22%, respectively. Furthermore, at 12 months, 87% of the IDDS patients described their quality of life as fair to excellent, and 87% said they would repeat the implant procedure.
Commentary. Although the report is promising and illustrates the importance of longitudinal outcome studies, the follow-up rates fell to 79% at 6 months and 56% at 12 months. The attrition rate not only limits efficacy analyses but also the recognition of complication rates (ie, infection, dislodging, and cerebrospinal fluid leak) that are likely to rise with time in these procedures. As the Editor-in-Chief Rollin Gallagher, MD, MPH, points out in his editorial, given the difficulty of conducting double-blind, placebo-controlled trials of surgical procedures, a prospective open-label design may be the best that can be achieved and hence the importance of robust follow-up. One hopes the National Registry method will allow for future studies of predictors and treatment effects and suggest types of patients who might benefit from earlier intervention.

Publication Type:
Clinical Trial

Rating: 3b

Deer T, Krames ES, Hassenbusch SJ, Burton A, Caraway D, Dupen S, Eisenach J, Erdek M, Grigsby E, Kim P, Levy R, McDowell G, Mekhail N, Panchal S, Prager J, Rauck R, Saulino M, Sitzman T, Staats P, Stanton-Hicks M, Stearns L, Willis KD, Witt W, Follett K, Huntoon M, Liem L, Rathmell J, Wallace M, Buchser E, Cousins M, Ver Donck A. Polyanalgesic Consensus Conference 2007: Recommendations for the Management of Pain by Intrathecal (Intraspinal) Drug Delivery: Report of an Interdisciplinary Expert Panel. Neuromodulation: Technology At The Neural Interface. Volume 10, Number 4, 2007, p. 300-328.

Timothy Deer, MD, West Virginia University, 400 Court Street, Suite 304, Charleston, WV 25301, USA. E-mail: DocTDeer@aol.com

Background: Expert panels of physicians and nonphysicians in the field of intrathecal therapies convened in 2000 and 2003 to make recommendations for the rational use of intrathecal analgesics based on the preclinical and clinical literature known up to those times. An expert panel of physicians convened in 2007 to update previous recommendations and to form guidelines for the rational use of intrathecal opioid and nonopioid agents. Methods: A review of preclinical and clinical published relevant studies from 2000 to 2006 was undertaken and disseminated to a convened expert panel of physicians and nonphysicians. Focused discussions were held on the rational use of intrathecal agents and a survey asking questions regarding intrathecal therapies management was given to the panelists. Results: The panelists, after review of the literature from 2000 to 2006 and discussion, created an updated algorithm for the rational use of intrathecal opioid and nonopioid agents in patients with nonmalignant and end-of-life pain. Of note is that the panelists felt that ziconotide, based on new and relevant literature and experience, should be updated to a line one intrathecal drug.

Rating: 8b

Note: Neurmodualtion has not yet been accepted for inclusion in MEDLINE, and this "conference" was sponsored by Elan, the manufacturer of Prialt (ziconotide).
Other comments: On pages 313 and 314 it appears the Panel of Experts moved this medication to level 1 based on the following:
1. (Reference 165). This was a case study of one subject (age 13 years) with CRPS.
2. (Reference 169). This study weaned all patients from IT drugs and replaced them with systemic opioids. Clinical judgment was used for this part of the protocol. Inclusion protocol was "severe chronic pain." The double-blind treatment period was 3 weeks. The mean oral morphine equivalents per patient were around 300 mg. At week 1 the difference in pain relief was statistical, but this was not found at week 2. At week 3 the proportion of treatment responders did not differ significantly between the two groups. This was the 3rd double blind, placebo controlled study with Prialt that formed the basis of the recent approval by the FDA.
3. (Reference 166): not listed on PubMed
On page 320 it was noted that Prialt was given a "special box" reference due to limited/targeted use and wide panel of known adverse effects. There is no discussion of dose escalation or opioid hyperalgesia (in reference to morphine). The use of an admixture of morphine and Prialt was based on reference 173, an abstract presentation. The conference was not only supported by Elan but the document clearly was directed at supporting Prialt. The participants are all highly ethical individuals but the document does not represent EBM. The main problem with the Polyanalgesic Conference recommendations is the support by Elan. As an outsider looking at their recommendations, this would appear to potentially undermine some of their suggestions.

Dell'Osso B, Altamura AC, Mundo E, Marazziti D, Hollander E. Diagnosis and treatment of obsessive-compulsive disorder and related disorders. Int J Clin Pract. 2007;61:98-104.

Department of Psychiatry, Compulsive, Impulsive and Anxiety Disorders Program, Mount Sinai School of Medicine, New York, NY, USA. bernardo.dellosso@mssm.edu

Obsessive-compulsive disorder (OCD) is currently recognised as one of the most common psychiatric disorders as well as one of the most disabling of all medical disorders. Obsessive-compulsive related disorders (OCRDs), often comorbid with OCD, include many distinct psychiatric conditions (i.e. some somatoform disorders, eating disorders, impulse control disorders and some neurological conditions) which have overlapping symptoms and compulsive qualities with OCD. Although effective treatments exist, OCD and related disorders are often underdiagnosed and undertreated. Serotonin reuptake inhibitors (SRIs) and cognitive behavioural therapy (CBT) represent the first-line treatment for OCD and related disorders. However, the time and the doses of the medications used in the treatment of OCD and related disorders differ from those recommended in depressive disorders. In addition, remission is not common for patients with OCD and related disorders in clinical practice, and poor responders as well as refractory cases may benefit from different treatment strategies including integrated treatment, pharmacological augmentation and brain stimulation techniques.

PMID: 17229184

Rating: 5c

Dersh J, Gatchel RJ, Mayer T, Polatin P, Temple OR. Prevalence of psychiatric disorders in patients with chronic disabling occupational spinal disorders. Spine. 2006 May 1;31(10):1156-62.

PRIDE Research Foundation, Dallas, TX, USA.

STUDY DESIGN: A prevalence study. OBJECTIVES: To assess the prevalence of psychiatric disorders among a large group of patients with chronic disabling occupational spinal disorders (CDOSDs), using a reliable and valid diagnostic instrument. SUMMARY OF BACKGROUND DATA: Although unrecognized and untreated psychiatric disorders have been found to interfere with successful treatment of CDOSD patients, little data are currently available regarding the psychiatric characteristics of patients claiming work-related injuries that result in CDOSDs. METHODS: Psychiatric disorders in a consecutive group of CDOSD patients (n = 1,323) attending a tertiary referral center for patients with CDOSD were diagnosed using the Diagnostic and Statistical Manual of Mental Disorders. RESULTS.: Overall prevalence of psychiatric disorders was found to be significantly elevated in CDOSD patients compared with base rates in the general population. A majority (65%) of patients were diagnosed with at least one current disorder (not including Pain Disorder, which is nearly universal in this population), compared with only 15% of the general population. Major Depressive Disorder (56%), Substance Use Disorders (14%), Anxiety Disorders (11%), and Axis II Personality Disorders (70%) were the most

common diagnoses. CONCLUSIONS: Clinicians treating CDOSD patients must be aware of the high prevalence of psychiatric disorders in this population. They must also be prepared to use mental health professionals to assist them in identifying and stabilizing these patients. Failure to follow a biopsychosocial approach to treatment will likely contribute to prolonged disability in a substantial number of these chronic pain patients.

PMID: 16648753

Rating: 4a

Dersh J, Gatchel RJ, Polatin P, Mayer T. Prevalence of psychiatric disorders in patients with chronic work-related musculoskeletal pain disability. J Occup Environ Med. 2002 May;44(5):459-68.

PRIDE Research Foundation, Dallas, TX, USA.

The cost and prevalence of chronic work-related musculoskeletal pain disability in industrialized countries are extremely high. Although unrecognized psychiatric disorders have been found to interfere with the successful rehabilitation of these disability patients, few data are currently available regarding the psychiatric characteristics of patients claiming work-related injuries that result in chronic disability. To investigate this issue, a consecutive group of patients with work-related chronic musculoskeletal pain disability (n = 1595), who started a prescribed course of tertiary rehabilitation, were evaluated. Psychiatric disorders were diagnosed according to the Diagnostic and Statistical Manual of Mental Disorders. Results revealed that overall prevalences of psychiatric disorders were significantly elevated in these patients compared with base rates in the general population. A majority (64%) of patients were diagnosed with at least one current disorder, compared with only 15% of the general population. However, prevalences of psychiatric disorders were elevated in patients only after the work-related disability. Such findings suggest that clinicians treating these patients must be aware of the high prevalence of psychiatric disorders and be prepared to use mental health professionals to assist in identifying and stabilizing these patients. Failure to follow a biopsychosocial approach to treatment will likely contribute to prolonged pain disability in a substantial number of these patients.

PMID: 12024691

Rating: 4a

Deshpande A, Furlan A, Mailis-Gagnon A, Atlas S, Turk D. Opioids for chronic low-back pain. Cochrane Database Syst Rev. 2007;(3):CD004959.

University Health Network, TWH-Comprehensive Pain Unit, 399 Bathurst St, 4th Floor, Toronto, Ontario, Canada, M5T 2S8. adeshpan@uhnres.utoronto.ca

BACKGROUND: The use of opioids in the long-term management of chronic low-back pain (LBP) appears to be increasing. Despite this trend, the benefits and risks of these medications remain unclear. OBJECTIVES: To determine the efficacy of opioids in adults with chronic LBP. SEARCH STRATEGY: We electronically searched CENTRAL, CINAHL and PsycINFO to May 2006; MEDLINE and EMBASE to May 2007. We supplemented our search by reviewing references in relevant systematic reviews and identified trials. SELECTION CRITERIA: We included randomized or quasi-randomized controlled trials assessing the use of opioids (as monotherapy or in combination with other therapies) for longer than four weeks, in adults with chronic LBP. Studies were included if they compared non-injectable opioids to other treatments. Comparisons between opioids were excluded. DATA COLLECTION AND ANALYSIS: Two authors independently assessed methodological quality and extracted data onto a pre-designed form. Results were statistically pooled using RevMan 4.2. We reported on pain and function using standardized mean difference (SMD) with 95% confidence interval (95% CI) and on side effects using absolute risk difference (RD) with 95% CI. MAIN RESULTS: We included four trials. Three compared tramadol to placebo. Pooled results revealed that tramadol was more effective than placebo for pain relief, SMD 0.71 (95% CI 0.39 to 1.02), and improving function, SMD 0.17 (95% CI 0.04 to 0.30). The two most common side effects of tramadol were headaches, RD 9% (95% CI 6% to 12%) and nausea, RD 3% (95% CI 0% to 6%). One trial comparing opioids to another analgesic (naproxen) found opioids were statistically significant for relieving pain but not improving function. When re-calculated, the results were not statistically significant for either pain relief (SMD -0.58; 95% CI -1.42 to 0.26) or improving function (SMD -0.06; 95% CI -0.88 to 0.76) . AUTHORS' CONCLUSIONS: Despite concerns surrounding the use of opioids for long-term management of chronic LBP, there remain few high-quality trials assessing their efficacy. The trials in this review, although achieving high internal validity scores, were characterized by a lack of generalizability, inadequate description of study populations, poor intention-to treat analysis, and limited interpretation of functional improvement. Based on our results, the benefits of opioids in clinical practice for the long-term management of chronic LBP remains questionable. Therefore, further high-quality studies that more closely simulate clinical practice are needed to assess the usefulness, and potential risks, of opioids for individuals with chronic LBP.

PMID: 17636781

Rating: 1c

Diaz RL, Gardeazabal J, Manrique P, Ratón JA, Urrutia I, Rodríguez-Sasiain JM, Aguirre C. Greater allergenicity of topical ketoprofen in contact dermatitis confirmed by use. Contact Dermatitis. 2006;54:239-43.

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The use of topical non-steroidal anti-inflammatory drugs (NSAIDs) is very popular in spite of their doubtful efficacy and high number of generally not serious, but preventable, adverse effects, especially

photoallergy. The allergenic potential of different topical NSAIDs was determined by performing a retrospective observational study of the period 1996-2001 and comparing the cases of allergy and photoallergy with the use of each topical NSAID. The diagnoses were obtained from a review of the clinical records of patch/photopatch testing carried out in the dermatology departments of 2 public hospitals in Bizkaia (Spain). The use of the different topical NSAIDs was obtained from invoices sent to the National Health System and the Reporting odds ratio (ROR) and Proportional reporting ratio (PRR) disproportionality estimates of the FEDRA database of the Spanish Pharmacovigilance System. A total of 139 contact reactions to topical NSAIDs were found with ketoprofen being responsible for 28% of the allergies and 82% of the contact photoallergies in spite of not being the most used topical NSAID (third in the ranking, diclofenac was the first). The ROR for ketoprofen was 3.9 (2.4-6.4) and the PRR 3.4 (2.1-5.5), thus confirming the possibility of a warning signal. The results support the need for regulatory action on topical ketoprofen.

PMID: 16689806

Rating: 4b

Ducharme J, Acute pain and pain control: State of the art, Annals of Emergency Medicine, Volume 35, Number 6, June 2000
Recognition and treatment of pain in the emergency department has undergone an evolution in the past decade. Emergency clinicians, educators, and researchers have begun to address the undertreatment of pain as well as challenge the long-standing dogmas concerning pain treatment. Well-described barriers, both psychological and educational, contribute to our providing inadequate pain relief. This state-of-the-art update describes the current perception of our practice with regard to pain relief and how it can be modified. Pain and pain control is such a broad and complex topic that only new advances and important principles relevant to the practice of emergency medicine are presented. Headache, pediatric pain, and procedural sedation and analgesia are not covered in this article as they will be addressed in future state-of-the-art articles.

Dworkin RH, Backonja M, Rowbotham MC, Allen RR, Argoff CR, Bennett GJ, Bushnell MC, Farrar JT, Galer BS, Haythornthwaite JA, Hewitt DJ, Loeser JD, Max MB, Saltarelli M, Schmader KE, Stein C, Thompson D, Turk DC, Wallace MS, Watkins LR, Weinstein SM. Advances in neuropathic pain: diagnosis, mechanisms, and treatment recommendations. Arch Neurol. 2003 Nov;60(11):1524-34.

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Chronic neuropathic pain, caused by lesions in the peripheral or central nervous system, comes in many forms. We describe current approaches to the diagnosis and assessment of neuropathic pain and discuss the results of recent research on its pathophysiologic mechanisms. Randomized controlled clinical trials

of gabapentin, the 5% lidocaine patch, opioid analgesics, tramadol hydrochloride, and tricyclic antidepressants provide an evidence-based approach to the treatment of neuropathic pain, and specific recommendations are presented for use of these medications. Continued progress in basic and clinical research on the pathophysiologic mechanisms of neuropathic pain may make it possible to predict effective treatments for individual patients by application of a pain mechanism-based approach.

Publication Types:
Review

PMID: 14623723

Rating: 5a

Dworkin RH, O'connor AB, Backonja M, Farrar JT, Finnerup NB, Jensen TS, Kalso EA, Loeser JD, Miaskowski C, Nurmikko TJ, Portenoy RK, Rice AS, Stacey BR, Treede RD, Turk DC, Wallace MS. Pharmacologic management of neuropathic pain: Evidence-based recommendations. Pain. 2007 Oct 5; [Epub ahead of print]

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Patients with neuropathic pain (NP) are challenging to manage and evidence-based clinical recommendations for pharmacologic management are needed. Systematic literature reviews, randomized clinical trials, and existing guidelines were evaluated at a consensus meeting. Medications were considered for recommendation if their efficacy was supported by at least one methodologically-sound, randomized clinical trial (RCT) demonstrating superiority to placebo or a relevant comparison treatment. Recommendations were based on the amount and consistency of evidence, degree of efficacy, safety, and clinical experience of the authors. Available RCTs typically evaluated chronic NP of moderate to severe intensity. Recommended first-line treatments include certain antidepressants (i.e., tricyclic antidepressants and dual reuptake inhibitors of both serotonin and norepinephrine), calcium channel alpha2-delta ligands (i.e., gabapentin and pregabalin), and topical lidocaine. Opioid analgesics and tramadol are recommended as generally second-line treatments that can be considered for first-line use in select clinical circumstances. Other medications that would generally be used as third-line treatments but that could also be used as second-line treatments in some circumstances include certain antiepileptic and antidepressant medications, mexiletine, N-methyl-d-aspartate receptor antagonists, and topical capsaicin. Medication selection should be individualized, considering side effects, potential beneficial or deleterious effects on comorbidities, and whether prompt onset of pain relief is necessary. To date, no medications have demonstrated efficacy in lumbosacral radiculopathy, which is probably the most common type of NP. Long-term studies, head-to-head comparisons between medications, studies involving combinations of medications, and RCTs examining treatment of central NP are lacking and should be a priority for future research.

PMID: 17920770

Rating: 1b

Dyck PJ, Norell JE, Dyck PJ. Non-diabetic lumbosacral radiculoplexus neuropathy: natural history, outcome and comparison with the diabetic variety. Brain. 2001 Jun;124(Pt 6):1197-207.

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Diabetic lumbosacral radiculoplexus neuropathy (DLSRPN) (other names include diabetic amyotrophy) is well recognized, unlike the non-diabetic lumbosacral radiculoplexus neuropathy (LSRPN), which has received less attention. Our objective was to characterize the natural history and outcome of LSRPN and to assess whether it is similar to the diabetic variety in its symptoms, course, electrophysiological features, quantitative sensory and autonomic findings, and the underlying pathophysiology. We studied 57 patients with LSRPN and 33 patients with DLSRPN. We found that the age of onset, course, kind and distribution of symptoms and impairments, laboratory findings and outcomes are essentially alike. Both disorders are a lumbosacral plexus neuropathy associated with weight loss, often beginning focally or asymmetrically in the thigh or leg but usually progressing to involve the initially unaffected segment and the contralateral side. Both have prolonged morbidity due to pain, paralysis, autonomic involvement and sensory loss. In biopsied distal LSRPN nerves, we found changes similar to those found in DLSRPN-alterations typical of ischaemic injury and of microvasculitis. The long-term outcome was determined in 42 LSRPN patients: two had become diabetic, seven had relapsed and only three had recovered completely, although all had improved. We conclude that: (i) LSRPN is a subacute, asymmetrical, painful and debilitating neuropathy of the lower limbs associated with weight loss, and we think it is under-recognized; (ii) recovery from the long-term impairments of LSRPN is usually delayed and incomplete and only a small minority of patients develop diabetes mellitus; (iii) LSRPN mirrors the diabetic variety in its clinical features, course, pathological findings (ischaemic injury from microvasculitis) and long-term outcome; and (iv) LSRPN should be set apart from chronic inflammatory demyelinating polyradiculoneuropathy and from systemic necrotizing vasculitis. We infer an autoimmune basis for LSRPN and emphasize the need for controlled trials of immune-modulating therapy.

PMID: 11353735

Rating: 4b

Dysvik E, Natvig GK, Eikeland OJ, Brattberg G. Results of a multidisciplinary pain management program: a 6- and 12-month follow-up study. Rehabil Nurs. 2005 Sep-Oct;30(5):198-206.

Faculty of Social Sciences, Department of Health Studies, University of Stavanger, Norway. elin.dysvik@uis.no

The aim of this study was to evaluate an 8-week multidisciplinary pain management program offered to patients suffering from chronic pain. The study initially included 88 participants, and 61 of the sample completed a follow-up program conducted at 6 and 12 months after the initial programs. The pain management program was based on a cognitive behavioral approach with active patient participation in learning new coping skills. The intervention consisted of supervised dialog, physical activity, and education. The main goals were change of focus from pain and disability to resources and functional coping strategies. It was hypothesized that the positive changes gained at posttest registration after an 8-week program on coping, health-related quality of life, and pain intensity would be maintained during follow-up sessions. The results indicated that these hypotheses were mainly supported and further pain reduction, decreased emotion-focused coping, better social functioning, and overall physical and mental health gains were observed. The participants who did not complete the follow-up program did not differ from the patients who completed the program on background variables investigated. The study also supported the claim that professional nurses are competent to lead such programs and to evaluate treatment results. Clinical and research implications are discussed.

PMID: 16175925

Rating: 4b

Edwards JE, Oldman A, Smith L, Collins SL, Carroll D, Wiffen PJ, McQuay HJ, Moore RA. Single dose oral aspirin for acute pain. The Cochrane Database of Systematic Reviews 2006 Issue 3 Copyright © 2006 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Plain language summary,
Aspirin is an effective analgesic for acute pain of moderate to severe intensity with a clear dose-response. Drowsiness and gastric irritation were seen as significant adverse effects even though the studies were single-dose. The pain relief achieved with aspirin was very similar milligram for milligram to that seen with paracetamol.

Rating 1a

Eisenberg E, McNicol ED, Carr DB. Efficacy and safety of opioid agonists in the treatment of neuropathic pain of nonmalignant origin: systematic review and meta-analysis of randomized controlled trials. JAMA. 2005 Jun 22;293(24):3043-52.

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In the United States, an estimated 2 million persons have neuropathic pain that is often resistant to therapy. The use of opioids for neuropathic pain remains controversial. For this meta-analysis, twenty-two articles met inclusion criteria and were classified as short-term (less than 24 hours; n = 14) or intermediate-term (median = 28 days; n = 8) trials. The short-term trials had contradictory results. In contrast, all 8 intermediate-term trials demonstrated opioid efficacy for spontaneous neuropathic pain. The study concluded, "Short-term studies provide only equivocal evidence regarding the efficacy of opioids in reducing the intensity of neuropathic pain. Intermediate-term studies demonstrate significant efficacy of opioids over placebo for neuropathic pain, which is likely to be clinically important. Reported adverse events of opioids are common but not life-threatening."

Publication Types:
Meta-Analysis
Review

PMID: 15972567

Rating: 1b

Eisenberg E, McNicol E, Carr DB. Opioids for neuropathic pain. Cochrane Database Syst Rev. 2006; 3:CD006146.

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BACKGROUND: The use of opioids for neuropathic pain remains controversial. Studies have been small, have yielded equivocal results, and have not established the long-term risk-benefit ratio of this treatment. OBJECTIVES: To assess the efficacy and safety of opioid agonists for the treatment of neuropathic pain. SEARCH STRATEGY: We searched the Cochrane Central Register of Controlled Trials (2nd Quarter 2005), MEDLINE (1966 to June 2005), and EMBASE (1980 to 2005 Week 27) for articles in any language, and reference lists of reviews and retrieved articles. SELECTION CRITERIA: Trials were included in which opioid agonists were given to treat central or peripheral neuropathic pain of any etiology, pain was assessed using validated instruments, and adverse events were reported. Studies in which drugs other than opioid agonists were combined with opioids or opioids were administered epidurally or intrathecally were excluded. DATA COLLECTION AND ANALYSIS: Data were extracted by two independent investigators and included demographic variables, diagnoses, interventions, efficacy, and adverse effects. MAIN RESULTS: Twenty-three trials met the inclusion criteria and were classified as short-term (less than 24 hours; n = 14) or intermediate-term (median = 28 days; range = eight to 70 days; n = 9). The short-term trials had contradictory results. In contrast all nine intermediate-term trials demonstrated opioid efficacy for spontaneous neuropathic pain. Meta-analysis of seven intermediate-term studies showed mean post-treatment visual analog scale scores of pain intensity after opioids to be 13 points lower on a scale from zero to 100 than after placebo (95%

confidence interval -16 to -9; P < 0.00001). The most common adverse events were nausea (33% opioid versus 9% control: number needed to treat to harm (NNH) 4.2) and constipation (33% opioid versus 10% control: NNH 4.2), followed by drowsiness (29% opioid versus 12% control: NNH 6.2), dizziness (21% opioid versus 6% control: NNH 7.1), and vomiting (15% opioid versus 3% control: NNH 8.3). Where reported, 23 (11%) of 212 participants withdrew because of adverse events during opioid therapy versus nine (4%) of 202 receiving placebo. AUTHORS' CONCLUSIONS: Short-term studies provide only equivocal evidence regarding the efficacy of opioids in reducing the intensity of neuropathic pain, whereas intermediate-term studies demonstrate significant efficacy of opioids over placebo, which is likely to be clinically important. Reported adverse events of opioids are common but not life threatening. Further randomized controlled trials are needed to establish long-term efficacy, safety (including addiction potential), and effects on quality of life.

PMID: 16856116

Rating: 1A

Eisenberg E, River Y, Shifrin A, Krivoy N. Antiepileptic drugs in the treatment of neuropathic pain. Drugs. 2007:67(9):1265-89.

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Antiepileptic drugs are an effective treatment for various forms of neuropathic pain of peripheral origin, although they rarely provide complete pain relief. Multiple multicentre randomised controlled trials have shown clear efficacy of gabapentin and pregabalin for postherpetic neuralgia and painful diabetic neuropathy. Theses drugs can be rapidly titrated and are well tolerated. Topiramate, lamotrigine, carbamazepine and oxcarbazepine are alternatives for the treatment of painful diabetic neuropathy, but should be titrated slowly. Carbamazepine remains the drug of choice for trigeminal neuralgia; however, oxcarbazepine and lamotrigine are potential alternatives.There is an apparent need for large-scale randomised controlled trials on the efficacy of antiepileptic drugs in neuropathic pain in general, and in cancer-related neuropathic pain and neuropathic pain of central origin in particular. Trials with long-term follow-up are required to establish the long-term efficacy of antiepileptic drugs in neuropathic pain. There is only limited scientific evidence to support the idea that drug combinations are likely to be more efficacious and safer than each drug alone; further studies are warranted in this area.

PMID: 17547471

Rating: 5a

Ekstrom P, Carling L, Wetterhus S, Wingren PE, Anker-Hansen O, Lundegardh G, Thorhallsson E, Unge P. Prevention of peptic ulcer and dyspeptic symptoms with omeprazole in patients receiving

continuous non-steroidal anti-inflammatory drug therapy. A Nordic multicentre study. Scand J Gastroenterol. 1996 Aug;31(8):753-8.

Dept. of Surgery, Sandvikens Hospital, Sweden.

BACKGROUND: Non-steroidal anti-inflammatory drugs (NSAIDs) are known to cause gastroduodenal lesions and dyspeptic symptoms. METHODS: Patients with a history of dyspepsia or uncomplicated peptic ulcer disease and with a need for continuous NSAID treatment were randomized to receive either 20 mg omeprazole once daily or placebo. Gastroduodenal ulcers, erosions, and dyspeptic symptoms were evaluated after 1 and 3 months. RESULTS: During a 3-month study period 4.7% (4 of 85) of omeprazole-treated patients developed peptic ulcer, compared with 16.7% (15 of 90) of patients treated with placebo. This prophylactic effect of omeprazole was sustained independently of previous peptic ulcer history or Helicobacter pylori status. Development of dyspeptic symptoms requiring active treatment, either alone or in combination with ulcer(s) or erosions, occurred in 15.3% (15 of 85) of patients treated with omeprazole and 35.6% of those who received placebo. CONCLUSIONS: Omeprazole, 20 mg once daily, provides effective prophylactic therapy in patients at risk of developing NSAID-associated peptic ulcers or dyspeptic symptoms.

Publication Types:
Clinical Trial
Multicenter Study
Randomized Controlled Trial

PMID: 8858742

Rating: 2b

Ensalada LH. The importance of illness behavior in disability management.
Occup Med. 2000 Oct-Dec;15(4):739-54, iv. Review.
Abstract:
Abnormal illness behaviors, ranging from non-deliberate distortion to intentional deception, are associated with clinical phenomena that lie along a continuum from unconscious symptom exaggeration to psychiatric disorders and malingering. Failure to recognize abnormal illness behavior leads to inappropriate treatment and erroneous estimates of impairment or disability. This review is divided into three sections. First, basic terms are defined, including dissimulation, distortion, deception, misattribution, false imputation, and malingering. Second, syndromes characterized by abnormal illness behavior are described, including somatization, somatoform disorders, factitious disorders, and symptom magnification. Third, methods for detecting deception are illustrated, including maximum voluntary effort assessment, objective personality inventories, and symptom validity testing.
Publication Type: Review

Erdogan M, Erdogan A, Erbil N, Karakaya HK, Demircan A. Prospective, Randomized, Placebo-controlled Study of the Effect of TENS on postthoracotomy pain and pulmonary function. World J Surg. 2005 Dec;29(12):1563-70.

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We investigated the efficacy of transcutaneous electrical nerve stimulation (TENS) for postthoracotomy pain control in a prospective, randomized, double-blind, placebo-controlled study. We studied two groups of patients undergoing posterolateral thoracotomy. In group 1, TENS was used postoperatively on 60 patients for 5 days. Group 2 contained 56 patients without TENS. In both groups a visual analog scale (VAS) was used to indicate if analgesia was needed. When the VAS was higher than 4, an analgesic was administered. We observed the forced expiratory volume in 1 second (FEV(1)), the forced vital capacity (FVC), partial arterial oxygen pressure (PaO2), partial arterial carbon dioxide pressure (PaCO2), and how many doses of analgesia were given at postoperative 0 (extubation time), 2, 6, 12, 24, 48, 72, and 120 hours. TENS was not employed in patients with cardiac or neurologic disease. In group 1, TENS reduced the need to administer opioids during the 5-day postoperative period. This result is statistically significant (P = 0.013). Additionally, following the sixth postoperative hour, TENS increased the spirometric breath function. The FEV1, FVC, and PaO2 were high and PaCO2 was low when the first group is compared to the second. All these results are statistically significant (P = 0.012, P = 0.01, P = 0.024, and P = 0.02 respectively). We observed that TENS produced no evidence of side effects or intolerance in the patients of group 1. TENS is thus beneficial for pain relief following thoracotomy and has no side effects. Consequently, the routine use of TENS following thoracic surgery is recommended.

PMID: 16331341

Rating: 2c

Eriksen J, Sjogren P, Bruera E, Ekholm O, Rasmussen NK. Critical issues on opioids in chronic non-cancer pain: an epidemiological study. Pain. 2006;125:172-9.

Multidisciplinary Pain Centre, H:S Rigshospitalet, Copenhagen, Denmark.

The aim of the study was epidemiologically to evaluate the long-term effects of opioids on pain relief, quality of life and functional capacity in long-term/chronic non-cancer pain. The study was based on data from the 2000 Danish Health and Morbidity Survey. As part of a representative National random sample of 16,684 individuals (>16 years of age), 10,066 took part in an interview and completed a self-administered questionnaire. Cancer patients were excluded. The interview and the self-administered questionnaire included questions on chronic/long-lasting pain (>6 months), health-related quality of life (SF-36), use of the health care system, functional capabilities, satisfaction with medical pain treatment

and regular or continuous use of medications. Participants reporting pain were divided into opioid and non-opioid users. The analyses were adjusted for age, gender, concomitant use of anxiolytics and antidepressants and pain intensity. Pain relief, quality of life and functional capacity among opioid users were compared with non-opioid users. Opioid usage was significantly associated with reporting of moderate/severe or very severe pain, poor self-rated health, not being engaged in employment, higher use of the health care system, and a negative influence on quality of life as registered in all items in SF-36. Because of the cross-sectional nature causative relationships cannot be ascertained. However, it is remarkable that opioid treatment of long-term/chronic non-cancer pain does not seem to fulfil any of the key outcome opioid treatment goals: pain relief, improved quality of life and improved functional capacity.

PMID: 16842922

Rating: 3a

Erman MK. Therapeutic options in the treatment of insomnia. J Clin Psychiatry. 2005;66 Suppl 9:18-23.

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Pharmacologic and nonpharmacologic therapies both have roles in the treatment of insomnia. The benzodiazepines, when first introduced, were a major improvement over earlier treatments for insomnia in terms of their safety and efficacy. Since then, the nonbenzodiazepine benzodiazepine receptor agonists have been developed, which have provided advantages over the older medications and are currently first-line medication treatment for insomnia. Although antidepressants, antipsychotics, and anticonvulsants are often prescribed for the treatment of insomnia, they are not approved by the U.S. Food and Drug Administration for this indication and have side effects that are sometimes severe. New types of medications that have different modes of action from the benzodiazepine receptor agonists are now being developed, and one, a selective melatonin receptor agonist, has recently been approved for treatment of insomnia. Nonpharmacologic therapies can also help patients learn how to fall asleep faster and improve sleep quality. It is important for physicians to teach patients good sleep hygiene as part of their treatment. Cognitive-behavioral therapy is effective in the treatment of insomnia, alone and in combination with pharmacotherapy, but finding a qualified provider can be difficult and the patient must be willing to take the time to learn the therapies and wait for them to show effect.

Rating 5b

Ettinger AB, Argoff CE. Use of antiepileptic drugs for nonepileptic conditions: psychiatric disorders and chronic pain. Neurotherapeutics. 2007 Jan;4(1):75-83.

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Antiepileptic drugs (AEDs) are commonly utilized for nonepileptic conditions, including various psychiatric disorders and pain syndromes. Evidence for their benefit in these nonepileptic conditions varies widely among different drugs, but there is, in general, a paucity of published multicenter randomized double-blind trials. Variable levels of evidence suggest that lamotrigine and the vagal nerve stimulator have antidepressant properties. Carbamazepine, valproate, lamotrigine, and oxcarbazepine appear to have mood stabilizing properties while gabapentin, pregabalin, and tiagabine have anxiolytic benefits. Barbiturates, topiramate, and possibly phenytoin may precipitate or exacerbate depression. Underlying depression and anxiety symptoms may be exacerbated by levetiracetam, while psychotic symptoms have rarely been reported with topiramate, levetiracetam, and zonisamide. Pregabalin, gabapentin, carbamazepine, and oxcarbazepine have been used to treat neuropathic pain such as postherpetic neuralgia, and diabetic polyneuropathy. Topiramate and divalproex sodium have utility in the prophylaxis or acute treatment of migraine. Further rigorous studies are needed to clarify the utility of AEDs in nonepileptic conditions.

PMID: 17199018

Rating: 5b

Ezzo J, Berman B, Hadhazy VA, Jadad AR, Lao L, Singh BB. Is acupuncture effective for the treatment of chronic pain? A systematic review. Pain. 2000 Jun;86(3):217-25.

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Pain is the major complaint of the estimated one million U.S. consumers who use acupuncture each year. Although acupuncture is widely available in chronic pain clinics, the effectiveness of acupuncture for chronic pain remains in question. Our aim was to assess the effectiveness of acupuncture as a treatment for chronic pain within the context of the methodological quality of the studies. MEDLINE (1966-99), two complementary medicine databases, 69 conference proceedings, and the bibliographies of other articles and reviews were searched. Trials were included if they were randomized, had populations with pain longer than three months, used needles rather than surface electrodes, and were in English. Data were extracted by two independent reviewers using a validated instrument. Inter-rater disagreements were resolved by discussion. Fifty one studies met inclusion criteria. Clinical heterogeneity precluded statistical pooling. Results were positive in 21 studies, negative in 3 and neutral in 27. Three fourths of the studies received a low-quality score and low-quality trials were significantly associated with positive results (P=0.05). High-quality studies clustered in designs using sham acupuncture as the control group, where the risk of false negative (type II) errors is high due to large sample size requirements. Six or more acupuncture treatments were significantly associated with

positive outcomes (P=0.03) even after adjusting for study quality. We conclude there is limited evidence that acupuncture is more effective than no treatment for chronic pain; and inconclusive evidence that acupuncture is more effective than placebo, sham acupuncture or standard care. However, we have found an important relationship between the methodology of the studies and their results that should guide future research.

Publication Types:
Meta-Analysis

PMID: 10812251

Rating: 2b

FDA. MedWatch: Methadone Hydrochloride. Death, Narcotic Overdose, and Serious Cardiac Arrhythmias. 11/2006.

FDA has reviewed reports of death and life-threatening adverse events such as respiratory depression and cardiac arrhythmias in patients receiving methadone. These adverse events are the possible result of unintentional methadone overdoses, drug interactions, and methadone's cardiac toxicities (QT prolongation and Torsades de Pointes). Physicians prescribing methadone should be familiar with methadone's toxicities and unique pharmacologic properties. Methadone's elimination half-life (8-59 hours) is longer than its duration of analgesic action (4-8 hours). Methadone doses for pain should be carefully selected and slowly titrated to analgesic effect even in patients who are opioid-tolerant. Physicians should closely monitor patients when converting them from other opioids and changing the methadone dose, and thoroughly instruct patients how to take methadone. Healthcare professionals should tell patients to take no more methadone than has been prescribed without first talking to their physician.

Rating: 6a

FDA News. FDA Approves First Drug for Treating Fibromyalgia. June 21, 2007

The U.S. Food and Drug Administration today approved Lyrica (pregabalin), the first drug to treat fibromyalgia, a disorder characterized by pain, fatigue and sleep problems. Lyrica reduces pain and improves daily functions for some patients with fibromyalgia. "Today's new approval marks an important advance, and provides a reason for optimism for the many patients who will receive pain relief with Lyrica," said Steven Galson, M.D., M.P.H., director of FDA's Center for Drug Evaluation and Research. "However, consumers should understand that some patients did not experience benefit in clinical trials. We still have more progress to make for treatment of this disorder." Persons with fibromyalgia typically experience long-lasting or chronic pain, as well as muscle stiffness and tenderness. Fibromyalgia affects about 3 million to 6 million people in the United States each year. The

disorder mostly affects women and typically develops in early-to-middle adulthood. There is no test for the diagnosis of fibromyalgia. Doctors make a diagnosis by conducting physical examinations, evaluating symptoms, and ruling out other conditions. Individuals with fibromyalgia have been shown to experience pain differently from other people. Studies have shown that such patients have decreased pain after taking Lyrica, but, the mechanism by which Lyrica produces such an effect is unknown. Two double-blind, controlled clinical trials, involving about 1,800 patients, support approval for use in treating fibromyalgia with doses of 300 milligrams or 450 milligrams per day. The most common side effects of Lyrica include mild-to-moderate dizziness and sleepiness. Blurred vision, weight gain, dry mouth, and swelling of the hands and feet also were reported in clinical trials. The side effects appeared to be dose-related. Lyrica can impair motor function and cause problems with concentration and attention. FDA advises that patients talk to their doctor or other health care professional about whether use of Lyrica may impair their ability to drive. Lyrica already is approved for treating partial seizures, pain following the rash of shingles and pain associated with diabetes nerve damage (diabetic neuropathy). Lyrica is manufactured by New York-based Pfizer Inc. Pfizer has agreed to perform a study of the drug in children with fibromyalgia and a study in breastfeeding women.

Rating: 8b

FDA. Potential Signals of Serious Risks/New Safety Information Identified by the Adverse Event Reporting System (AERS). January - March 2008

The table below lists the names of products and potential signals of serious risks/new safety information that were identified for these products during the period January - March 2008 in the AERS database. The appearance of a drug on this list does not mean that FDA has concluded that the drug has the listed risk. It means that FDA has identified a potential safety issue, but does not mean that FDA has identified a causal relationship between the drug and the listed risk. If after further evaluation the FDA determines that the drug is associated with the risk, it may take a variety of actions including requiring changes to the labeling of the drug, requiring development of a Risk Evaluation and Mitigation Strategy (REMS), or gathering additional data to better characterize the risk. FDA wants to emphasize that the listing of a drug and a potential safety issue on this Web site does not mean that FDA is suggesting prescribers should not prescribe the drug or that patients taking the drug should stop taking the medication. Patients who have questions about their use of the identified drug should contact their health care provider. FDA will complete its evaluation of each potential signal/new safety information and issue additional public communications as appropriate.

Potential Signals of Serious Risks/New Safety Information Identified by the Adverse Event Reporting System (AERS) January - March 2008

Product Name: Active Ingredient (Trade) or Product Class	Potential Signal of Serious Risk/New Safety Information
Arginine Hydrochloride Injection (R-Gene 10)	Pediatric overdose due to labeling / packaging confusion

Desflurane (Suprane) Cardiac arrest
Duloxetine (Cymbalta) Urinary retention
Etravirine (Intelence) Hemarthrosis
Fluorouracil Cream (Carac) and Ketoconazole Cream (Kuric) Adverse events due to name confusion
Heparin Anaphylactic-type reactions
Icodextrin (Extraneal) Hypoglycemia
Insulin U-500 (Humulin R) Dosing confusion
Ivermectin (Stromectol) and Warfarin Drug interaction
Lapatinib (Tykerb) Hepatotoxicity
Lenalidomide (Revlimid) Stevens Johnson Syndrome
Natalizumab (Tysabri) Skin melanomas
Nitroglycerin (Nitrostat) Overdose due to labeling confusion
Octreotide Acetate Depot (Sandostatin LAR) Ileus
Oxycodone Hydrochloride Controlled-Release (Oxycontin) Drug misuse, abuse and overdose
Perflutren Lipid Microsphere (Definity) Cardiopulmonary reactions
Phenytoin Injection (Dilantin) Purple Glove Syndrome
Quetiapine (Seroquel) Overdose due to sample pack labeling confusion
Telbivudine (Tyzeka) Peripheral neuropathy
Tumor Necrosis Factor (TNF) Blockers Cancers in children and young adults

Rating: 8a

Federation of State Medical Boards of the U.S. Inc. Model Guidelines for the Use of Controlled Substances for the Treatment of Pain. 1998.
http://www.medsch.wisc.edu/painpolicy/domestic/model.htm (November 27, 2000)
Abstract:
The Board will judge the validity of prescribing based on the physician's treatment of the patient and on available documentation, rather than on the quantity and chronicity of prescribing. The goal is to control the patient's pain for its duration while effectively addressing other aspects of the patient's functioning, including physical, psychological, social and work-related factors. The following guidelines are not intended to define complete or best practice, but rather to communicate what the Board considers to be within the boundaries of professional practice.
Publication Type: Guideline

Federation of State Medical Boards, Model Guidelines for the Use of Controlled Substances for the Treatment of Pain, March 23, 2004

The Federation of State Medical Boards recently brought together medical board representatives, experts in pain management and addiction medicine and representatives from state and federal government to

review proposed revisions to the Federation's Model Guidelines for the Use of Controlled Substances for the Treatment of Pain. The review was undertaken to reflect new medical insights in pain management, especially regarding the undertreatment of pain. "State medical boards recognize undertreatment of pain as a public health priority," said James N. Thompson, M.D., chief executive officer for the Federation of State Medical Boards. "They actively support pain management as an important part of good medical practice."

For years, fear of scrutiny by state and federal agencies has caused physician reluctance to prescribe pain medication to patients. Today, underprescribing those same medications is considered as much a breach of the appropriate standard of care as overprescribing. In fact, the Oregon and California medical boards already have disciplined physicians for the undertreatment of pain and New Mexico revised its medical practice act to specify that undertreatment of pain may be grounds for unprofessional conduct.

The revised guidelines seek to assist state medical boards by:

- Addressing the inadequate management of pain and barriers to appropriate treatment;
- Encouraging states to consider undertreatment to be a violation equal to overtreatment;
- Emphasizing the dual obligation of government to develop a system that prevents abuse, trafficking and diversion of controlled substances while at the same time ensuring their availability for legitimate medical purposes; and
- Revising definitions of addiction, chronic pain and physical dependence to reflect current consensus and expertise in the medical community.

The revised Model Policy for the Use of Controlled Substances for the Treatment of Pain will be submitted to the Federation's House of Delegates in May for consideration as policy. Since the release in 1998 of the Model Guidelines, more than 300,000 copies have been distributed nationally and 22 state medical boards have adopted all or part of the guidelines.

Rating: 5b

Feinberg SD. ACPA Chronic Pain Medications Supplement. American Chronic Pain Association, Inc. 2008

The ACPA Chronic Pain Medications Supplement 2008 provides a short review of all available medication treatments for pain in patient-oriented language. However, a lot of health care professionals, claims people, case managers and attorneys find it useful as well.

Sedatives, anti-anxiety medications, & tranquilizers: Proper sleep hygiene is critical to the individual with chronic pain and often is hard to obtain. Various medications may provide short-term benefit. While sleeping pills, so-called minor tranquilizers, and anti-anxiety agents are commonly prescribed in chronic pain, pain specialists rarely, if ever, recommend them for long-term use. They can be habit-forming, and they may impair function and memory more than opioid pain relievers. There is also concern that they may increase pain and depression over the long-term. Zolpidem tartrate (Ambien®) is a non-benzodiazepine and is used for the short-term treatment of insomnia (difficulty falling asleep, staying asleep, or early awakening).

Rating: 8b

Feuerstein M, Berkowitz SM, Haufler AJ, Lopez MS, Huang GD.Working with low back pain: workplace and individual psychosocial determinants of limited duty and lost time. American Journal of Independent Medicine. 2001 Dec;40(6):627-38.
Abstract:
BACKGROUND: Few studies have identified the risk factors associated with lost time in employees working with occupational low back pain (OLBP) despite the presence of pain. Such data could assist in the development of evidenced-based secondary prevention programs. METHODS: The present investigation was a case-control study (n = 421) of demographic, health behavior, ergonomic, workplace and individual psychosocial factors hypothesized to be associated with lost time in young, full-time employees (i.e., soldiers) with OLBP. Analyses of the burden of OLBP in terms of the number of days on limited duty and lost time status were also computed. RESULTS: Logistic regression analysis indicated that female gender, education beyond HS/GED, longer time working in military, higher levels of daily life worries, no support from others, higher levels of ergonomic exposure, stressful work, increased peer cohesion, and greater perceived effort at work placed a worker at a greater likelihood for OLBP-related lost work time. Lower levels of innovation, involvement, and supervisor support were also associated with lost time. Linear regression indicated that the number of days of lost time and limited duty was associated with lower levels of physical health and higher levels of symptom severity. CONCLUSIONS: The results support the potential utility of interventions targeting ergonomic, workplace and individual psychosocial risk factors in secondary prevention. Published 2001 Wiley-Liss, Inc
Publication Type: Case Control, 421 cases

Finnerup NB, Otto M, McQuay HJ, Jensen TS, Sindrup SH. Algorithm for neuropathic pain treatment: an evidence based proposal. Pain. 2005 Dec 5;118(3):289-305. Epub 2005 Oct 6.

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New studies of the treatment of neuropathic pain have increased the need for an updated review of randomized, double-blind, placebo-controlled trials to support an evidence based algorithm to treat neuropathic pain conditions. Available studies were identified using a MEDLINE and EMBASE search. One hundred and five studies were included. Numbers needed to treat (NNT) and numbers needed to harm (NNH) were used to compare efficacy and safety of the treatments in different neuropathic pain syndromes. The quality of each trial was assessed. Tricyclic antidepressants and the anticonvulsants gabapentin and pregabalin were the most frequently studied drug classes. In peripheral neuropathic pain, the lowest NNT was for tricyclic antidepressants, followed by opioids and the anticonvulsants gabapentin and pregabalin. For central neuropathic pain there is limited data. NNT and NNH are

currently the best way to assess relative efficacy and safety, but the need for dichotomous data, which may have to be estimated retrospectively for old trials, and the methodological complexity of pooling data from small cross-over and large parallel group trials, remain as limitations.

Publication Types:
Review

PMID: 16213659

Rating: 5a

Finnerup NB, Otto M, Jensen TS, Sindrup SH. An evidence-based algorithm for the treatment of neuropathic pain. MedGenMed. 2007 May 15;9(2):36.

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OBJECTIVE: The purpose of this article is to discuss an evidence-based algorithm that can be implemented by the primary care physician in his/her daily clinical practice for the treatment of patients with neuropathic pain conditions. METHOD: A treatment algorithm for neuropathic pain was formulated on the basis of a review of 105 high-quality, randomized, placebo-controlled clinical trials. The number needed to treat (NNT) and number needed to harm (NNH) were used to compare the safety and effectiveness of current treatments for neuropathic pain syndromes. Most of the clinical trials reviewed in the analysis assessed tricyclic antidepressants (TCAs) and antiepileptic drugs (AEDs). RESULTS: TCAs had the lowest NNT followed by opioids and AEDs, such as gabapentin and pregabalin. The nature of the retrospective calculation of the NNT and NNH involves obvious limitations because of the pooling of studies with different experimental designs and outcomes. CONCLUSION: Patients presenting with neuropathic pain are becoming a more frequent occurrence for the primary care physician as the population ages. Evidence-based treatment options allow for the most efficient and effective pharmacotherapy regimen to be implemented.

Rating: 1b

Finsen V, Persen L, Lovlien M, Veslegaard EK, Simensen M, Gasvann AK, Benum P. Transcutaneous electrical nerve stimulation after major amputation. J Bone Joint Surg Br. 1988 Jan;70(1):109-12.

Trondheim University Hospital, Department of Orthopaedic Surgery, Norway.

We studied the effect of transcutaneous electrical nerve stimulation (TENS) on stump healing and postoperative and late phantom pain after major amputations of the lower limb. A total of 51 patients were randomised to one of three postoperative treatment regimens: sham TENS and chlorpromazine

medication, sham TENS only, and active low frequency TENS. There were fewer re-amputations and more rapid stump healing among below-knee amputees who had received active TENS. Sham TENS had a considerable placebo effect on pain. There were, however, no significant differences in the analgesic requirements or reported prevalence of phantom pain between the groups during the first four weeks. The prevalence of phantom pain after active TENS was significantly lower after four months but not after more than one year.

PMID: 3257494

Rating: 2c

Fishbain D, Evidence-based data on pain relief with antidepressants, Ann Med. 2000 Jul;32(5):305-16.

University of Miami School of Medicine, Department of Psychiatry, University of Miami Comprehensive Pain and Rehabilitation Center at South Shore Hospital, USA. cprc@um-cprc.com

This structured review addresses the issue of whether antidepressants have an antinociceptive (analgesic) effect for chronic pain independent of their antidepressant effect. In order to answer this question, human acute pain studies, individual placebo-controlled studies for the treatment of specific chronic pain syndromes, and metaanalytic studies were reviewed and placed into table format. Analysis of this evidence led to the following conclusions: The evidence was consistent in indicating that overall antidepressants may have an antinociceptive effect in chronic pain, and that these drugs were effective for neuropathic pain. There was also some evidence that these drugs could be effective for psychogenic or somatoform disorder-associated pain. This evidence also strongly suggested that serotonergic-noradrenergic antidepressants may have a more consistent antinociceptive effect than the serotonergic antidepressants. Finally, this evidence indicated that antidepressants could be effective for pain associated with some specific pain syndromes, such as chronic low back pain, osteoarthritis or rheumatoid arthritis, fibrositis or fibromyalgia, and ulcer healing. Possible reasons for the conflicting results of studies in this area are presented, and problems that could limit the validity of the conclusions of this review are discussed.

PMID: 10949061

Rating: 5b

Fisher R, Hassenbusch S, Krames E, Leong M, Minehart M, Prager J, Staats P, Webster L, Willis KD.A Consensus Statement Regarding the Present Suggested Titration for Prialt (Ziconotide). Neuromodulation 2005; 8:153–154.

This was a titration that stated the following:

Because of the side-effect profile of this drug, the recommended maximum titration rate approved by the FDA on December 28, 2004 and stated in the package insert is considered, unanimously, by the undersigned authors of this editorial and the vast majority of Prialt clinical investigators, to be two and one-half to five times too rapid.
They also stated:

Given the severity of the side-effects of this drug, it is recommended by a consensus of the most experienced clinical investigators (signatures below), that the "mantra" regarding the initiation of intrathecal Prialt for pain control should be to "Start Low and Go Slow

The rinse process is also very important to the infusion of this drug.

Rating: 8a

Flor H, Fydrich T, Turk DC. Efficacy of multidisciplinary pain treatment centers: a meta-analytic review. Pain. 1992 May;49(2):221-30.

Department of Clinical and Physiological Psychology, University of Tubingen, Germany.

Sixty-five studies that evaluated the efficacy of multidisciplinary treatments for chronic back pain were included in a meta-analysis. Within- and between-group effect sizes revealed that multidisciplinary treatments for chronic pain are superior to no treatment, waiting list, as well as single-discipline treatments such as medical treatment or physical therapy. Moreover, the effects appeared to be stable over time. The beneficial effects of multidisciplinary treatment were not limited to improvements in pain, mood and interference but also extended to behavioral variables such as return to work or use of the health care system. These results tend to support the efficacy of multidisciplinary pain treatment; however, these results must be interpreted cautiously as the quality of the study designs and study descriptions is marginal. Suggestions for improvement in research designs as well as appropriate reports of research completed are provided.

PMID: 1535122

Rating: 1a

Flotte ER. Flotte's Outline of Neurosurgery. University of Mississippi. 2004.

Neurosurgery Student Syllabus (Put together by Edward Flotte, MD, Assistant Professor, Department of Neurosurgery, University of Mississippi Medical Center)

Rating: 9b

Flor H, Birbaumer N. Comparison of the efficacy of electromyographic biofeedback, cognitive-behavioral therapy, and conservative medical interventions in the treatment of chronic musculoskeletal pain. J Consult Clin Psychol. 1993 Aug;61(4):653-8.

Institute of Medical Psychology and Behavioral Neurobiology, University of Tübingen, Federal Republic of Germany.

In this study, three types of treatments for chronic musculoskeletal pain were compared. Fifty-seven patients who suffered from chronic back pain and 21 patients who suffered from temporomandibular pain and dysfunction were randomly assigned to either electromyographic (EMG) biofeedback, cognitive-behavioral therapy, or conservative medical treatment. At posttreatment, improvements were noted in all three treatment groups, with the biofeedback group displaying the most substantial change. At the 6- and 24-month follow-up, only the biofeedback group maintained significant reductions in pain severity, interference, affective distress, pain-related use of the health care system, stress-related reactivity of the affected muscles, and an increase in active coping self-statements. Treatment outcome was predicted by chronicity and treatment-specific variables. Analysis of attrition showed a significant effect for therapist and extent of somatic pathology. Results suggest that pain patients who suffer from musculoskeletal pain problems and display few physical disabilities may profit the most from short-term EMG biofeedback treatment.

PMID: 8370861

Rating: 2c

Fordyce WE. Opioids and treatment targets. APS Bull. 1991;1:276-283.

Rehabilitation Medicine and Pain Service, University of Washington School of Medicine, Seattle.

Pain is reconceptualized in learning-based behavioral terms. Methods to assess behavioral elements of pain and to discuss nonmedical influences on pain with patients as well as behaviorally based tactics for early and long-term management and reactivation are discussed in this article.

Publication Types:
Review

PMID: 1840386

Rating: 5b

Forman JP, Rimm EB, Curhan GC. Frequency of analgesic use and risk of hypertension among men. Arch Intern Med. 2007;167:394-9.

Channing Laboratory, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA 02115, USA. jforman@partners.org

METHODS: The association between analgesic use and risk of incident hypertension was analyzed in a prospective cohort analysis of 16 031 male health professionals. CONCLUSIONS: The frequency of nonnarcotic analgesic use is independently associated with a moderate increase in the risk of incident hypertension.

PMID: 17325302

Rating: 3a

Foster L, Clapp L, Erickson M, Jabbari B. Botulinum toxin A and chronic low back pain. A randomized, double blind study. Neurology 2001;56:1290-93.
Department of Physical Medicine & Rehabilitation, Walter Reed Army Medical Center, Washington, DC, USA.
Abstract:
OBJECTIVES: To investigate the efficacy of botulinum toxin A in chronic low back pain and associated disabilities. METHODS: Thirty-one consecutive patients with chronic low back pain who met the inclusion criteria were studied: 15 received 200 units of botulinum toxin type A, 40 units/site at five lumbar paravertebral levels on the side of maximum discomfort, and 16 received normal saline. Each patient's baseline level of pain and degree of disability was documented using the visual analogue scale (VAS) and the Oswestry Low Back Pain Questionnaire (OLBPQ). The authors reevaluated the patients at 3 and 8 weeks (visual analogue scale) and at 8 weeks (OLBPQ). RESULTS: At 3 weeks, 11 of 15 patients who received botulinum toxin (73.3%) had >50% pain relief vs four of 16 (25%) in the saline group (p = 0.012). At 8 weeks, nine of 15 (60%) in the botulinum toxin group and two of 16 (12.5%) in the saline group had relief (p = 0.009). Repeat OLBPQ at 8 weeks showed improvement in 10 of 15 (66.7%) in the botulinum toxin group vs three of 16 (18.8%) in the saline group (p = 0.011). No patient experienced side effects. CONCLUSION: Paravertebral administration of botulinum toxin A in patients with chronic low back pain relieved pain and improved function at 3 and 8 weeks after treatment.
Publication Type: RCT, 31 cases
PMID: 11376175

Forouzanfar T, Kemler MA, Weber WE, Kessels AG, Van Kleef M, Spinal cord stimulation in complex regional pain syndrome: cervical and lumbar devices are comparably effective, Br J Anaesth. 2004 Jan 22

Pain Management and Research Centre, Department of Anaesthesiology, University Hospital Maastricht, Maastricht, The Netherlands.

BACKGROUND: Spinal cord stimulation (SCS) has been used since 1967 for the treatment of patients with chronic pain. However, long-term effects of this treatment have not been reported. The present study investigated the long-term effects of cervical and lumbar SCS in patients with complex regional pain syndrome type I. METHODS: Thirty-six patients with a definitive implant were included in this study. A pain diary was obtained from all patients before treatment and 6 months and 1 and 2 years after implantation. All patients were asked to complete a seven-point Global Perceived Effect (GPE) scale and the Euroqol-5D (EQ-5D) at each post-implant assessment point. RESULTS: The pain intensity was reduced at 6 months, 1 and 2 years after implantation ($P<0.05$). However, the repeated measures ANOVA showed a statistically significant, linear increase in the visual analogue scale score ($P=0.03$). According to the GPE, at least 42% of the cervical SCS patients and 47% of the lumbar SCS patients reported at least 'much improvement'. The health status of the patients, as measured on the EQ-5D, was improved after treatment ($P<0.05$). This improvement was noted both from the social and from the patients' perspective. Complications and adverse effects occurred in 64% of the patients and consisted mainly of technical defects. There were no differences between cervical and lumbar groups with regard to outcome measures. CONCLUSION: SCS reduced the pain intensity and improves health status in the majority of the CRPS I patients in this study. There was no difference in pain relief and complications between cervical and lumbar SCS.

PMID: 14742334

Rating: 4c

Forouzanfar T, Köke AJ, van Kleef M, Weber WE. Treatment of complex regional pain syndrome type I. Eur J Pain. 2002;6:105-22.

Pain Management and Research Centre, Department of Anesthesiology, University Hospital Maastricht, The Netherlands. TFOR@sane.azm.nl

Reflex sympathetic dystrophy (RSD), also known as complex regional pain syndrome type I (CRPS I), is a disabling neuropathic pain syndrome. Controversy exists about the effectiveness of therapeutic interventions for the management of RSD/CRPS I. In order to ascertain appropriate therapies we conducted a review of existing randomized controlled trials of therapies for this disabling disease. Eligible trials were identified from the Cochrane, Pubmed, Embase and MEDLINE databases from 1966 through June 2000, from references in retrieved reports and from references in review articles. Twenty-six studies concerning treatment modalities were identified. Eighteen studies were randomized placebo-controlled trials and eight studies were randomized active-controlled trials. Three independent investigators reviewed articles for inclusion criteria using a 15-item checklist. Seventeen of the trials were of high quality according to the 15-item criteria. There was limited evidence for the effectiveness of these interventions because of the heterogeneity of treatment modalities. The search for trials concerning prevention of RSD/CRPS I resulted in two eligible studies. Both were of high quality and

dealt with different interventions. There is limited evidence for their preventive effect. Copyright 2002 European Federation of Chapters of the International Association for the Study of Pain.

PMID: 11900471

Rating: 1b

Fotopoulou S. Honey and Cinnamon. Copenhagen University. October 08, 2008.

Arthritis: Take one part honey to two parts of lukewarm water and add a small teaspoon of cinnamon powder, make a paste and massage it on the itching part of the body slowly. It is noticed that the pain recedes within a minute or two. Or arthritis patients may daily, morning and night take one cup of hot water with two spoons of honey and one small teaspoon of cinnamon powder. If drunk regularly even chronic arthritis can be cured. In a recent research done at the Copenhagen University, it was found that when the doctors treated their patients with a mixture of one tablespoon Honey and half teaspoon cinnamon powder before breakfast, they found that within a week out of the 200 people so treated practically 73 patients were totally relieved of pain and within a month, mostly all the patients who could not walk or move around because of arthritis started walking without pain.

Rating: 10c

Fransen M, Woodward M, Norton R, Coggan C, Dawe M, Sheridan N. Risk factors associated with the transition from acute to chronic occupational back pain.
Spine. 2002 Jan 1;27(1):92-8.
Abstract:
CONCLUSIONS: "Simple self-report measures of individual, psychosocial, and workplace factors administered when earnings-related compensation for back pain is claimed initially can identify individuals with increased odds for development of chronic occupational disability."
Publication Type: Case Control Study, 854 cases

Feuerstein TJ, Chronic pain treatment with antidepressants – Metaanalysis. Schmerz. 1997 Jun 13;11(3):213-26.

Sektion Klinische Neuropharmakologie der Neurologischen Universitatsklinik, Neurozentrum, Freiburg.

Both preclinical and clinical evidence support the usefulness of antidepressants in chronic pain treatment. Monoamine uptake inhibitors influence the neurotransmissions of noradrenaline (NA) and/or serotonin (5-HT); their effect on nociception is thought to take place predominantly within the spinal cord. Antidepressant drugs seem to differ in their properties as analgesics and as thymoleptics. The

present work is aimed at correlating the special mechanism of action of antidepressants in diminishing nocicepetion with the pharmacological profile of these drugs in clinical pain treatment. From a preclinical, experimental point of view, it can be expected, that mixed type uptake blockers should be superior to selective NA or 5-HT uptake inhibitors. The analgesic profile of antidepressants was established by a metaanalysis of clinical trials on the effect of these drugs, given alone or in combination with other analgetics, in chronic pain syndromes. 57 Clinical trials were separated into 5 groups according to their scientific quality: [1] placebo-controlled double-blind studies with high power; [2] placebo-controlled double-blind studies with low power; [3-4] open controlled studies or studies with historical controls; [5] case reports. A study was positive if the tested antidepressant was more effective than placebo or the compared drug or seemed beneficial with respect to the interval of its previous absence. The most effective antidepressants in chronic pain treatment only included unselective monoamine reuptake inhibitors in the following rank order: amitriptyline > clomipramine >/= desipramine >/= imipramine >/= doxepin. A statement about the appropriate dosage of these drugs in chronic pain treatment, however, must wait for properly conducted dose finding studies which include the measurement of plasma concentrations.

PMID: 12799822

Rating: 1b

Frade LC, Lauretti GR, Lima IC, Pereira NL. The antinociceptive effect of local or systemic parecoxib combined with lidocaine/clonidine intravenous regional analgesia for complex regional pain syndrome type I in the arm. Anesth Analg. 2005 Sep;101(3):807-11, table of contents.

Rua-Campos Sales, 330, apto. 44, Ribeirao Preto-Sao Paulo 14015-110, Brazil.

We evaluated the efficacy of local or systemic parecoxib combined with lidocaine/clonidine IV regional analgesia in complex regional pain syndrome (CRPS) type 1 in a dominant upper limb. Thirty patients with CRPS type 1 were divided into three groups. The control group (CG) received both IV saline in the healthy limb and IV loco-regional 1 mg/kg of lidocaine + 30 mug of clonidine, diluted to a 10-mL volume with saline. The systemic parecoxib group (SPG) received a regional block similar to that administered to the CG but with systemic 20 mg of parecoxib, whereas the IV regional anesthesia with parecoxib group (IVRAPG) received an extra IV 5 mg of loco-regional parecoxib compared with the CG. The block was performed once a week for 3 consecutive weeks. Analgesia was evaluated by the 10-cm visual analog scale (VAS) and rescue analgesic consumption. The IVRAPG showed less daily ketoprofen (milligrams) consumption in the second and third weeks compared with the other groups ($P < 0.05$). The IVRAPG also showed less ketoprofen consumption when comparing the first and second week with the third week ($P < 0.05$). The VAS score comparison among groups revealed that groups were similar during the first and second week observation, although the IVRAPG showed smaller VAS scores in the third week compared with both CG and SPG ($P < 0.05$). We conclude the IV 5 mg of

parecoxib was an effective antiinflammatory drug combined with clonidine/lidocaine loco-regional block in CRPS type 1.

PMID: 16115995

Rating: 2c

Fredheim OM, Moksnes K, Borchgrevink PC, Kaasa S, Dale O. Clinical pharmacology of methadone for pain. Acta Anaesthesiol Scand. 2008 Mar 6; [Epub ahead of print].

Pain and Palliation Research Group, Department of Circulation and Medical Imaging, Faculty of Medicine, Norwegian University of Science and Technology, Trondheim, Norway.

Background: This topical review addresses methadone's pharmacology, its application in malignant and non-malignant pain conditions, practical issues related to methadone for the treatment of pain and its influence on QTc time. Methods: Relevant papers were identified in PubMed and EMBASE. Results: Methadone is advocated by experts as a second line opioid when first line opioids fail to provide a satisfactory balance between pain control and side effects (opioid switching). Although randomized-controlled studies are lacking, current evidence suggests that switching to methadone in this situation reduces pain intensity. However, interindividual variability in its pharmacokinetics make its application challenging and metabolism by CYP 3A4 and 2B6 implies a substantial risk of drug-drug interactions. Several ways of switching to methadone have been presented, with a gradual switch during 3 days or 'stop and go' as the dominating strategies. Episodes of torsade de pointes arrhythmia during methadone treatment have been reported in patients with other risk factors for arrhythmia, while small prospective studies have reported a small, lasting and stable increase in QTc time. The extensive use of methadone for opioid replacement in addicts has added additional patient barriers to its use for pain control. Conclusion: In spite of challenges related to the variable pharmacokinetics and concerns regarding increase in QTc time, current evidence indicates that opioid switching to methadone improves pain control in a substantial proportion of patients who are candidates for opioid switching. Measures must be instituted to secure that patients receiving methadone for pain are not considered opioid addicts.

PMID: 18331375

Rating: 1c

Freeman R, Durso-Decruz E, Emir B. Efficacy, safety and tolerability of pregabalin treatment of painful diabetic peripheral neuropathy: findings from 7 randomized, controlled trials across a range of doses. Diabetes Care. 2008 Mar 20 [Epub ahead of print].

Department of Neurology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts, U.S.A.

OBJECTIVE to evaluate the efficacy, safety, and tolerability of pregabalin across the effective dosing range; to determine differences in the efficacy of TID and BID dosage schedules; and to use time to event analysis to determine the time to onset of a sustained therapeutic effect using data from 7 trials of pregabalin in painful diabetic neuropathy (DPN). METHODS Data were pooled across 7 double-blind, randomized, placebo-controlled trials using pregabalin to treat painful DPN with dosages of 150, 300, and 600 mg/d, administered TID or BID. Only 1 trial included all 3 of these dosages and TID dosing was used in 4. All studies shared fundamental selection criteria and treatment durations ranged from 5-13 weeks. RESULTS pooled analysis showed pregabalin significantly reduced pain and pain-related sleep interference associated with DPN (150, 300 and 600 mg/d administered TID vs placebo all P </=0.007). Only the 600 mg/d dosage showed efficacy when administered BID (P </=0.001). Pain and sleep interference reductions associated with pregabalin appear to be positively correlated with dosage; the greatest effect was observed in patients treated with 600 mg/d. Kaplan-Meier analysis revealed the median time to onset of a sustained (>/=30% at end-point) 1-point improvement was 4 days in patients treated with pregabalin 600 mg/d; 5 days in patients treated with pregabalin 300 mg/d; 13 days in patients receiving pregabalin 150 mg/d; and 60 days in patients receiving placebo. The most common treatment-emergent adverse events were dizziness, somnolence and peripheral edema. CONCLUSIONS Treatment with pregabalin across its effective dosing range is associated with significant, dose-related improvement in pain in patients with DPN.

PMID: 18356405

Rating: 1b

Friedman AP, DiSerio FJ. Symptomatic treatment of chronically recurring tension headache: a placebo-controlled, multicenter investigation of Fioricet and acetaminophen with codeine. Clin Ther. 1987;10(1):69-81.

Neurological Associates of Tucson, Tucson Medical Park, Arizona.

A double-blind, randomized, multicenter investigation was conducted to compare the efficacy and safety of Fioricet, acetaminophen with codeine, and placebo for the symptomatic treatment of tension headache. At the onset of a typical headache, the patients took two capsules of their assigned study medication and rated responses over the next four hours in three target symptoms areas: pain, emotional or psychic tension, and muscle contractions or stiffness in the head and neck. Physicians made global assessments of the same symptom responses and of adverse reactions for each patient. One hundred ninety-eight patients were evaluated. Both active analgesic preparations were more effective than placebo in relieving pain and muscle stiffness or contractions. Fioricet, but not acetaminophen with codeine, was significantly better than placebo in alleviating emotional or psychic tension; Fioricet was also significantly better than acetaminophen with codeine in relieving this symptom. Certain analyses

suggested the possibility that Fioricet had a faster and more sustained analgesic effect than acetaminophen with codeine. By the end of the four-hour trial, significantly more patients achieved complete pain relief with Fioricet than with acetaminophen with codeine. The quality and quantity of adverse reactions did not differ significantly among the treatment groups. None was serious, and all abated without medical intervention.

PMID: 3329967

Rating: 2b

Fritz JM, Cleland JA, Brennan GP. Does adherence to the guideline recommendation for active treatments improve the quality of care for patients with acute low back pain delivered by physical therapists? Med Care. 2007 Oct;45(10):973-80.

Rehabilitation Agency, Intermountain Healthcare, Salt Lake City, Utah, USA. julie.fritz@hsc.utah.edu

BACKGROUND: Numerous practice guidelines have been developed for patients with low back pain in an attempt to reduce inappropriate variations and improve the cost-effectiveness of care. Guideline implementation has received more research attention than the impact of adherence to guideline recommendations on outcomes and costs of care. OBJECTIVE: Examine the association between adherence to the guideline recommendation to use active versus passive treatments with clinical outcomes and costs for patients with acute low back pain receiving physical therapy. RESEARCH DESIGN: Retrospective review of patients with acute low back pain receiving physical therapy in 2004-2005. Adherence to the recommendation for active treatment was determined from billing records. Clinical and financial outcomes were compared between patients receiving adherent or nonadherent care. SUBJECTS: A total of 1190 patients age 18-60 years old with low back pain of less than 90 days duration in 10 clinics in 1 geographic region. MEASURES: Clinical outcomes included the numeric pain rating and Oswestry disability questionnaire taken initially and at the completion of treatment. Financial outcomes included the number of sessions and charges for physical therapy care. RESULTS: Adherence rate was 40.4%. Adherence was greater for patients receiving workers' compensation ($P < 0.05$). Patients receiving adherent care had fewer visits and lower charges ($P < 0.05$), and showed more improvement in disability [adjusted mean difference for percentage improvement 25.8%, 95% confidence interval (CI): 21.3-30.4, $P < 0.001$] and pain (adjusted mean difference for percentage improvement 22.4%, 95% CI: 17.5-27.3, $P < 0.001$). Patients receiving adherent care were more likely to have a successful physical therapy outcome (64.7% vs. 36.5%, $P < 0.001$). CONCLUSIONS: Adherence to the guideline recommendation for active care was associated with better clinical outcomes and reduced cost.

PMID: 17890995

Rating: 4a

Fudin J. What Is the Maximum Safe Dose of Opioids? Medscape Pharmacists. 2008; ©2008 Medscape. 02/21/2008

Jeffrey Fudin, BS, PharmD, Adjunct Associate Professor, Albany College of Pharmacy/Union University, Albany, New York; Clinical Pharmacy Specialist, Stratten VA Medical Center, Albany, New York

Charts and tables are readily available from multiple sources that attempt to correlate certain doses of oxycodone to other opioid narcotics. "Maximum safe dose" is patient-specific and dependent on current and previous opioid exposure, as well as on whether the patient is using such medications chronically.When using single-agent opioid preparations (noncombination products), there is no maximum dose when appropriately titrated. The dose should be slowly escalated until adequate pain relief is seen or side effects preclude further escalation. When using combination opioid products containing acetaminophen, aspirin, or ibuprofen (such as Percocet, Percodan, and Combunox), the dose limiting toxicity is generally attributable to acetaminophen, aspirin, or ibuprofen respectively. The maximum amount of acetaminophen should be no more than 4 g/day considering all combined acetaminophen in 24 hours. Using more than 4 g/day of acetaminophen can cause acute hepatic failure. Aspirin and ibuprofen have their own inherent toxicities, including but not limited to possible gastrointestinal bleeding, kidney dysfunction, hypertension, etc. When switching between different opioid preparations, a narcotic analgesic conversion calculator or equi-analgesic table may be used as a guide. A conversion calculator is available at Globalrph.com. Equi-analgesic tables are readily available from multiple sources, including NovaPain and the American Pain Society. However, many equi-analgesic tables provide different information, depending on the source and the manner in which equivalency was calculated. There are drawbacks to these equivalency tables, in part because many do not consider a recommended 15% dose reduction for opioid cross-tolerance. Some resources actually recommend that a dose reduction of up to 50% is appropriate when switching from one opioid to an alternative. Another common problem with conversion tables is that many are based on single doses rather than steady-state concentrations, so certain data will not apply to chronic opioid users. Most opioid conversion tables fail to elucidate the potential problems when converting a patient to methadone from another opioid, or from another opioid to methadone. Methadone conversion requires careful consideration because of its long half-life and unusual pharmacokinetic profile compared with most other opioids. In addition, converting methadone to morphine, for example, is not bidirectional. Consider that the half-life of methadone is 15-30 hours. When switching from an established dose of methadone to another opioid, we must consider that measurable methadone serum levels will be around for days. Therefore, when placing a patient on a new opioid, even with the discontinuation of methadone, both drugs are now readily available to the mu receptors, increasing the overall risk for opioid toxicity. When newly converting a patient on methadone from another opioid, the equivalent dose conversion changes in a triphasic pattern: For example, the ratio of morphine (or a morphine equivalent) < 90 mg/day to methadone is 4:1; the ratio for morphine 90 mg/day - 300 mg/day is 8:1; and for morphine > 300 mg/day, the ratio is 12:1.

Rating: 9b

Furlan AD, Sandoval JAS, Mailis A. Spinal cord stimulation for chronic pain (Protocol for a Cochrane Review). In: The Cochrane Library, Issue 1, 2004. Chichester, UK: John Wiley & Sons, Ltd.

Spinal Cord Stimulation (SCS), first called Dorsal Column Stimulation (DCS), is a treatment that has been used for more than 30 years, but only in the past five years has it met with widespread acceptance and recognition by the medical community (Barolat 2000). It emerged as a clinical application of the gate-control theory (Melzack 1965), starting with a clinical report about its first application in patients by Norman Shealy in 1967(Shealy 1975). In the first decade after its introduction, SCS was extensively practiced and applied to wide spectrum of pain diagnoses, probably indiscriminately. The results at follow-up were poor and the method soon fell in disrepute. As a result, in the late 1970s and 1980s SCS was, at least in the United States, still used in only few specialized pain centers. In Europe, SCS was not introduced until the early 1970s and then practiced to a very limited extent. In the last decade there has been growing awareness that SCS is a reasonably effective therapy for many patients suffering from neuropathic pain for which there is no alternative therapy. There are several reasons for this development, the principal one being that the indications have been more clearly identified. The enhanced design of electrodes, leads, and receivers/stimulators has substantially decreased the incidence of reoperations for device failure (Meyerson 2000). Further, the introduction of the percutaneous electrode implantation has enabled trial stimulation, which is now commonly recognized as an indispensable step in assessing whether the treatment is appropriate for individual patients.

The antisympathetic effect of SCS is the likely reason for its great activity in peripheral ischaemia (Cook 1973), cardiac ischaemia (Sandric 1984, Lanza 2001), and at least some cases of complex regional pain syndrome (Type I and II) (Kemler 2000). In addition, SCS has also been used extensively for the management of other chronic pain states such as failed back surgery syndrome (North 1994), phantom pain, postamputation stump pain, diabetic neuropathy (Tesfaye 1996), post-herpetic neuralgia (Meglio 1989a; Meglio 1989b; Meglio 1989c) and multiple sclerosis (Cook 1973, Kumar 1991).
SCS involves the use of an electrical generator which delivers pulses by means of an electrode placed in the epidural space adjacent to a targeted spinal cord area, which is causing the pain. The leads, which are special devices containing the set of electrodes, can be implanted by laminectomy or percutaneously. The number and type of electrodes (unipolar, bipolar or multipolar) and the parameters of stimulation (amplitude, pulse width, electrode selection) may vary according to the roots involved and the intensity of the pain. Power is supplied by an implanted battery, or transcutaneously by an external transmitter of radio-frequency. Both types have a computerized telemetry system that allows the programming of a specific pattern of stimulation.

Nowadays, protocols for SCS implantation stipulate a screening trial period with temporary percutaneous placement of the leads and using an external generator. This phase, which could last from several days to several weeks, allows for assessment of the amount of pain relief obtained with usual

activities. If the trial is positive (at least 50% of pain relief) (Kemler 2000), depending on the surgeon's criteria, laminectomy could be indicated, and the temporal leads replaced by permanent ones. If percutaneous permanent leads are used in the trial, then these are generally left in place and the additional equipment, such as the generator and the extension, is implanted.
It is established that SCS abolishes continuous and evoked pain (tactile/thermal allodynia) so acute, nociceptive pain (such as wound pain and arthralgia) is unaffected (Meyerson 2000). Although the exact mechanism of action of SCS is still poorly understood, the experimental evidence shows that the sensitivity of the neural tissue is significantly altered by the frequency and amplitude variations. Therefore, the application of electric stimuli decreases the activity of dorsal horn cells (DH), including the hyperexcitability of the presumably noxious ones. There is evidence in animal models that the phenomenon of peripheral hypersensitivity with allodynia and hyperalgesia is the result of central sensitization which reflects a loss of tonic GABA-mediated inhibition as well as an increase of excitatory neurotransmitters in DH cells (Woolf 1994; Devor 1996). SCS is shown to induce decreased release of excitatory amino acids (EAA), glutamate and aspartate, concomitant with an increase of the GABA release from DH cells (Cui 1997). The same group also found involvement of adenosine in inhibitory neuromodulation of neuropathic pain which overlaps with the GABA action (Cui 1997, Meyerson 2000).
The only attempt to gather comprehensively the information on this issue by means of a systematic review was undertaken by Turner et al (Turner 1995) who tried to analyze the long-term risks and benefits of SCS for patients with failed surgery syndrome. This study has been criticized for the poor quality of the included studies (lack of randomization and blinding) and methodological flaws. Therefore, SCS as a form of therapy remains unproven (McQuay 1998). Despite the limited evidence for SCS efficacy because of the lack of controlled studies, the use of spinal stimulation for pain relief has increased exponentially during the last decade. In 1995 it was estimated that 14000 stimulators were being implanted worldwide each year (Linderoth 1995), and in Europe in 1997 the figure was 5000 units per annum (Simpson 1997). Since the publication of Turner's review a number of clinical trials have been published, and it is the objective of this review to assess the current evidence.

Rating: 5b

Furlan AD, Mailis A, Papagapiou M. Are we paying a high price for surgical sympathectomy? A systematic literature review of late complications. J Pain. 2000 Winter;1(4):245-57.

Comprehensive Pain Program and Toronto Western Hospital Research Institute, Toronto Western Hospital, Ontario, Canada.

The purpose of this article was to systematically review the literature in order to assess (1) the current indications for surgical sympathectomy and (2) the incidence of late complications collectively and per indication. All types of upper or lower limb surgical sympathectomies are included. An extensive search strategy looked for controlled trials and observational studies or case series with an english abstract. Out of 1,024 abstracts from MEDLINE and 221 from EMBASE, 135 articles reporting on 22,458 patients

and 42,061 procedures (up to april 1998) fulfilled the inclusion criteria. Weighted means were used to control for heterogeneity of data. No controlled trials were found. The main indication was primary hyperhidrosis in 84.3% of the patients. Compensatory hyperhidrosis occurred in 52.3%, gustatory sweating in 32.3%, phantom sweating in 38.6%, and horner's syndrome in 2.4% of patients, respectively, with cervicodorsal sympathectomy, more often after open approach. Neuropathic complications (after cervicodorsal and lumbar sympathectomy) occurred in 11.9% of all patients. Compensatory hyperhidrosis occurred 3 times more often if the indication was palmar hyperhidrosis instead of neuropathic pain (52.3% versus 18.2%), whereas neuropathic complications occurred 3 times more often if the treatment was for neuropathic pain instead of palmar hyperhidrosis (25.2% versus 9.8%). Surgical sympathectomy, irrespective of approach, is accompanied by several potentially disabling complications. Detailed informed consent is recommended when surgical sympathectomy is contemplated.

PMID: 14622605

Rating: 1c

Furlan AD, Sandoval JA, Mailis-Gagnon A, Tunks E. Opioids for chronic noncancer pain: a meta-analysis of effectiveness and side effects, CMAJ. 2006;174:1589-94.

Comprehensive Pain Program, Toronto Western Hospital, Ont.

BACKGROUND: Chronic noncancer pain (CNCP) is a major health problem, for which opioids provide one treatment option. However, evidence is needed about side effects, efficacy, and risk of misuse or addiction. METHODS: This meta-analysis was carried out with these objectives: to compare the efficacy of opioids for CNCP with other drugs and placebo; to identify types of CNCP that respond better to opioids; and to determine the most common side effects of opioids. We searched MEDLINE, EMBASE, CENTRAL (up to May 2005) and reference lists for randomized controlled trials of any opioid administered by oral or transdermal routes or rectal suppositories for CNCP (defined as pain for longer than 6 mo). Extracted outcomes included pain, function or side effects. Methodological quality was assessed with the Jadad instrument; analyses were conducted with Revman 4.2.7. RESULTS: Included were 41 randomized trials involving 6019 patients: 80% of the patients had nociceptive pain (osteoarthritis, rheumatoid arthritis or back pain); 12%, neuropathic pain (postherpetic neuralgia, diabetic neuropathy or phantom limb pain); 7%, fibromyalgia; and 1%, mixed pain. The methodological quality of 87% of the studies was high. The opioids studied were classified as weak (tramadol, propoxyphene, codeine) or strong (morphine, oxycodone). Average duration of treatment was 5 (range 1-16) weeks. Dropout rates averaged 33% in the opioid groups and 38% in the placebo groups. Opioids were more effective than placebo for both pain and functional outcomes in patients with nociceptive or neuropathic pain or fibromyalgia. Strong, but not weak, opioids were significantly superior to naproxen and nortriptyline, and only for pain relief. Among the side effects of opioids, only constipation and nausea were clinically and statistically significant. INTERPRETATION: Weak and strong opioids

outperformed placebo for pain and function in all types of CNCP. Other drugs produced better functional outcomes than opioids, whereas for pain relief they were outperformed only by strong opioids. Despite the relative shortness of the trials, more than one-third of the participants abandoned treatment.

PMID: 16717269

Rating: 1b

Furlan AD, Sjölund BH. Igniting the spark? Pain. 2007 Jul;130(1-2):1-3. Epub 2007 May 22.

Comment on: Johnson M, Martinson M. Efficacy of electrical nerve stimulation for chronic musculoskeletal pain: A meta-analysis of randomized controlled trials. Pain. 2007 Jul;130(1-2):157-65.

PMID: 17521812

Rating: 11b

There has been another letter to the editor about this article from Furlan et al. They state the following:
1. The methodological quality of the studies that the meta-analysis was based on was low.
2. There was still a need to demonstrate the benefits of ENS to other modalities to assess the pain conditons that are most responsive
3. What is the most appropriate duration.

This author did not pick up the above discrepencies in disease states.
Furlan writes for Cochrane

Editorial -- Igniting the spark?
Since its re-invention (Wall and Sweet, 1967) electrical nerve stimulation to relieve pain has been challenged as a clinical method to relieve pain (e.g. McQuay and Moore, 1998) Early single center studies did little to clarify the clinical relevance of these techniques, due to fragmentary description of the stimuli employed, to vague criteria for the patients included and for the pain relief obtained and to no or insufficiently defined controls and blinding. However, the clarification of short term biological effects of the stimulation (Sjo¨lund et al., 1977; Sjo¨lund and Eriksson, 1979; Johnson et al., 1989) as well as encouraging support by user statistics (Fishbain et al., 1996) has contributed to the continued application of this family of techniques (Transcutaneous Electrical Nerve Stimulation, acupuncture-like TENS, electro-acupuncture and Peripheral Electrical Nerve Stimulation) but to a most varying degree.
While for acute pain, definitions like postsurgical pain or early and late pain in delivery with observations merely close to the intervention may be adequate for evaluation (e.g. Carroll et al., 1997; Bjordal et al., 2003), the situation is different for chronic pain conditions. Here, a more precise and mechanism-oriented characterization of the pain conditions treated (Woolf et al., 1998) along with collecting important contextual parameters of the patients (Sjo¨lund, 2007) should form the basis of long

term clinical studies (cf. Coffey and Lozano, 2006). It is of course also necessary to use relevant outcomes that are monitored for a reasonable follow up period. These goals are not easy to achieve in a large number of patients without the economical support of large (e.g. pharmaceutical) companies and data from large studies are therefore lacking.

Meta-analysis has become a powerful tool to assess the effectiveness of interventions. Since the birth of the Cochrane Collaboration in 1990 there has been an explosion of methodology to find relevant studies, to critically appraise and to combine them statistically. Recently developed techniques make it possible to determine if a meta-analysis is misleading due to publication bias (Begg and Mazumdar, 1994; Egger et al., 1997). It is also feasible to assess the robustness of the conclusions of a meta-analysis by conducting sensitivity analysis. Meta-regression is a technique that can be used to determine why studies included in a meta-analysis reach different conclusions.

In the past, the evidence about the effectiveness of electrical nerve stimulation (ENS) for the treatment of pain was combined in various systematic reviews of randomized controlled trials (RCTs). However most of these systematic reviews focused on a specific regional pain condition or a particular type of ENS and therefore were not able to combine the studies using statistical methods because they included only a subset of RCTs.

In this issue, Johnson and Martinson report on a meta-analysis of 38 studies published in 29 papers of any type of electrical nerve stimulation (ENS) for all kinds of chronic musculoskeletal pain including 1227 patients. They were able to calculate standardized mean differences for all studies and combine them into a single meta-analysis.

One of the benefits of meta-analysis is that by combining various studies it increases the overall power to detect a statistically significant difference that was not possible in each individual trial due to small sample size. On the other hand, some people view this as a disadvantage, because combining different studies may neutralize a negative study with a positive study, meaning that clinically important differences might explain differences and therefore it is not appropriate to combine heterogeneous studies. In this situation, a meta-regression analysis would be the appropriate choice.

Among the many therapeutic options for chronic pain, ENS is a family of modalities that may stimulate the release of endogenous opioids (Han et al., 1991; Sluka et al., 1999) and/or influence the excitability of the sensory nervous system by other mechanisms (Marchand et al., 1995; Sluka et al., 1998; Radhakrishnan et al., 2003), with few contraindications, without major side effects, and it is relatively inexpensive. It should be remembered, though, that even in its simplest form, some expertise is required to teach its application, i.e. to effectively activate sensory afferents (Sjo¨lund et al., 1990) in clinical practice.

Johnson and Martinson showed that on average, the pain relief provided by ENS was nearly three times the pain relief provided by placebo. Despite the fact that the methodological quality of the studies in this area is still low, the meta-analysis presented by Johnson and Martinson demonstrates that ENS is better than placebo therapies. However, there is still a need to demonstrate the benefits of ENS compared to other modalities and therapies, to assess what kind of pain conditions are most responsive to ENS and to estimate the most appropriate duration of therapy. There are now considerable data on which electrical pulse pattern that are most effective in animal pain models (Sjo¨lund, 1985, 1988; Gopalkrishnan and

Sluka, 2000; Radhakrishnan and Sluka, 2005) but this knowledge has to be validated for chronic pain in humans.

Furukawa TA, Watanabe N, Churchill R. Combined psychotherapy plus antidepressants for panic disorder with or without agoraphobia. Cochrane Database Syst Rev. 2007;(1):CD004364.

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BACKGROUND: Panic disorder can be treated with pharmacotherapy, psychotherapy or in combination, but the relative merits of combined therapy have not been well established. OBJECTIVES: To review evidence concerning short- and long-term advantages and disadvantages of combined psychotherapy plus antidepressant treatment for panic disorder with or without agoraphobia, in comparison with either therapy alone. SEARCH STRATEGY: The Cochrane Collaboration Depression, Anxiety and Neurosis Controlled Trials Registers (CCDANCTR-Studies and CCDANCTR-References) were searched on 11/10/2005, together with a complementary search of the Cochrane Central Register of Controlled Trials and MEDLINE, using the keywords antidepressant and panic. A reference search, SciSearch and personal contact with experts were carried out. SELECTION CRITERIA: Two independent review authors identified randomised controlled trials comparing the combined therapy against either of the monotherapies among adult patients with panic disorder with or without agoraphobia. DATA COLLECTION AND ANALYSIS: Two independent review authors extracted data using predefined data formats, including study quality indicators. The primary outcome was relative risk (RR) of "response" i.e. substantial overall improvement from baseline as defined by the original investigators. Secondary outcomes included standardised weighted mean differences in global severity, panic attack frequency, phobic avoidance, general anxiety, depression and social functioning and relative risks of overall dropouts and dropouts due to side effects. MAIN RESULTS: We identified 23 randomised comparisons (representing 21 trials, 1709 patients), 21 of which involved behaviour or cognitive-behaviour therapies. In the acute phase treatment, the combined therapy was superior to antidepressant pharmacotherapy (RR 1.24, 95% confidence interval (CI) 1.02 to 1.52) or psychotherapy (RR 1.17, 95% CI 1.05 to 1.31). The combined therapy produced more dropouts due to side effects than psychotherapy (number needed to harm (NNH) around 26). After the acute phase treatment, as long as the drug was continued, the superiority of the combination over either monotherapy appeared to persist. After termination of the acute phase and continuation treatment, the combined therapy was more effective than pharmacotherapy alone (RR 1.61, 95% CI 1.23 to 2.11) and was as effective as psychotherapy (RR 0.96, 95% CI 0.79 to 1.16). AUTHORS' CONCLUSIONS: Either combined therapy or psychotherapy alone may be chosen as first line treatment for panic disorder with or without agoraphobia, depending on patient preference.

PMID: 17253502

Rating: 1b

Gaines, J., et al. The Effect of Neuromuscular Electrical Stimulation on Arthritis Knee Pain in Older Adults with Osteoarthritis of the Knee. Applied Nursing Research 2004. August; Volume 17, Number 3: 201-06.

Rating: 2c

Quality: Low. Total Rating: 3.0. Comment: Does not meet inclusion criteria for evidence-based review. [CA DWC]

Galantino ML, Bzdewka TM, Eissler-Russo JL, Holbrook ML, Mogck EP, Geigle P, Farrar JT, The impact of modified Hatha yoga on chronic low back pain: a pilot study, Altern Ther Health Med. 2004 Mar-Apr;10(2):56-9.

Program in Physical Therapy, Richard Stockton College of New Jersey, USA.

PURPOSE: The purpose of this randomized pilot study was to evaluate a possible design for a 6-week modified hatha yoga protocol to study the effects on participants with chronic low back pain. PARTICIPANTS: Twenty-two participants (M = 4; F = 17), between the ages of 30 and 65, with chronic low back pain (CLBP) were randomized to either an immediate yoga based intervention, or to a control group with no treatment during the observation period but received later yoga training. METHODS: A specific CLBP yoga protocol designed and modified for this population by a certified yoga instructor was administered for one hour, twice a week for 6 weeks. Primary functional outcome measures included the forward reach (FR) and sit and reach (SR) tests. All participants completed Oswestry Disability Index (ODI) and Beck Depression Inventory (BDI) questionnaires. Guiding questions were used for qualitative data analysis to ascertain how yoga participants perceived the instructor, group dynamics, and the impact of yoga on their life. ANALYSIS: To account for drop outs, the data were divided into better or not categories, and analyzed using chi-square to examine differences between the groups. Qualitative data were analyzed through frequency of positive responses. RESULTS: Potentially important trends in the functional measurement scores showed improved balance and flexibility and decreased disability and depression for the yoga group but this pilot was not powered to reach statistical significance. Significant limitations included a high dropout rate in the control group and large baseline differences in the secondary measures. In addition, analysis of the qualitative data revealed the following frequency of responses (1) group intervention motivated the participants and (2) yoga fostered relaxation and new awareness/learning. CONCLUSION: A modified yoga-based intervention may benefit individuals with CLB, but a larger study is necessary to provide definitive evidence. Also, the impact on depression and disability could be considered as important outcomes for further study. Additional functional outcome measures should be explored. This pilot study supports the need for more research investigating the effect of yoga for this population.

PMID: 15055095

Rating: 2c

Galer BS, Bruehl S, Harden RN. IASP diagnostic criteria for complex regional pain syndrome: a preliminary empirical validation study. International Association for the Study of Pain. Clin J Pain. 1998 Mar;14(1):48-54.

Department of Neurology and Anesthesiology, Multidisciplinary Pain Center, University of Washington School of Medicine, Seattle 98105, USA.

OBJECTIVE: To assess the ability of the International Association for the Study of Pain Complex Regional Pain Syndrome (CRPS) diagnostic criteria and associated features to discriminate between CRPS patients and patients with painful diabetic neuropathy. DESIGN: Prospective assessment of signs and symptoms in a series of CRPS and diabetic neuropathy patients. SETTING: University of Washington Multidisciplinary Pain Center. PATIENTS: A consecutive series of 18 CRPS patients and 30 diabetic neuropathy patients. INTERVENTIONS: Patients completed a 10-item patient history questionnaire assessing symptoms of CRPS prior to medical evaluation. The evaluating physician completed a 10-item patient examination questionnaire assessing objective signs of CRPS. OUTCOME MEASURES: The analyses conducted were designed to test the ability of CRPS signs and symptoms and associated features to discriminate between CRPS patients and diabetic neuropathy patients. RESULTS: Data analysis suggested that CRPS decision rules may lead to overdiagnosis of the disorder. Diagnosis based on self-reported symptoms can be diagnostically useful in some circumstances. The addition of trophic tissue changes, range of motion changes, and "burning" quality of pain did not improve diagnostic accuracy, but the addition of motor neglect signs did. Test of a CRPS scoring system resulted in improved accuracy relative to current criteria and decision rules. CONCLUSIONS: Poorly understood disorders lacking prototypical signs/symptoms and diagnostic laboratory testing must rely on the development of reliable diagnostic guidelines. The results of this study should assist in the further refinement of the CRPS diagnostic criteria.

PMID: 9535313

Rating: 4b

Gallagher RM. Primary care and pain medicine. A community solution to the public health problem of chronic pain. Medical Clinics of North America. 01-May-1999; 83(3): 555-83, v.

The author emphasizes that pain is an important public health problem that demands attention. He discusses ineffective management and its causes, administrative and socioeconomic problems

perpetuating poor care, problems in technology transfer, organizational models, specialists and subspecialists, and other topics.

Publication Type: Review

Gallagher RM. Treatment planning in pain medicine. Integrating medical, physical, and behavioral therapies. Medical Clinics of North America. 01-May-1999; 83(3): 823-49, viii.

This article addresses a systematic approach to the treatment of chronic pain. The first section presents a biopsychosocial model of pain. The second section presents an application of the biopsychosocial approach to the clinical assessment and management of clinical cases with chronic pain. Physicians who selectively and skillfully integrate treatment and coordinate the needed resources are more successful in managing many difficult pain patients and improve their performance with common problems in practice, such as headache and backache. This is a difficult challenge in medicine's present state of flux. Modern pain treatment abounds with paradox, some would say reflecting the evolution of medicine itself. Society is beginning to limit dollars for health care and demanding accountability for cost-effectiveness of treatment through the use of uniform outcome measures of performance. These values collide with the public's expectation of better care of pain and access to expensive technology that promises to cure pain. This battle is being fought in the HMOs, which limit access to specialists when access to the right specialist may improve cost-effectiveness. Outcomes research is showing that new organizational models are needed to provide cost-effective care of pain through timely, selective, and sometimes simultaneous use of several treatment modalities focused on functional restoration. Yet the reimbursement for the services provided in these models is declining, and administrative structures oriented to traditional specialty practices, which interfere with integration, are emphasized to encourage accountability. Therefore, pain medicine must work not only to improve the science of pain management, but also to evolve the administrative structures that enable new products to be distributed effectively to the public. The field must continue research to establish reliable methods of skillfully managing pain in a timely fashion to prevent chronicity and its consequences, while, through education and administrative change, endeavoring to limit the wasteful practices that have dominated chronic pain treatment heretofore. Creating attitudes of self-help through knowledge and pain management training is complementary to the selective use of the advances in technology that have occurred in response to the explosion of neurosciences and clinical research.

Rating: 5b

Gammaitoni A, Gallagher RM, Welz-Bosna M. Topical ketamine gel: possible role in treating neuropathic pain. Pain Med. 2000;1:97-100.

Pain Medicine and Comprehensive Rehabilitation Center, MCP Hahnemann School of Medicine Graduate Hospital, Philadelphia, PA, USA.

Neuropathic pain is often resistant to opioids, so other medication classes, such as tricyclic antidepressants, anticonvulsants, and local anesthetics, are often used. Central sensitization, or pain 'wind-up', may perpetuate chronic neuropathic pain even when ongoing peripheral sensory input is absent. Wind-up is thought to cause allodynia, hyperalgesia, and hyperpathia. Receptors such as NMDA, AMPA, and M-glu have recently been identified for their role in central sensitization or pain 'wind-up'. Ketamine has been proposed recently for neuropathic pain secondary to its NMDA receptor activity. The current application as a topical gel stems from the theory that ketamine has peripheral action at both opioid and Na+-K+ channels. This case study involved 5 patients from 25 to 70 years old (3 RSD, 1 lumbar radiculopathy, 1 post-herpetic neuralgia). Dose used was determined by site and surface area of involvement and ranged from 0.093 mg/kg to 9.33 mg/kg. All five patients reported significant pain relief at initial application and wished to continue treatment. The average numerical analogue scale (NAS) score preapplication was 8.8. The average 15 minutes post application NAS was 1.6. Patients reported alterations in temperature sensation, feelings of relaxation and decreased tension in the area of application, and pain relief. Reduction in numerical pain scores postapplication of ketamine gel ranged from 53-100% using a 1-10 numerical pain intensity scale. No significant side effects were reported. Ketamine Gel may provide clinicians with a new option in the battle against chronic neuropathic pain. Until further information is available and larger trials can be conducted, we can only recommend this type of therapy for refractory cases in which all primary and secondary options have been exhausted.

PMID: 15101968

Rating: 5c

Gatchel RJ; Gardea MA. Psychosocial issues: their importance in predicting disability, response to treatment, and search for compensation. Neurologic Clinics. 01-Feb-1999; 17(1): 149-66

The conceptualization of pain and its progression into chronic disability has evolved from unidimensional models to more integrative, biopsychosocial models that take into account the many biological, psychosocial, social, and economic factors that may significantly contribute to the low back pain experience. This chapter reviews various studies that have demonstrated our growing understanding of these complex, interactive processes in helping to predict those who develop chronic disability as well as those who respond best to treatment attempts. Further, we examine the issue of compensation and how it too is intricately intertwined with the other variables contributing to lower back pain disability.

Publication Type: Review

Gatchel R., Polatin P. and Kinney R. Predicting Outcome of Chronic Back Pain Using Clinical Predictors of Psychopathology: A Prospective Analysis. Health Psychology 1995:14 (5);415-20.

Abstract:

This study evaluated whether a comprehensive assessment of psychosocial measures is useful in characterizing those acute low back pain patients who subsequently develop chronic pain disability problems. A cohort of 324 patients was evaluated, with all patients being administered a standard battery psychological assessment tests. A structured telephone interview was conducted 6 months after the psychological assessment to evaluate return-to-work status. Analyses, conducted to differentiate between those patients who were back at work at 6 months versus those who were not because of the original back injury, revealed the importance of 3 measures: self-reported pain and disability, the presence of a personality disorder, and scores on Scale 3 of the Minnesota Multiphasic Personality Inventory. These results demonstrate the presence of a psychosocial disability variable that is associated with those injured workers who are likely to develop chronic disability problems.

Comments by Dr. Whitney of the Colorado Division of Workers' Compensation:

Design: Prospective cohort study

Population/sample size:
- 324 patients seen for acute low back pain in 3 outpatient clinics
- No more than 6 weeks of lumbar symptoms
- Mean age 35, 64% men, 36% women

Main outcome measures:
- Associations between measured psychological characteristics and working status at 6 month follow-up structured telephone interview
- Scales were Million Visual Analog Scale (VAS) for pain at baseline; Structured Clinical Interview for DSM-III-R (SCID) for Axis I disorders; SCID-II for Axis II disorders at time of baseline assessment; injury severity assessed by blinded chart review by physician; physical demands of job
- Minnesota Multiphasic Personality Inventory (MMPI) when possible 1 week after baseline assessment (56% of subjects had complete MMPI data)
- At 6 month interview, 274 were working, 36 were disabled/not working because of initial back injury, 14 not classifiable
- Disability more common among non-Caucasians; disabled had less education than working group; age, gender, marital status not different between groups
- Disabled group had higher pain VAS and MMPI Hysteria scores; also had near-significant (p=.067) greater number of Axis II personality disorders
- Multivariable logistic model on group without MMPI scores associated disability with older age, non-Caucasian race, pain VAS score, and Axis II disorder; model on group with valid MMPI scores associated disability with pain VAS score, Axis II disorder, and MMPI Hysteria score
- Injury severity and physical demands of job not different between groups

Authors' conclusions:
- Psychosocial variables more important in development of back pain-related disability than injury severity and job demands
- Physicians need to be alert for psychosocial factors in acute pain patients

Comments:
- Correlation between MMPI and Axis II personality disorders not stated; this would lend support to interpretation of data
- 95% confidence intervals for Axis II odds ratio in Table 3 include odds ratio of one; pain VAS appears to be most robust predictor of disability, since it is the only variable whose 95% CI does not include one
- Cannot infer what psychosocial information ought to be elicited at initial office visit; SCID and MMPI not practical for routine clinical use

Rating: 3b, 324 cases

Gatchel RJ, Mayer TG, Kidner CL, McGeary DD. Are gender, marital status or parenthood risk factors for outcome of treatment for chronic disabling spinal disorders? J Occup Rehabil. 2005 Jun; 15(2):191-201.

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Recent clinical research has suggested that single working mothers may differ in their response to health treatment and outcomes, relative to their married female or male counterparts. The present study explored, on an a priori basis, the existence and extent of differences in chronic pain rehabilitation outcomes of pain report, return-to-work and future health utilization for single working mothers, relative to other patients. A cohort of 1,679 consecutive chronically disabled work related spinal disorder (CDWRSD) patients were placed into one of eight groups as a function of gender, marital status (single/married), and parenthood (with/without children). All patients completed an assessment battery measuring psychosocial variables at pre- and post-treatment, and a structured clinical interview evaluating socioeconomic outcomes at 1 year following completion of a 5-7 week functional restoration program. Results revealed that single females with children differed from all other groups in racial representation, with 57.1% of these individuals being African American, widely disparate from the prevailing local ethnicity. Single females and males with children were represented by a higher incidence of cervical injuries (25.0% and 26.7%, respectively) than all other groups (5.4-16.6%, $p < .001$). Contrary to expectation, the 8 groups did not differ significantly in program completion rate, work return, work retention, health utilization, recurrent injury or case settlement rates at one-year follow-up. The single females with children group did display greater levels of depression pre-treatment compared to the other groups. However, at post-treatment, these differences no longer existed. This investigation is one of the first to examine if the combination of gender and parenthood distinguishes significantly

among CDWRSD patients. Overall, contrary to expectation, the single mothers did not show any significant differences in CDWRSD outcome at one-year post-rehab follow-up, and the single mothers and fathers showed no differences in depression or pain severity post-treatment. Thus, in spite of the societal belief to the contrary, it seems that single parent patients can show similar chronic pain rehabilitation outcomes, relative to other CDWRSD patients, after a prescribed course of tertiary functional restoration rehabilitation.

PMID: 15844676

Rating: 4b

Gatchel RJ. Psychosocial factors that can influence the self-assessment of function. J Occup Rehabil. 2004 Sep;14(3):197-206.

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What has plagued the evaluation process in this area has been the level of agreement in the wide variation in the measures used to document a construct such as pain, as well as changes in that construct as reflected in the measurement of function. The present article reviews the major psychosocial barriers to assessment/recovery that have been implicated as influencing the self-assessment of function. The following are discussed: secondary gain; secondary loss; emotional distress (such as anger, anxiety and depression); psychopathology; somatization and symptom magnification; compliance and resistance; patient comprehension/mental status; and iatrogenic effects.

Publication Types:
Review

PMID: 15156778

Rating: 5a

Gatchel RJ, Polatin PB, Noe C, Gardea M, Pulliam C, Thompson J. Treatment- and cost-effectiveness of early intervention for acute low-back pain patients: a one-year prospective study. J Occup Rehabil. 2003 Mar;13(1):1-9.

Eugene McDermott Center for Pain Management, University of Texas Southwestern Medical Center at Dallas, Dallas, Texas, USA. robert.gatchel@utsouthwestern.edu

In an attempt to prevent acute low-back pain from becoming a chronic disability problem, an earlier study developed a statistical algorithm which accurately identified those acute low-back pain patients

who were at high risk for developing such chronicity. The major goal of the present study was to evaluate the clinical effectiveness of employing an early intervention program with these high-risk patients in order to prevent the development of chronic disability at a 1-year follow-up. Approximately 700 acute low-back pain patients were screened for their high-risk versus low-risk status. On the basis of this screening, high-risk patients were then randomly assigned to one of two groups: a functional restoration early intervention group (n = 22), or a nonintervention group (n = 48). A group of low-risk subjects (n = 54) who did not receive any early intervention was also evaluated. All these subjects were prospectively tracked at 3-month intervals starting from the date of their initial evaluation, culminating in a 12-month follow-up. During these follow-up evaluations, pain disability and socioeconomic outcomes (such as return-to-work and healthcare utilization) were assessed. Results clearly indicated that the high-risk subjects who received early intervention displayed statistically significant fewer indices of chronic pain disability on a wide range of work, healthcare utilization, medication use, and self-report pain variables, relative to the high-risk subjects who do not receive such early intervention. In addition, the high-risk nonintervention group displayed significantly more symptoms of chronic pain disability on these variables relative to the initially low-risk subjects. Cost-comparison savings data were also evaluated. These data revealed that there were greater cost savings associated with the early intervention group versus the no early intervention group. The overall results of this study clearly demonstrate the treatment- and cost-effectiveness of an early intervention program for acute low-back pain patients.

PMID: 12611026

Rating: 3c

Gatchel RJ. 2005. Clinical Essentials of Pain Management. Washington, DC: American Psychological Association; 2005.

Clinical Essentials of Pain Management lays out an empirically documented program for treating patients experiencing acute and chronic pain, two of the most common symptoms in modern society. Going beyond traditional biomedical remedies, Robert Gatchel offers a comprehensive viewpoint that takes into consideration not only biological, but also psychological and social variables.

Rating: 9b

Gatchel RJ, Mayer TG, Theodore BR. The pain disability questionnaire: relationship to one-year functional and psychosocial rehabilitation outcomes. J Occup Rehabil. 2006 Mar;16(1):75-94.

Department of Psychology, College of Science, University of Texas at Arlington, Arlington, TX, USA.

OBJECTIVE: The Pain Disability Questionnaire (PDQ) is a new functional assessment instrument designed for evaluating chronic disabling musculoskeletal disorders. It is useful for assessing

function/disability as affected by pain. This is the first study to assess the predictive validity of the PDQ in its relationship to 1-year post-treatment work- and health-related outcomes in a chronic disabling occupational musculoskeletal disorder (CDOMD) population. DESIGN: A prospective cohort of CDOMD patients (n=150) completed a prescribed functional restoration rehabilitation program, with PDQ and other psychosocial measures evaluated before and immediately after treatment. A structured telephonic interview for objective work- and health-related outcomes took place 1-year following treatment. RESULTS: Lower rates of work retention were associated with more severe pre-treatment PDQ scores. Higher post-treatment PDQ were associated with decreased return-to-work rates, decreased work retention and a greater percentage seeking health care from a new provider. In addition, PDQ scores were also associated with psychosocial measures such as depression and perceived pain intensity, as well as alternative measures of disability. CONCLUSIONS: Results demonstrated the ability of this simple and psychometrically-sound disability rating scale for systematic functional assessment in predicting treatment outcomes in patients with CDOMD. Results support the further use of the PDQ as a standard treatment outcomes measure in this area of musculoskeletal disorders.

PMID: 16752090

Rating: 3c

Gavin, I., et al. Identification of Human Cell Responses to Hexavalent Chromium. Environmental and Molecular Mutagenesis. 2007. Volume 48: 650-57.

Rating: 5c

Quality: N/A. Total Rating: N/A. Comment: Does not meet inclusion criteria for evidence-based review. [CA DWC]

Ghoname EA, Craig WF, White PF, Ahmed HE, Hamza MA, Henderson BN, Gajraj NM, Huber PJ, Gatchel RJ, Percutaneous electrical nerve stimulation for low back pain: a randomized crossover study, JAMA 1999 Mar 3;281(9):818-23

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The objective of this study was to compare the effectiveness of a novel nonpharmacologic pain therapy, percutaneous electrical nerve stimulation (PENS), with transcutaneous electrical nerve stimulation (TENS) and flexion-extension exercise therapies in patients with long-term LBP. For 29 men and 31 women with LBP secondary to degenerative disk disease, 4 therapeutic modalities (sham-PENS, PENS, TENS, and exercise therapies) were each administered for a period of 30 minutes 3 times a week for 3 weeks. In the results, PENS was significantly more effective in decreasing VAS pain scores after each treatment than sham-PENS, TENS, and exercise therapies. The average daily oral intake of nonopioid

analgesics was decreased to 1.3 pills per day with PENS compared with 2.5, 2.2, and 2.6pills per day with sham-PENS, TENS, and exercise, respectively. Compared with the other 3 modalities, 91 % of the patients reported that PENS was the most effective in decreasing their LBP. The PENS therapy was also significantly more effective in improving physical activity, quality of sleep, and sense of well-being. The SF-36 survey confirmed that PENS improved post treatment function more than sham-PENS, TENS, and exercise. The study concluded, "In this sham-controlled study, PENS was more effective than TENS or exercise therapy in providing short-term pain relief and improved physical function in patients with long-term LBP."

Publication Types:
- Clinical Trial
- Randomized Controlled Trial

PMID: 10071003

Rating: 2b

Comments by Dr. Whitney of the Colorado Division of Workers' Compensation:

Design: Randomized crossover trial.

Population/sample size:
- 60 patients (29 men, 31 women) with 3 months or more of low back pain due to 'radiologically confirmed degenerative disk disease'
- Excluded if long-term use of opioid analgesics, change in character/severity of back pain in last 3 months, acute sciatica, past use of non-traditional therapies, pending workers' compensation claim

Main outcome measures:
- Visual analog scale scores for pain, level of activity, quality of sleep; SF-36 physical and mental component scores before and after receiving each of four interventions: percutaneous electrical nerve stimulation (PENS), sham PENS, transcutaneous electrical nerve stimulation (TENS), and supervised exercise
- Each patient received each intervention 30 minutes 3 times a week for 3 weeks, with 1 week between interventions
- PENS associated with greater improvements in SF-36 scores than TENS, sham PENS, or exercise at end of 4 week periods of each intervention
- PENS associated with greater improvements in VAS scores for pain, activity, and sleep & with greater reduction in analgesic use
- PENS preferred by 91% of patients as 'most desirable modality'

Authors' conclusions:

- PENS more effective than TENS & exercise in short-term relief of low back pain
- Prolonged trial of PENS with longer follow-up needed to measure long-term effects
- Ongoing exercise program needs to be incorporated in PENS therapy

Comments:
- "Radiologically confirmed" disk disease may not be valid classification, since imaging tests not shown to identify discogenic pain
- Carryover effects (1 week between interventions) not measured; this makes sense if effect of PENS is less than 1 week after discontinuation
- TENS usually applied prn; this trial applied TENS on fixed schedule & does not constitute a valid comparison of PENS with actual TENS use

Rating: 2c, RCT, 60 cases

Ghostine SY, Comair YG, Turner DM, Kassell NF, Azar CG. Phenoxybenzamine in the treatment of causalgia. Report of 40 cases. J Neurosurg. 1984 Jun;60(6):1263-8.

Forty consecutive cases of causalgia treated during a 7-year period are presented. The patients ranged in age between 17 and 55 years, and all patients were males who received their nerve injuries from missile or shrapnel wounds. The greater occipital nerve was involved in two cases, median nerve in 10, sciatic nerve in 12, brachial plexus in seven, cauda equina in five, and multiple nerves in four cases. Each patient was treated with phenoxybenzamine, a postsynaptic alpha 1-blocker and presynaptic alpha 2-blocking agent. The drug was given orally in gradually increasing increments until a maximum daily dose of 40 to 120 mg was reached. Duration of treatment was usually 6 to 8 weeks. Total resolution of pain was achieved in all cases. The follow-up period ranged between 6 months and 6 years. Side effects of phenoxybenzamine were minimal and transient, consisting primarily of mild orthostatic hypotension and ejaculatory problems. We conclude that oral phenoxybenzamine is a simple, safe, and effective treatment of causalgia.

PMID: 6726371

Rating: 4b

Giesecke T, Williams DA, Harris RE, Cupps TR, Tian X, Tian TX, Gracely RH, Clauw DJ. Subgrouping of fibromyalgia patients on the basis of pressure-pain thresholds and psychological factors. Arthritis Rheum. 2003 Oct;48(10):2916-22.

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OBJECTIVE: Although the American College of Rheumatology (ACR) criteria for fibromyalgia are used to identify individuals with both widespread pain and tenderness, individuals who meet these

criteria are not a homogeneous group. Patients differ in their accompanying clinical symptoms, as well as in the relative contributions of biologic, psychological, and cognitive factors to their symptom expression. Therefore, it seems useful to identify subsets of fibromyalgia patients on the basis of which of these factors are present. Previous attempts at identifying subsets have been based solely on psychological and cognitive features. In this study, we attempt to identify patient subsets by incorporating these features as well as the degree of hyperalgesia/tenderness, which is a key neurobiologic feature of this illness. METHODS: Ninety-seven individuals meeting the ACR criteria for fibromyalgia finished the same battery of self-report and evoked-pain testing. Analyzed variables were obtained from several domains, consisting of 1) mood (evaluated by the Center for Epidemiologic Studies Depression Scale [for depression] and the State-Trait Personality Inventory [for symptoms of trait-related anxiety]), 2) cognition (by the catastrophizing and control of pain subscales of the Coping Strategies Questionnaire), and 3) hyperalgesia/tenderness (by dolorimetry and random pressure-pain applied at suprathreshold values). Cluster analytic procedures were used to distinguish subgroups of fibromyalgia patients based on these domains. RESULTS: Three clusters best fit the data. Multivariate analysis of variance (ANOVA) confirmed that each variable was differentiated by the cluster solution (Wilks' lambda [degrees of freedom 6,89] = 0.123, $P < 0.0001$), with univariate ANOVAs also indicating significant differences (all $P < 0.05$). One subgroup of patients ($n = 50$) was characterized by moderate mood ratings, moderate levels of catastrophizing and perceived control over pain, and low levels of tenderness. A second subgroup ($n = 31$) displayed significantly elevated values on the mood assessments, the highest values on the catastrophizing subscale, the lowest values for perceived control over pain, and high levels of tenderness. The third group ($n = 16$) had normal mood ratings, very low levels of catastrophizing, and the highest level of perceived control over pain, but these subjects showed extreme tenderness on evoked-pain testing. CONCLUSION: These data help support the clinical impression that there are distinct subgroups of patients with fibromyalgia. There appears to be a group of fibromyalgia patients who exhibit extreme tenderness but lack any associated psychological/cognitive factors, an intermediate group who display moderate tenderness and have normal mood, and a group in whom mood and cognitive factors may be significantly influencing the symptom report.

PMID: 14558098
Rating: 3b

Gijsman HJ, Geddes JR, Rendell JM, Nolen WA, Goodwin GM. Antidepressants for bipolar depression: a systematic review of randomized, controlled trials. Am J Psychiatry. 2004 Sep;161(9):1537-47.

Scutari Clinic, St. Thomas' Hospital, Lambeth Palace Rd., London, U.K. harm.gijsman@doctors.net.uk

OBJECTIVE: This study reviewed the evidence from randomized, controlled trials on the efficacy and safety of antidepressants in the short-term treatment of bipolar depression. METHOD: The authors performed a systematic review and meta-analysis of randomized, controlled trials. They searched the Cochrane Collaboration Depression, Anxiety, and Neurosis Controlled Trials Register, incorporating results of searches of MEDLINE, EMBASE, CINAHL, PsycLIT, PSYNDEX, and LILACS. The main

outcome measures were the proportion of patients who clinically responded to treatment and the rate of switching to mania. RESULTS: Twelve randomized trials were included, with a total of 1,088 randomly assigned patients. Five trials compared one or more antidepressants with placebo: 75% of these patients were receiving a concurrent mood stabilizer or an atypical antipsychotic. Antidepressants were more effective than placebo. Antidepressants did not induce more switching to mania (the event rate for antidepressants was 3.8% and for placebo, it was 4.7%). Six trials allowed comparison between two antidepressants. The rate of switching for tricyclic antidepressants was 10%, and for all other antidepressants combined, it was 3.2%. CONCLUSIONS: Antidepressants are effective in the short-term treatment of bipolar depression. The trial data do not suggest that switching is a common early complication of treatment with antidepressants. It may be prudent to use a selective serotonin reuptake inhibitor or a monoamine oxidase inhibitor rather than a tricyclic antidepressant as first-line treatment. Given the limited evidence, there is a compelling need for further studies with longer follow-up periods and careful definition and follow-up of emerging mania and partial remission.

PMID: 15337640
Rating: 1b

Gillis, B., et al. Identification of Human cell responses to benzene and benzene metabolites. Genomics. 2007. Number 90: 324-33.

Rating: 5c

Quality: N/A. Total Rating: N/A. Comment: Does not meet inclusion criteria for evidence-based review. [CA DWC]

Gilron I, Bailey JM, Tu D, Holden RR, Weaver DF, Houlden RL. Morphine, gabapentin, or their combination for neuropathic pain. N Engl J Med. 2005 Mar 31;352(13):1324-34.

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BACKGROUND: The available drugs to treat neuropathic pain have incomplete efficacy and dose-limiting adverse effects. We compared the efficacy of a combination of gabapentin and morphine with that of each as a single agent in patients with painful diabetic neuropathy or postherpetic neuralgia. METHODS: In this randomized, double-blind, active placebo-controlled, four-period crossover trial, patients received daily active placebo (lorazepam), sustained-release morphine, gabapentin, and a combination of gabapentin and morphine--each given orally for five weeks. The primary outcome measure was mean daily pain intensity in patients receiving a maximal tolerated dose; secondary outcomes included pain (rated according to the Short-Form McGill Pain Questionnaire), adverse effects, maximal tolerated doses, mood, and quality of life. RESULTS: Of 57 patients who underwent randomization (35 with diabetic neuropathy and 22 with postherpetic neuralgia), 41 completed the trial.

Mean daily pain (on a scale from 0 to 10, with higher numbers indicating more severe pain) at a maximal tolerated dose of the study drug was as follows: 5.72 at baseline, 4.49 with placebo, 4.15 with gabapentin, 3.70 with morphine, and 3.06 with the gabapentin-morphine combination (P<0.05 for the combination vs. placebo, gabapentin, and morphine). Total scores on the Short-Form McGill Pain Questionnaire (on a scale from 0 to 45, with higher numbers indicating more severe pain) at a maximal tolerated dose were 14.4 with placebo, 10.7 with gabapentin, 10.7 with morphine, and 7.5 with the gabapentin-morphine combination (P<0.05 for the combination vs. placebo, gabapentin, and morphine). The maximal tolerated doses of morphine and gabapentin were lower (P<0.05) with the combination than for each drug as single agent. At the maximal tolerated dose, the gabapentin-morphine combination resulted in a higher frequency of constipation than gabapentin alone (P<0.05) and a higher frequency of dry mouth than morphine alone (P<0.05). CONCLUSIONS: Gabapentin and morphine combined achieved better analgesia at lower doses of each drug than either as a single agent, with constipation, sedation, and dry mouth as the most frequent adverse effects. Copyright 2005 Massachusetts Medical Society.

Publication Types:
- Clinical Trial
- Randomized Controlled Trial

PMID: 15800228
Rating: 2b
Clinical Question: Is the combination of gabapentin (Neurontin) and morphine more effective for neuropathic pain than either drug alone?
Setting: Outpatient (specialty)
Study Design: Crossover trial (randomized)
Allocation: Concealed
Synopsis: Gabapentin and morphine are widely used for neuropathic pain, but it is unclear whether the combination is better than either drug alone. The authors of this small study used a crossover design. Each patient took each drug or a combination of drugs and served as his or her own control. This study design makes it possible to identify statistically significant results with a relatively small sample size. The 57 patients in the study had diabetic neuropathy or postherpetic neuralgia that was at least moderate in severity and had been present for at least three months. Those with postherpetic neuralgia were somewhat older than those with diabetic neuropathy (mean age: 68 versus 60 years). They stopped taking any medications for neuralgia and kept a pain diary for seven days to establish their baseline level of symptoms.
Patients were then assigned randomly to one of four treatment sequences. Each sequence included the following maximal target dosages for the four treatment regimens: (1) sustained-release morphine in a dosage of 60 mg twice daily, (2) gabapentin in a dosage of 3,200 mg daily in three divided doses, (3) sustained-release morphine in a dosage of 30 mg twice daily plus gabapentin in a dosage of 800 mg three times daily, and (4) active placebo with a low dose of lorazepam (Ativan; not believed to be effective for neuropathic pain, but patients were more likely to believe they were taking an active drug

because of its side effects). Each treatment period lasted five weeks, with the dosage slowly escalated during the first three weeks, outcomes measured during the fourth week, and the drugs tapered and stopped during the fifth week. Older and smaller patients had somewhat lower target dosages than the dosages listed above (60 mg for morphine alone and 2,400 mg for gabapentin alone). Most patients did not reach the maximal dosage; the mean final dosages for morphine and gabapentin when used in combination were 35 mg and 1,700 mg per day, respectively.
Only 41 of 57 patients completed the study; most of the others dropped out during the first treatment period. The primary outcome was the mean pain intensity on a scale from zero to 10 during the fourth week when patients were receiving the maximal dosage of each drug. Average pain intensity was 5.70 at baseline and was decreased to 4.50 with placebo, 4.15 with gabapentin, 3.70 with morphine, and 3.10 with the combination of gabapentin and morphine. The differences between the individual active drugs and the combination were statistically significant but of marginal clinical significance. In general, on a 10-point scale, a difference of less than 1 to 1.5 points is not clinically important. Patients receiving morphine alone or in combination with gaba-pentin had significant side effects; 21 percent receiving the combination had constipation, sedation, and dry mouth.
Bottom Line: The combination of gabapentin and morphine provides a small but clinically unimportant benefit over either drug alone. Tricyclic antidepressants have been shown in other studies to be as effective as gabapentin and are much less expensive, but were not studied in this trial. (Level of Evidence: 1b)

Gilron I, Watson CP, Cahill CM, Moulin DE. Neuropathic pain: a practical guide for the clinician. CMAJ. 2006;175:265-75.

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Neuropathic pain, caused by various central and peripheral nerve disorders, is especially problematic because of its severity, chronicity and resistance to simple analgesics. The condition affects 2%-3% of the population, is costly to the health care system and is personally devastating to the people who experience it. The diagnosis of neuropathic pain is based primarily on history (e.g., underlying disorder and distinct pain qualities) and the findings on physical examination (e.g., pattern of sensory disturbance); however, several tests may sometimes be helpful. Important pathophysiologic mechanisms include sodium-and calcium-channel upregulation, spinal hyperexcitability, descending facilitation and aberrant sympathetic-somatic nervous system interactions. Treatments are generally palliative and include conservative nonpharmacologic therapies, drugs and more invasive interventions (e.g., spinal cord stimulation). Individualizing treatment requires consideration of the functional impact of the neuropathic pain (e.g., depression, disability) as well as ongoing evaluation, patient education, reassurance and specialty referral. We propose a primary care algorithm for treatments with the most favourable risk-benefit profile, including topical lidocaine, gabapentin, pregabalin, tricyclic antidepressants, mixed serotonin-norepinephrine reuptake inhibitors, tramadol and opioids. The field of neuropathic pain research and treatment is in the early stages of development, with many unmet goals.

In coming years, several advances are expected in the basic and clinical sciences of neuropathic pain, which will provide new and improved therapies for patients who continue to experience this disabling condition.

PMID: 16880448

Rating: 5b

Gilron I, Coderre TJ. Emerging drugs in neuropathic pain. Expert Opin Emerg Drugs. 2007;12:113-26.

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Neuropathic pain is a personally devastating and costly condition affecting 3-8% of the population. Existing treatments have limited effectiveness and produce relatively frequent adverse effects. Preclinical research has identified many promising pharmacological targets; however, reliable predictors of success in humans remain elusive. At least 50 new molecular entities have reached clinical development including: glutamate antagonists, cytokine inhibitors, vanilloid-receptor agonists, catecholamine modulators, ion-channel blockers, anticonvulsants, opioids, cannabinoids, COX inhibitors, acteylcholine modulators, adenosine receptor agonists and several miscellaneous drugs. Eight drugs are in Phase III trials at present. Strategies that may show promise over existing treatments include topical therapies, analgesic combinations and, in future, gene-related therapies. Recent years have heralded an explosion of pharmaceutical development in neuropathic pain, reflecting advanced knowledge of neurobiology and a heightened perception of the commercial value of neuropathic pain therapeutics. In the interest of improving patient care, the authors recommend implementing comparative studies throughout the development process in order to demonstrate the increased value of novel agents.

PMID: 17355217

Rating: 5b

Göbel H, Heinze A, Reichel G, Hefter H, Benecke R; Dysport myofascial pain study group. Efficacy and safety of a single botulinum type A toxin complex treatment (Dysport) for the relief of upper back myofascial pain syndrome: results from a randomized double-blind placebo-controlled multicentre study. Pain. 2006 Nov;125(1-2):82-8.

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Botulinum type A toxin (BoNT-A) has antinociceptive and muscle-relaxant properties and may help relieve the symptoms of myofascial pain syndrome. In this study we evaluated the efficacy and tolerability of BoNT-A (Dysport) in patients with myofascial pain syndrome of the upper back. We

conducted a prospective, randomized, double-blind, placebo-controlled, 12-week, multicentre study. Patients with moderate-to-severe myofascial pain syndrome affecting cervical and/or shoulder muscles (10 trigger points, disease duration 6-24 months) were randomized to Dysport or saline. Injections were made into the 10 most tender trigger points (40 units per site). The primary outcome was the proportion of patients with mild or no pain at week 5. Secondary outcomes included changes in pain intensity and the number of pain-free days per week. Tolerability and safety were also assessed. At week 5, significantly more patients in the Dysport group reported mild or no pain (51%), compared with the patients in the placebo group (26%; p=0.002). Compared with placebo, Dysport resulted in a significantly greater change from baseline in pain intensity during weeks 5-8 ($p<0.05$), and significantly fewer days per week without pain between weeks 5 and 12 (p=0.036). Treatment was well tolerated, with most side effects resolving within 8 weeks. In conclusion, in patients with upper back myofascial pain syndrome, injections of 400 Ipsen units of Dysport at 10 individualised trigger points significantly improved pain levels 4-6 weeks after treatment. Injections were well tolerated.

PMID: 16750294

Rating: 2c

Gold BD, Scheiman JM, Sabesin SM, Vitat P. Updates on the management of upper gastrointestinal disorders in the primary care setting: NSAID-related gastropathies and pediatric reflux diseases. J Fam Pract. 2007;56:S1-S12.

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Nonsteroidal anti-inflammatory drugs (NSAIDs) are among the most widely used medications in the United States, owing to their analgesic, anti-inflammatory, and antipyretic properties. Aspirin, which is also an NSAID, is frequently used for cardiovascular (CV) prophylaxis. However, the use of "traditional" NSAIDs results in serious upper gastrointestinal (GI) adverse events in nearly one fourth of patients. Cyclooxygenase-2 (COX-2)-selective inhibitors are beneficial in alleviating GI adverse events, but with the possible trade-off of causing CV adverse events in at-risk patients. Hence, balancing the CV risks of COX-2 inhibitors with the higher GI risks of nonselective NSAIDs remains a major clinical challenge. The management of gastroesophageal reflux disease (GERD) continues to garner significant attention among physicians who care for adults. However, there is an increasing awareness that this disorder may originate in childhood. Pediatric GERD is likely to share a similar pathophysiology with adult GERD. Early detection and treatment in children may yield better adult disease outcomes, improved quality of life, and a decreased overall health care burden. This review article examines important considerations pertaining to the management of some specific upper GI disorders seen in the primary care setting, namely NSAID-associated gastropathies and pediatric reflux disease. Its content is derived from the proceedings of a satellite symposium that was held during the 2006 American Academy of Family Physicians' Scientific Assembly in Washington, DC.

PMID: 17343806

Rating: 5a

Goldberg, M., et al. Multi-Day Low Dose Ketamine Infusion for the Treatment of Complex Regional Pain Syndrome. Pain Physician. 2005;Volume 8, Number 2: 175-19.

Rating: 2c

Quality: Low. Total Rating: 1.0. Comment: Does not meet inclusion criteria for evidence-based review. [CA DWC]

Goldenberg DL, Burckhardt C, Crofford L. Management of fibromyalgia syndrome. JAMA. 2004 Nov 17;292(19):2388-95.

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The optimal management of fibromyalgia syndrome (FMS) is unclear. This was a search of all human trials (randomized controlled trials and meta-analyses of randomized controlled trials) of FMS, and a total of 505 articles were reviewed. The study concluded, "current evidence suggests efficacy of low-dose tricyclic antidepressants, cardiovascular exercise, cognitive behavioral therapy, and patient education. A number of other commonly used FMS therapies, such as trigger point injections, have not been adequately evaluated. Despite the chronicity and complexity of FMS, there are pharmacological and nonpharmacological interventions available that have clinical benefit. Based on current evidence, a stepwise program emphasizing education, certain medications, exercise, cognitive therapy, or all 4 should be recommended."

Publication Types:
- Guideline
- Practice Guideline
- Review

PMID: 15547167

Rating: 1b

Fibromyalgia, as defined by the presence of widespread bodily pain and the presence of excessive tenderness at 11 out of 18 pressure points, affects about 2 percent of the U.S. population. Fibromyalgia often is associated with mood disorders and comorbidities, and psychosocial factors often are

implicated. Overall, patients with fibromyalgia appear to have an altered response to pain. Goldenberg and colleagues review the evidence-based findings of the American Pain Society's commissioned report on fibromyalgia treatment.
Evidence was categorized as "strong" if there was support from a meta-analysis or more than one randomized controlled trial (RCT); "moderate" if positive findings from one RCT or consistent positive findings came from several RCT's or multiple non-RCT studies; and "weak" with positive results from lower-quality trials. Outcome measures were predominantly levels of pain; they also included physical, psychologic, and social function.
From a pharmacologic perspective, the strongest evidence supported the efficacy of tricyclic antidepressants such as amitriptyline (Elavil) and cyclobenzaprine (Flexeril). Moderate evidence suggested benefit from selective serotonin reuptake inhibitors as well as from two new dual serotonin and norepinephrine uptake inhibitors, milnacipran (Ixel) and duloxetine (Cymbalta). The analgesic tramadol (Ultram) also was modestly effective. Evidence is lacking for other analgesics, such as nonsteroidal anti-inflammatory drugs and opioids. Benefit also was modestly associated with the anticonvulsant pregabalin (Lyrica). Results from a trial using gabapentin (Neurontin) are pending, and many other medications, such as benzodiazepines and corticosteroids are lacking evidence or have weak evidence of efficacy.
Of the nonmedical therapies, the strongest evidence supports aerobic exercise. Moderate evidence exists to support the use of muscle-strengthening exercises. Cognitive behavior therapy (CBT) also is effective, with strong evidence showing decreased pain and improved function. Other psychologic interventions also appear to be beneficial. In particular, multidisciplinary approaches that combine exercise, CBT, and other modalities appear to maintain treatment gains over long periods. Relaxation, hypnosis, biofeedback, massage, and warm water baths have moderate clinical support.
One drawback of most trials is their short duration. The authors recommend a step-wise approach beginning with thorough patient education, followed by a trial of low-dose tricyclic antidepressants, an exercise program, and CBT. For refractory cases, referral and combination medications are warranted.

Goldenberg DL. Pharmacological treatment of fibromyalgia and other chronic musculoskeletal pain. Best Pract Res Clin Rheumatol. 2007;2:499-511.

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The pharmacologic management of fibromyalgia is based on the emerging evidence that pain in this disorder is primarily related to central pain sensitization. There is strong evidence that tricyclic antidepressants are effective, and moderate evidence for the effectiveness of serotonin reuptake inhibitors and dual serotonin-norepinephrine reuptake inhibitors. Recent work suggests that the anti-seizure medications pregabalin and gabepentin are also effective. The only analgesic demonstrated to be helpful is tramadol.

PMID: 17602996

Rating: 5b

Goldberg RT; Pachas WN; Keith D. Relationship between traumatic events in childhood and chronic pain. Disability Rehabilitation. 01-Jan-1999; 21(1): 23-30.
Abstract:
PURPOSE: The purpose was to examine the relationships between traumatic events in childhood, such as sexual and physical abuse, alcoholism, and drug addiction, and three types of chronic pain: facial pain, myofascial pain, and fibromyalgia. A fourth group, a heterogeneous group of other pain, was used as a comparison group. METHOD: Ninety one patients with chronic pain, age range 20-60, were consecutively recruited from the outpatient clinics of a rehabilitation hospital and a general hospital. Patients were given four measures for completion at evaluation: Childhood History Questionnaire; Childhood Traumatic Events Scale; McGill Melzack Pain Questionnaire; Pain Disability Index. Chi-square was used to test significant differences among four pain groups on sexual, physical, and verbal abuse; alcoholism; drug dependence; medications; major upheaval, childhood illness, death of a family member or friend, and separation or divorce of parents. Logistic regression was used to predict membership in the four pain groups. RESULTS: All pain groups had a history of abuse exceeding 48%: fibromyalgia, 64.7%; myofascial, 61.9%; facial, 50%; other pain, 48.3%. All groups had a history of family alcohol dependence exceeding 38%, and a history of drug dependence ranging from 5.8 to 19.1%. A combined history of pain, child physical abuse, and alcoholism was prevalent in 12.9 to 35.3%. Logistic regression showed patients who were female, with an alcoholic parent, using non-narcotic drugs were more likely to be members of the facial, myofascial, and fibromyalgia groups. CONCLUSIONS: Child traumatic events are significantly related to chronic pain. Since the problem of child abuse is broader than physical and sexual abuse, health and rehabilitation agencies must shift from individualized treatment to interdisciplinary treatment of the family and patient.
Major Subjects:
- Child Abuse / * psychology
- Facial Pain / epidemiology / * psychology
- Fibromyalgia / epidemiology / * psychology
- Myofascial Pain Syndromes / epidemiology / * psychology

Publication Type: Case Control Study, 91 cases
Gonge H, Jensen LD, Bonde JP. Do psychosocial strain and physical exertion predict onset of low-back pain among nursing aides? Scand J Work Environmental Health. 2001 Dec;27(6):388-94.

Abstract:

OBJECTIVES: The aim of this study was to investigate psychosocial factors and physical exertion at work in relation to the onset of low-back pain. METHODS: The study was carried out as a case-crossover investigation of nursing aides caring for the elderly. Cases were identified among 157 nursing

aides over a period of 2 years. Psychosocial factors, physical exertion, and low-back pain were reported daily in diary questionnaires over three consecutive days at work, repeated in six periods of 3 days. For each subject, case observations were identified as pain onset from one day to the next and matched with reference observations with no pain onset from the same person. Prospective data collection allowed analyses to be conducted with and without a lag in time between exposure and pain onset. RESULTS: The results of the analyses with time lag (longitudinal) did not support the hypothesis that psychosocial and physical strain from 1 day of work predicts pain onset the following day. However, physical exertion, stress, and, to some extent, time pressure were associated with pain on the day of onset. CONCLUSION: The effect period, if any, of exposure to physical exertion, stress, and time pressure on the onset of acute low-back pain is considered to be less than 24 hours.

Publication Type: Case Control Study, 157 cases

Gore M, Dukes E, Rowbotham DJ, Tai KS, Leslie D. Clinical characteristics and pain management among patients with painful peripheral neuropathic disorders in general practice settings. Eur J Pain. 2007;11:652-64.

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Alleviating chronic pain is a global healthcare priority. Understanding the medical profile and current treatment patterns in patients with painful neuropathic disorders (PNDs) is crucial to the development of effective pain management strategies. Thus, our objective was to describe the demographic and clinical characteristics of persons with PNDs and their use of pain medications. Using the general practice research database, we categorized PNDs in two ways: Pure PNDs (which include diabetic neuropathy, postherpetic neuralgia, etc.; N=16,690) and Mixed PNDs (which include back/neck pain with neuropathic involvement; N=14,309). On average, PND patients were 55 years old (Pure, 55.4 [SD=16.9] years; Mixed, 54.3 [SD=16.4] years). Over a third had other chronic pain-related (Pure, 37.5%; Mixed, 37.1%) and nearly a quarter had non-pain related (Pure, 28.1%; Mixed, 24.1%) comorbidities. Use of medications with clinically demonstrated efficacy in PNDs was higher among patients with Pure PNDs (tricyclic antidepressants [Pure, 16.6%; Mixed, 10.1%]; 2nd generation antidepressants [Pure, 11.0%; Mixed, 9.7%]; and antiepileptics [Pure, 12.2%; Mixed, 2.6%]), whereas use of NSAIDs (Pure, 43.1%; Mixed, 65.2%) and opioids (Pure, 8.5%; Mixed, 14.3%) was higher among patients with Mixed PNDs. Average daily doses of select neuropathic pain-related medications among PND patients (Pure and Mixed) were lower than those recommended for neuropathic pain. Among both Pure and Mixed PND patients, use and doses of evidenced-based neuropathic pain-related medications was low, and lower than the use of NSAIDs (a medication class with no proven efficacy for PNDs) in each group, suggesting possible sub-optimal neuropathic pain management among these patients.

PMID: 17126045

Rating: 4c

Gowing L, Ali R, White J. Opioid antagonists under heavy sedation or anaesthesia for opioid withdrawal. Cochrane Database Syst Rev. 2006 Apr 19;(2):CD002022.

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BACKGROUND: Withdrawal (detoxification) is necessary prior to drug-free treatment. It may also represent the end point of long-term opioid replacement treatment such as methadone maintenance. The availability of managed withdrawal is essential to an effective treatment system. OBJECTIVES: To assess the effectiveness of interventions involving the administration of opioid antagonists to induce opioid withdrawal with concomitant heavy sedation or anaesthesia, in terms of withdrawal signs and symptoms, completion of treatment and adverse effects. SEARCH STRATEGY: We searched the Drugs and Alcohol Group register (October 2003), Cochrane Central Register of Controlled Trials (The Cochrane Library, Issue 4, 2004), Medline (January 1966 to January 2005), Embase (January 1985 to January 2005), PsycINFO (1967 to January 2005), and Cinahl (1982 to December 2004) and reference lists of studies. SELECTION CRITERIA: Controlled trials comparing antagonist-induced withdrawal under heavy sedation or anaesthesia with another form of treatment, or a different regime of anaesthesia-based antagonist-induced withdrawal. DATA COLLECTION AND ANALYSIS: One reviewer assessed studies for inclusion and undertook data extraction and assessed quality. Inclusion decisions and the overall process were confirmed by consultation between all three reviewers. MAIN RESULTS: Six studies (five randomised controlled trials) involving 834 participants met the inclusion criteria for the review. Antagonist-induced withdrawal is more intense but less prolonged than withdrawal managed with reducing doses of methadone, and doses of naltrexone sufficient for blockade of opioid effects can be established significantly more quickly with antagonist-induced withdrawal than withdrawal managed with clonidine and symptomatic medications. The level of sedation does not affect the intensity and duration of withdrawal, although the duration of anaesthesia may influence withdrawal severity. There is a significantly greater risk of adverse events with heavy, compared to light, sedation (RR 3.21, 95% CI 1.13 to 9.12, P = 0.03) and probably also other forms of detoxification. AUTHORS' CONCLUSIONS: Heavy sedation compared to light sedation does not confer additional benefits in terms of less severe withdrawal or increased rates of commencement on naltrexone maintenance treatment. Given that the adverse events are potentially life-threatening, the value of antagonist-induced withdrawal under heavy sedation or anaesthesia is not supported. The high cost of anaesthesia-based approaches, both in monetary terms and use of scarce intensive care resources, suggest that this form of treatment should not be pursued.

PMID: 16625552

Raing: 1b

"Considerably more research evidence will be needed before any conclusions can be drawn regarding the effectiveness of managing withdrawal by administration of opioid antagonists under heavy sedation or anaesthesia. The risk of vomiting during sedation, respiratory depression and cardiac irregularities point to the approach being limited to facilities equipped for intubation, assisted ventilation and a high level of monitoring, and with the capacity to respond to adverse events that might occur. The approach must be regarded as experimental with both risks and benefits remaining uncertain."

Grabow TS, Raja SN. Complex Regional Pain Syndrome I (Reflex Sympathetic Dystrophy). Anesthesiology. Volume 96 • Number 5 • May 2002.

" Despite the long history of these disorders, the natural course and pathophysiology of CRPS types I and II are elusive, and hence, their therapies remain controversial."
Publication Type: Review
Rating: 5b

Grabow TS, Guarino Ah, Raja SN. Complex regional pain syndromes: Diagnosis and treatment. In: Benzon HT, Raja SN, Molloy RE, Liu SS, Fishman SM. Essentials of Pain Medicine and Regional Anesthesia. 2nd ed. Elisevier, 2005.

Rating: 9a

Graff-Radford SB. Myofascial pain: diagnosis and management. Curr Pain Headache Rep. 2004 Dec;8(6):463-7.

The Pain Center, Cedars-Sinai Medical Center, 444 South San Vicente Blvd., #1101, Los Angeles, CA 90048, USA. graffs@cshs.org.

Clinical understanding and management of myofascial pain is overlooked frequently when dealing with pain. Myofascial pain is defined as pain or autonomic phenomena referred from active trigger points, with associated dysfunction. The trigger point is a focus of hyperirritability in the muscle that, when compressed, is locally tender and, if sensitized, gives rise to referred pain and tenderness. The pain quality is dull or achy and associated with autonomic changes. Myofascial pain is poorly understood, which results too often in underdiagnosis and poor management. The pathogenesis likely has a central mechanism with peripheral clinical manifestations. The therapy for myofascial pain requires enhancing central inhibition through pharmacology or behavioral techniques and simultaneously reducing peripheral inputs through physical therapies including exercises and trigger point-specific therapy.

Publication Types:
- Review

PMID: 15509460

Rating: 5b

Grant, I. S., et al. Pharmacokinetics and Analgesic Effects of I.M. and Oral Ketamine. British Journal Anesthesiology. 1981; Volume 53, 805-10.

Rating: 2c

Quality: Low Total Rating: 2.5 Comment: Does not meet inclusion criteria for evidence-based review. [CA DWC]

Gross DP, Battie MC. Predicting timely recovery and recurrence following multidisciplinary rehabilitation in patients with compensated low back pain. Spine. 2005 Jan 15;30(2):235-40.

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STUDY DESIGN: Historical cohort study. OBJECTIVES: We investigated factors predictive of timely and sustained recovery following multidisciplinary rehabilitation in Workers' Compensation claimants with low back pain. SUMMARY OF BACKGROUND DATA: It is still unknown which factors predict better outcomes among back pain patients enrolled in intensive rehabilitation programs. Previously, few consistent predictors have been reported. METHODS: We created and tested predictive models using data from clinical and administrative databases of the Alberta Workers' Compensation Board. Predictive models were built on a cohort of subjects admitted for multidisciplinary rehabilitation in 1999 and tested on subjects admitted in 2000. Cox regression was used to evaluate days to time-loss benefit suspension and days to claim closure following admission for rehabilitation. Logistic regression was used to evaluate risk of future recurrence as judged through time-loss benefit resumption, claim reopening, or new back-related claims filing. RESULTS: Prediction models were variable between exploratory and confirmatory stages, and few variables were found to predict consistently. The number of preadmission healthcare visits was the most robust predictor of all recovery outcomes. Recurrence rates were 18% in 1999 and 22% in 2000. A higher number of preadmission healthcare visits and more previous back-related claims were associated with higher risk of recurrence. CONCLUSIONS: The number of preadmission healthcare visits was the most robust prognostic indicator with more healthcare visits related to delayed recovery and higher risk of recurrence. Recurrence rates following successful functional restoration were consistent with the episodic and recurrent nature of low back pain.

PMID: 15644763

Rating: 3b

Guay DR. Oxcarbazepine, topiramate, zonisamide, and levetiracetam: potential use in neuropathic pain. Am J Geriatr Pharmacother. 2003 Sep;1(1):18-37.

Department of Experimental and Clinical Pharmacology, Institute for the Study of Geriatric Pharmacotherapy, College of Pharmacy, University of Minnesota, Minneapolis, Minnesota, USA. guayx001@umn.edu

BACKGROUND: Oxcarbazepine, topiramate, zonisamide, and levetiracetam are the antiepileptic drugs (AEDs) most recently approved by the US Food and Drug Administration. Based on the experience with carbamazepine, gabapentin, and lamotrigine, these newer AEDs are being investigated for the management of neuropathic pain. OBJECTIVE: This article reviews preclinical and clinical data on the efficacy and tolerability of these 4 AEDs in the management of neuropathic pain, as well as the pharmacokinetics, drug-interaction potential, adverse effects, and dosing of these agents, with an emphasis on their use in older individuals. METHODS: Relevant studies were identified through a MEDLINE search of the Englidh-language literature published between 1986 and May 2003, a review of the reference lists of identified articles, and abstracts from the annual meetings of the American Academy of Neurology (1986-2002) and the 2003 Annual Meeting of the American Pain Society. Search terms were oxcarbazepine, topiramate, zonisamide, and levetiracetam. RESULTS: Oxcarbazepine and topiramate have been effective in animal models of neuropathic pain. Thirty-four publications on the efficacy and tolerability of the 4 agents were identified (25 case reports/case series, 6 randomized parallel-group studies, and 3 randomized crossover studies). The 9 randomized studies were restricted to oxcarbazepine and topiramate, and 23 (68%) publications were available in abstract form only. These preliminary data suggest that the 4 newer AEDs may be useful in a wide variety of neuropathic pain syndromes; however, additional data, including full-length peer-reviewed reports, are necessary before their true analgesic potential in neuropathic pain can be determined. All 4 agents have pharmacodynamic interactions with other psychotherapeutic drugs, potentiating adverse central nervous system events such as sedation. With the exception of levetiracetam, these drugs also have pharmacokinetic interactions with other drugs, although to a somewhat lesser extent than carbamazepine. These agents have some unique adverse effects not frequently monitored by clinicians, such as hyponatremia, nephrolithiasis, acute myopia with secondary angle-closure glaucoma, and weight loss. CONCLUSIONS: Based on preliminary data, oxcarbazepine, topiramate, zonisamide, and levetiracetam may be useful in the treatment of a wide variety of neuropathic pain syndromes, although full publication of the results of controlled trials is awaited. These agents are associated with specific adverse effects not commonly monitored by clinicians. Of the 4, levetiracetam appears to be easiest to use (ie, no need for dose adjustment in organ dysfunction, no need for laboratory monitoring) and best tolerated, and has not been associated with the unique toxicities seen with oxcarbazepine, topiramate, and zonisamide. The ultimate role of these agents in the therapeutic armamentarium against pain requires further research and experience. In the interim, these 4 agents should be used to treat neuropathic pain in the elderly only when carbamazepine, gabapentin, or lamotrigine cannot be used or when the response to the aforementioned agents is suboptimal.

PMID: 15555463

Rating: 1b

Guillaume D, Van Havenbergh A, Vloeberghs M, Vidal J, Roeste G. A clinical study of intrathecal baclofen using a programmable pump for intractable spasticity. Arch Phys Med Rehabil. 2005;86:2165-71.

Centre Neurologique et de Readaptation Fonctionnelle, Fraiture-en-Condroz, Belgium.

OBJECTIVE: To determine the impact of intrathecal baclofen (ITB) therapy on outcomes of functional independence, pain, subjective improvement, performance, and standard measures of spasticity. DESIGN: A noncomparative, multicenter, prospective cohort trial of patients with implanted pumps followed up over a 12-month period for the assessment of spasticity, pain, and function. SETTING: Twenty-four European centers of neurology or rehabilitation familiar with implantable pump technique participated. PARTICIPANTS: Patients with intractable spasticity (N=138) who responded positively to a trial dose of baclofen (n=133) and who began ITB therapy (n=129) were enrolled. INTERVENTION: Implantation of a Medtronic SynchroMed Infusion System with the administration of ITB therapy. MAIN OUTCOME MEASURES: Ashworth Scale assessment, Penn Spasm Frequency Scale scores, pain assessment, FIM instrument scores or WeeFIM scores for children, Canadian Occupational Performance Measure (COPM), and subjective ratings of overall relief were the tools administered. RESULTS: Muscle tone, spasm scores, and pain intensity reductions were observed. Overall FIM scores increased significantly in cognitive and motor function. COPM scores for both performance and satisfaction also improved significantly. Patients reported increased relief from pain and spasticity, supported by physician reports. Forty-three percent of patients reported adverse events, mostly related to patients' underlying conditions (20%), the device implant surgery (10%), or complications with the catheter (9%). CONCLUSIONS: ITB therapy using a programmable pump is clinically effective and well tolerated, despite a seemingly high level of adverse events, in patients with intractable spasticity of spinal or cerebral origin and may offer improvements in pain relief and function.

PMID: 16271565

Rating: 3b

Gürol Z, Hekimoğlu S, Demirdamar R, Sumnu M. Percutaneous absorption of ketoprofen. I. In vitro release and percutaneous absorption of ketoprofen from different ointment bases. Pharm Acta Helv. 1996;71:205-12.

Hacettepe University, Faculty of Pharmacy, Department of Pharmaceutical Technology, Ankara, Turkey.

Ketoprofen (KP) is a potent non-steroidal anti-inflammatory drug which is used for the treatment of rheumatoid arthritis. The oral administration of KP can cause gastric irritation and renal adverse effects. Topical application of the drug can bypass gastrointestinal disturbances and provide relatively consistent drug levels at the site of action. Since the efficacy of an ointment depends on the type of ointment base and the concentration of the drug, four different bases (white petrolatum, cold cream, hydrophilic ointment and Carbopol 940 gel) were used at 1, 3, 5, 7 and 10% concentrations of KP to evaluate the effect of ointment base and concentration. The general rank order of the drug release was found to be: Carbopol gel > hydrophilic ointment > cold cream > white petrolatum. There was a positive correlation between the concentration of KP and release rate for all bases except Carbopol gel. The in vivo percutaneous absorption of KP from different ointment bases at 3% concentration was studied by carrageenan-induced paw edema in mice. The rank order of the percent edema inhibition was as follows: Carbopol gel > or = hydrophilic ointment > cold cream > white petrolatum. There was a good correlation between the in vitro and in vivo results.

PMID: 8818309

Rating: 4b

Gusi N, Tomas-Carus P. Cost-utility of an 8-month aquatic training for women with fibromyalgia: a randomized controlled trial. Arthritis Res Ther. 2008 Feb 22;10(1):R24.

ABSTRACT: BACKGROUND: Physical therapy in warm-water has been effective and highly recommended in persons with fibromyalgia but its efficiency remains mainly unknown. Should patients or health care managers invest in this therapy? The aim of the current study was to assess the cost-utility of adding an aquatic exercise programme to the usual care of women with fibromyalgia. METHODS: Costs to the health care system and to society were considered in this study that included 33 participants, randomly assigned to an experimental group (n=17) or a control group (n=16). The intervention in the experimental group consisted of a one-hour, supervised, water-based exercise sessions, three times per week for 8 months. The main outcome measures were the health care costs and the number of quality-adjusted life-years (QALYs) using the time trade-off elicitation technique from the EQ-5D. Sensitivity analyses was performed for variations in the staff salary, number of women attending sessions and time spent going to the pool. The cost-effectiveness acceptability curves were created using a non-parametric bootstrap technique. RESULTS: The mean incremental treatment costs exceeded those for usual care per patient by 517 Euros for health care costs and 1032 Euros for societal costs. The mean incremental QALY associated with the intervention was 0.131 (95% CI: 0.011 to 0.290). Each QALY gained in association with the exercise programme cost an additional 3947 Euro/QALY (95% CI: 1782 to 47,000) for a health care perspective and 7878 Euro/QALY (3559 to 93818) from a societal perspective. The curves showed a 95% probability that the addition of the water-based programme is a cost-effective strategy if the ceiling of inversion is 14200 Euro/QALY from a health care perspective and 28300 Euro/QALY from a societal perspective. CONCLUSIONS: The addition of an aquatic exercise programme to the usual care for fibromyalgia in women, is cost-effective in terms of both health care

costs and societal costs. However, the characteristics of facilities (distance from the patients homes and number of patients that can be accommodated per session) are major determinants to consider before investing in such a programme. Trial registration: Current Controlled Trials ISRCTN53367487.

PMID: 18294367

Rating: 2c

Guzman J, Esmail R, Karjalainen K. et al. Multidisciplinary Rehabilitation for Chronic Low Back Pain: Systematic Review. BMJ 2001;322:1511-1516.

OBJECTIVE: To assess the effect of multidisciplinary biopsychosocial rehabilitation on clinically relevant outcomes in patients with chronic low back pain. DESIGN: Systematic literature review of randomised controlled trials. PARTICIPANTS: A total of 1964 patients with disabling low back pain for more than three months. MAIN OUTCOME MEASURES: Pain, function, employment, quality of life, and global assessments. RESULTS: Ten trials reported on a total of 12 randomised comparisons of multidisciplinary treatment and a control condition. There was strong evidence that intensive multidisciplinary biopsychosocial rehabilitation with functional restoration improves function when compared with inpatient or outpatient non-multidisciplinary treatments. There was moderate evidence that intensive multidisciplinary biopsychosocial rehabilitation with functional restoration reduces pain when compared with outpatient non-multidisciplinary rehabilitation or usual care. There was contradictory evidence regarding vocational outcomes of intensive multidisciplinary biopsychosocial intervention. Some trials reported improvements in work readiness, but others showed no significant reduction in sickness leaves. Less intensive outpatient psychophysical treatments did not improve pain, function, or vocational outcomes when compared with non-multidisciplinary outpatient therapy or usual care. Few trials reported effects on quality of life or global assessments. CONCLUSIONS: The reviewed trials provide evidence that intensive multidisciplinary biopsychosocial rehabilitation with functional restoration reduces pain and improves function in patients with chronic low back pain. Less intensive interventions did not show improvements in clinically relevant outcomes.

Publication Type: Systematic Review/Meta-Analysis

Rating: 1b

Gulevich SJ, Conwell TD, Lane J, Lockwood B, Schwettmann RS, Rosenberg N, Goldman LB. Stress Infrared Telethermography Is Useful in the Diagnosis of Complex Regional Pain Syndrome, Type I (Formerly Complex Regional Dystrophy). Clin J Pain 1997;13:50-59.

OBJECTIVE: To assess the sensitivity, specificity, and predictive value (PV) of stress infrared telethermography (IRT) in the complex regional pain syndrome, type I (CRPS-I). METHODS: One hundred eighty-five consecutive patients (47 men, 138 women) with 205 pairs of chronically painful

limbs (upper, lower, or both) were examined by pain specialists in neurology, physiatry, and anesthesia, who then reached a consensus diagnosis. A clinical diagnosis of CRPS-I required at least two of the following observations: burning pain, vasomotor changes, diaphoresis, trophic changes, allodynia. Patients with only one criterion were classified as possible CRPS-I; those with none were judged not to have CRPS-I. Patients and 24 asymptomatic control subjects underwent stress IRT, which was considered positive for CRPS-I if it showed three of the following: quantitative thermal emission of > or = 1.00 degree C, abnormal distal thermal gradient patterns, presence of a "thermal marker," and abnormal response to functional cold water autonomic stress testing. RESULTS: By clinical criteria, CRPS-I was diagnosed in 73 pairs of limbs; not CRPS-I was diagnosed in 70; and 62 pairs had possible CRPS-I. Excluding possible CRPS-I cases, there were 5 false-negative stress IRTs (sensitivity 93%) and 7 false-positive results (specificity 89%). Based on estimated 50% prior probability for our population, the positive PV is 90% and the negative PV 94%. None of the control subjects exhibited thermographic evidence of CRPS-I. CONCLUSION: Stress IRT is a sensitive and specific indicator of CRPS-I.

Publication Type: Case Control Study, 185 cases

Haddad RM, Kennedy CC, Caples SM, Tracz MJ, Bolona ER, Sideras K, Uraga MV, Erwin PJ, Montori VM. Testosterone and cardiovascular risk in men: a systematic review and meta-analysis of randomized placebo-controlled trials. Mayo Clin Proc. 2007;82:29-39.

Knowledge and Encounter Research Unit, Mayo Clinic College of Medicine, Rochester, Minn 55905, USA.

OBJECTIVE: To conduct a systematic review and meta-analysis of randomized trials that assessed the effect of testosterone use on cardiovascular events and risk factors in men with different degrees of androgen deficiency. METHODS: Librarian-designed search strategies were used to search the MEDLINE (1966 to October 2004), EMBASE (1988 to October 2004), and Cochrane CENTRAL (inception to October 2004) databases. The database search was performed again in March 2005. We also reviewed reference lists from included studies and content expert files. Eligible studies were randomized trials that compared any formulation of commercially available testosterone with placebo and that assessed cardiovascular risk factors (lipid fractions, blood pressure, blood glucose), cardiovascular events (cardiovascular death, nonfatal myocardial infarction, angina or claudication, revascularization, stroke), and cardiovascular surrogate end points (ie, laboratory tests indicative of cardiac or vascular disease). Using a standardized data extraction form, we collected data on participants, testosterone administration, and outcome measures. We assessed study quality with attention to allocation concealment, blinding, and loss to follow-up. RESULTS: The 30 trials included 1642 men, 808 of whom were treated with testosterone. Overall, the trials had limited reporting of methodological features that prevent biased results (only 6 trials reported allocation concealment), enrolled few patients, and were of brief duration (only 4 trials followed up patients for > 1 year). The median loss to follow-up across all 30 trials was 9%. Testosterone use in men with low testosterone levels led to inconsequential changes in blood pressure and glycemia and in all lipid fractions (total

cholesterol: odds ratio [OR], -0.22; 95% confidence interval [CI], -0.71 to 0.27; high-density lipoprotein cholesterol: OR, -0.04; 95% CI, -0.39 to 0.30; low-density lipoprotein cholesterol: OR, 0.06; 95% CI, -0.30 to 0.42; and triglycerides: OR, -0.27; 95% CI, -0.61 to 0.08); results were similar in patients with low-normal to normal testosterone levels. The OR between testosterone use and any cardiovascular event pooled across trials that reported these events (n = 6) was 1.82 (95% CI, 0.78 to 4.23). Several trials failed to report data on measured outcomes. For reasons we could not explain statistically, the results were inconsistent across trials. CONCLUSION: Currently available evidence weakly supports the inference that testosterone use in men is not associated with important cardiovascular effects. Patients and clinicians need large randomized trials of men at risk for cardiovascular disease to better inform the safety of long-term testosterone use.

PMID: 17285783

Rating: 1a

Hadler NM. Fibromyalgia, chronic fatigue, and other iatrogenic diagnostic algorithms. Do some labels escalate illness in vulnerable patients? Postgraduate Medicine. 1997 Aug;102(2):161-2, 165-6, 171-2 passim.

Contemporary medicine has the sophistication to identify the clinical settings in which the hunt for a diagnosis can be harmful to a patient's health. Which patients are best served by a prolonged search for a cause? Why has the disease-illness paradigm backfired for so many patients? Dr Hadler challenges readers to look at the difficult questions linked with diagnostic labels that might teach patients to stay sick.

Publication Type: Review

Halas CJ. Eszopiclone. Am J Health Syst Pharm. 2006;63:41-8.

Adult Critical Care, Penn State Milton S. Hershey Medical Center, Pharmacy, M.C. H079, 500 University Drive, Hershey, PA 17033, USA. chalas@psu.edu

PURPOSE: The pharmacology, pharmacokinetics, indications, clinical efficacy, adverse effects, drug interactions, dosing, and administration of eszopiclone are discussed. SUMMARY: The pharmacology of eszopiclone is not well understood. Eszopiclone is the S-isomer of racemic zopiclone. The relative bioavailability of oral racemic zopiclone is about 80%. Eszopiclone is rapidly absorbed after oral administration, with peak serum concentrations ranging from 1 to 1.3 hours. The efficacy of eszopiclone has been evaluated in healthy adults, including elderly patients, for the treatment of transient and chronic insomnia. Compared with placebo, eszopiclone has been shown to considerably reduce sleep induction and improve sleep maintenance, duration, quality, and depth, as well as next-day functioning. The most

common adverse effects reported are unpleasant taste, headache, and dry mouth. Dosing should be individualized, and the lowest effective dose should be used to minimize the risk of adverse events. The recommended starting dosage for nonelderly patients is 2 mg immediately before bedtime, with adjustment to 3 mg if clinically indicated. Dosage adjustment is necessary in patients with severe hepatic disease and in those receiving concomitant potent cytochrome P-450 isoenzyme 3A4 inhibitors. No dosage adjustment is required for patients with renal dysfunction. The cost of eszopiclone is 3.70 dollars per tablet for all dosage strengths (1-, 2-, and 3-mg tablets). CONCLUSION: Its favorable adverse-effect profile and approved labeling for the treatment of chronic insomnia makes eszopiclone a viable alternative for insomnia treatment. Published data are limited, however, and more clinical trials, including comparator studies, are needed to further evaluate the use of this drug.

PMID: 1637346

Rating: 5b

Haldorsen EM, Grasdal AL, Skouen JS, Risa AE, Kronholm K, Ursin H. Is there a right treatment for a particular patient group? Comparison of ordinary treatment, light multidisciplinary treatment, and extensive multidisciplinary treatment for long-term sick-listed employees with musculoskeletal pain. Pain. 2002 Jan;95(1-2):49-63.

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In general, randomized controlled studies concerning return to work have failed to demonstrate significant treatment effects for long-lasting musculoskeletal pain, and most treatments examined have not been economically beneficial. Individuals (n=654) sick-listed for at least 8 weeks with musculoskeletal pain, selected from the Norwegian mandatory sickness insurance system and volunteering to participate, were categorized into three groups differing in a prognosis score (good, medium, poor) for return to work, based on a brief, standardized screening of psychological and physiotherapy findings. They were then randomly assigned to three outpatient treatments with three different levels of intensity (ordinary treatment, light multidisciplinary, and extensive multidisciplinary treatment). The evaluation was based on 14 months follow-up data on return to work collected from social security records. The patients with good prognosis for return to work do equally well with ordinary treatment as with the two more intensive treatments. The patients with medium prognosis benefit equally from the two multidisciplinary treatments. The patients with poor prognosis receiving extensive multidisciplinary treatment returned to work at a higher rate than patients with poor prognosis receiving ordinary treatment, 55 vs. 37% ($P<0.05$) at 14 months. Multidisciplinary treatment is effective concerning return to work, when given to patients who are most likely to benefit from that treatment. Measures of pain or quality of life are not included in this study. The cost-benefit analysis of the economic returns of the light multidisciplinary and the extensive multidisciplinary treatment programs yields a positive net present social value of the treatment. A simple, standardized, screening instrument

including only psychological and physiotherapeutic observations may be a useful clinical tool for allocating patients with musculoskeletal pain to the right level of treatment.

PMID: 11790467

Rating: 2a

Halvorsen PA, Selmer R, Kristiansen IS. Different ways to describe the benefits of risk-reducing treatments: a randomized trial. Ann Intern Med. 2007 Jun 19;146(12):848-56.

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BACKGROUND: How physicians communicate the risks and benefits of medical care may influence patients' choices. Ways to communicate the benefits of risk-reducing drug therapies include the number needed to treat (NNT) to prevent adverse events, such as heart attacks or hip fractures, and gains in disease-free life expectancy or postponement of adverse events. Previous studies suggest that the magnitude of the NNT does not affect a layperson's decision about risk-reducing interventions, but postponement of an adverse event does affect such decisions. OBJECTIVE: To examine laypersons' responses to scenarios that describe benefits as postponing an adverse event or the equivalent NNT. DESIGN: Cross-sectional survey with random allocation to different scenarios. SETTING: General community. PARTICIPANTS: Respondents to a population-based health study. INTERVENTION: The survey presented scenarios regarding a hypothetical drug therapy to reduce the risk for heart attacks (1754 respondents) or hip fractures (1000 respondents). The data sources for both scenarios were clinical trials. Respondents were randomly assigned to a scenario with 1 of 3 outcomes after 5 years of treatment. For the drug to prevent heart attacks, the outcomes were postponement by 2 months for all patients, postponement by 8 months for 1 of 4 patients, or an NNT of 13 patients to prevent 1 heart attack. For the drug to prevent hip fractures, the outcomes were postponement by 16 days for all patients, postponement by 16 months for 3 of 100 patients, or an NNT of 57 patients to prevent 1 fracture. MEASUREMENTS: Consent to receive the intervention and perceived ease of understanding the treatment effect. RESULTS: The overall rate of response to the survey was 81%. In the heart attack scenarios, 93% of respondents who were presented with the NNT outcome consented to drug therapy, 82% who were presented with the outcome of large postponement for some patients consented to therapy, and 69% who were presented with the outcome of short postponement for all patients consented to therapy (chi-square, 89.6; $P < 0.001$). Corresponding consent rates for the hip fracture scenarios were 74%, 56%, and 34%, respectively (chi-square, 91.5, $P < 0.001$). Respondents who said that they understood the treatment effect were more likely to consent to therapy. LIMITATION: Decisions were based on hypothetical scenarios, not real clinical encounters. CONCLUSIONS: Treatment effects expressed in terms of NNT yielded higher consent rates than did those expressed as equivalent postponements. This result suggests that the description of the anticipated outcome may influence the patient's willingness to accept a recommended intervention.

PMID: 17577004

Rating: 2a

"How physicians communicate the risks and benefits of medical care may influence patient's choices," write Peder A. Halvorsen, MD, from the University of Southern Denmark in Odense, and colleagues. "Ways to communicate the benefits of risk-reducing drug therapies include the number needed to treat (NNT) to prevent adverse events, such as heart attacks or hip fractures, and gains in disease-free life expectancy or postponement of adverse events. Previous studies suggest that the magnitude of the NNT does not affect a layperson's decision about risk-reducing interventions, but postponement of an adverse event does affect such decisions."
Clinical Context: The NNT is a useful and relatively simple tool for practicing evidence-based medicine. This calculation can be applied to intervention studies and reflects the number of additional patients who need to receive an intervention to prevent 1 additional outcome. It is derived by calculating the reciprocal of the absolute risk reduction. Patients may react differently to a proposed intervention depending on how this intervention is introduced by the physician. The authors of the current study hypothesized that emphasizing the relative risk reduction of 2 hypothetical treatments instead of the NNT would yield higher rates of consent to treatment.
Pearls for Practice: The NNT, which reflects the number of additional patients who need to receive an intervention to prevent 1 more outcome, is derived by calculating the reciprocal of the absolute risk reduction. In the current study, using NNT was superior to achieve participant consent vs explanations focused on the postponements of outcomes for either all patients treated or a small, select group of patients treated.

Hans G. Buprenorphine--a review of its role in neuropathic pain. J Opioid Manag. 2007;3:195-206. Review.

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RESULTS:. Preclinical assessments of buprenorphine demonstrate its sustained antihyperalgesic effect in several models of neuropathic pain. Furthermore, these studies have demonstrated that, despite there being a ceiling effect for respiratory depression, no relevant analgesic ceiling effect is found with buprenorphine. CONCLUSIONS: Further studies are certainly warranted to identify the clinical neuropathic syndromes that are most sensitive to buprenorphine treatment, and to compare buprenorphine with other opioids in head-to-head trials of neuropathic pain.

PMID: 17957979

Rating: 1b

Han JS. Acupuncture and endorphins. Neurosci Lett. 2004 May 6;361(1-3):258-61.

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Acupuncture and electroacupuncture (EA) as complementary and alternative medicine have been accepted worldwide mainly for the treatment of acute and chronic pain. Studies on the mechanisms of action have revealed that endogenous opioid peptides in the central nervous system play an essential role in mediating the analgesic effect of EA. Further studies have shown that different kinds of neuropeptides are released by EA with different frequencies. For example, EA of 2 Hz accelerates the release of enkephalin, beta-endorphin and endomorphin, while that of 100 Hz selectively increases the release of dynorphin. A combination of the two frequencies produces a simultaneous release of all four opioid peptides, resulting in a maximal therapeutic effect. This finding has been verified in clinical studies in patients with various kinds of chronic pain including low back pain and diabetic neuropathic pain.

Publication Types:
Review
Review, Tutorial

PMID: 15135942

Rating: 5b

Harden R, Bruehl S, Gass S, et al. Signs and Symptoms of the Myofascial Pain Syndrome: A National Survey of Pain Management Providers. Clinical Journal of Pain 2000;16:64-72.

Conclusion: "There was general agreement across specialties that MPS is a legitimate diagnosis distinct from fibromyalgia."

Publication Type: Case Control Study, 1663 cases
Harden RN. "Chronic Opiod Therapy: Another Reappraisal," American Pain Society Bulletin, Jan-Feb 2002, at: http://www.ampainsoc.org/pub/bulletin/jan02/poli1.htm.

Abstract:

There should be little argument that the ultimate goals of rehabilitation (e.g., optimal functional recovery, decreased healthcare utilization, maximal self-actualization) are more valuable than simple long-term palliation (Stein, 1996). The long-term outcomes of interdisciplinary pain management techniques are so effective, and so many nonopioid drugs have been conclusively proven to help that these may obviate the need for chronic opioid therapy in many patients (Becker et al., 2000; Merskey,

1997; Rowbotham et al., 1991). However, because opioids are "easy" and represent a path of little resistance, they may prevent the patient (or the physician) from vesting in a difficult and uncomfortable rehabilitation course. A physician's choice to palliate and not rehabilitate is a profound clinical, ethical, and medico-economic decision that must not be taken lightly or be based on unfounded dogma.

Publication Type: Review

Harden RN, Bruehl S, Stanton-Hicks M, Wilson PR. Proposed new diagnostic criteria for complex regional pain syndrome. Pain Med. 2007 May-Jun;8(4):326-31.

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This topical update reports recent progress in the international effort to develop a more accurate and valid diagnostic criteria for complex regional pain syndrome (CRPS). The diagnostic entity of CRPS (published in the International Association for the Study of Pain's Taxonomy monograph in 1994; International Association for the Study of Pain [IASP]) was intended to be descriptive, general, and not imply etiopathology, and had the potential to lead to improved clinical communication and greater generalizability across research samples. Unfortunately, realization of this potential has been limited by the fact that these criteria were based solely on consensus and utilization of the criteria in the literature has been sporadic at best. As a consequence, the full potential benefits of the IASP criteria have not been realized. Consensus-derived criteria that are not subsequently validated may lead to over- or underdiagnosis, and will reduce the ability to provide timely and optimal treatment. Results of validation studies to date suggest that the IASP/CRPS diagnostic criteria are adequately sensitive; however, both internal and external validation research suggests that utilization of these criteria causes problems of overdiagnosis due to poor specificity. This update summarizes the latest international consensus group's action in Budapest, Hungary to approve and codify empirically validated, statistically derived revisions of the IASP criteria for CRPS.

PMID: 17610454

Rating: 5b

Table 3 Proposed clinical diagnostic criteria for CRPS
General definition of the syndrome: CRPS describes an array of painful conditions that are characterized by a continuing (spontaneous and/or evoked) regional pain that is seemingly disproportionate in time or degree to the usual course of any known trauma or other lesion. The pain is regional (not in a specific nerve territory or dermatome) and usually has a distal predominance of abnormal sensory, motor, sudomotor, vasomotor, and/or trophic
findings. The syndrome shows variable progression over time
To make the clinical diagnosis, the following criteria must be met:
(1) Continuing pain, which is disproportionate to any inciting event

(2) Must report at least one symptom in three of the four following categories:
(a) Sensory: Reports of hyperesthesia and/or allodynia
(b) Vasomotor: Reports of temperature asymmetry and/or skin color changes and/or skin color asymmetry
(c) Sudomotor/Edema: Reports of edema and/or sweating changes and/or sweating asymmetry
(d) Motor/Trophic: Reports of decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, nail, skin)
(3) Must display at least one sign at time of evaluation in two or more of the following categories:
(a) Sensory: Evidence of hyperalgesia (to pinprick) and/or allodynia (to light touch and/or temperature sensation and/or deep somatic pressure and/or joint movement)
(b) Vasomotor: Evidence of temperature asymmetry (>1°C) and/or skin color changes and/or asymmetry
(c) Sudomotor/Edema: Evidence of edema and/or sweating changes and/or sweating asymmetry
(d) Motor/Trophic: Evidence of decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, nail, skin)
4. There is no other diagnosis that better explains the signs and symptoms
For research purposes, diagnostic decision rule should be at least one symptom in all four symptom categories and at least one sign (observed at evaluation) in two or more sign categories.

Harke H, Gretenkort P, Ladleif HU, Rahman S. Spinal cord stimulation in sympathetically maintained complex regional pain syndrome type I with severe disability. A prospective clinical study. Eur J Pain. 2005 Aug;9(4):363-73.

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BACKGROUND AND PURPOSE: In this prospective trial we assessed the long-term effect of spinal cord stimulation (SCS) on the improvement of functional status in complex regional pain syndrome type I (CRPS I). METHODS: A prerequisite for eligibility to SCS treatment was the responsiveness of patients to sympathetic nerve block. In 29 patients with chronic sympathetically maintained CRPS I, the efficacy of SCS on deep pain, allodynia and functional disability was determined. Pain intensity was estimated during SCS free intervals of 45 min (inactivation test) every 3 months and compared with that under SCS treatment. RESULTS: On SCS treatment, both deep pain and allodynia could be permanently reduced from 10 to 0-2 on a 10 cm visual analogue scale (VAS) ($p<0.01$). During the inactivation tests, reoccurrence of pain up to 8 VAS (quartiles 6-8) was measured. Considerable impairments in daily living activities, objectified by the pain disability index, were also restored ($p<0.01$). After a follow-up period of 35.6+/-21 months, 12 of 16 patients with affected upper limb showed significant increase of the fist grip strength from 0 to 0.35 (quartiles 0.1-0.5) kg compared with 0.9 (quartiles 0.7-1.1) kg on the unaffected side ($p<0.01$). Eight of ten patients with lower limb disability resumed walking without crutches. Previous pain medication could be significantly reduced ($p<0.01$). CONCLUSIONS: As a

result of permanent pain relief under long-term SCS combined with physiotherapy, the functional status and the quality of life could be significantly improved in sympathetically maintained CRPS I.

PMID: 15979016

Rating: 2b

Hartrick CT, Kovan JP, Naismith P. Outcome prediction following sympathetic block for complex regional pain syndrome. Pain Pract. 2004;4:222-8.

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Evidence for the efficacy of sympathetic blocks as either diagnostic or therapeutic tools in complex regional pain syndrome (CRPS) remains anecdotal. Systematic evaluation has been confounded by inconsistent terminology, difficulties in objectively quantifying physical findings, and failure to control for co-morbid psychological factors. This study examines the relative contribution of physical and psychometric features as prospective predictors of outcome following sympathetic block in the treatment of CRPS. Twenty patients with CRPS characterized by mechanical allodynia and vasomotor/sudomotor disturbance were treated with sympathetic blocks. Long-term outcome was assessed at > 6 months following the last treatment using a mailed questionnaire. Pain relief and functional improvement were negatively influenced by anxiety ($P < 0.001$). When the improvement in the initial visual analog for pain (VAS) was 50% or greater following "diagnostic" sympathetic block, the percent improvement was highly correlated with improvement at long-term follow-up ($P < 0.001$). Higher "sensitivity" scores on the Neuropathic Pain Scale ($P < 0.001$), C fiber allodynia ($P < 0.01$) and Adelta-fiber allodynia ($P < 0.01$) on quantitative sensory testing, and pretreatment reported dynamic mechanical allodynia ($P < 0.02$) all predicted positive response to initial sympathetic block. While sympathetic blocks can be helpful in the reduction of mechanical allodynia, and thus the facilitation of physical and occupational therapy, ultimate response to a regime that includes medications is not predicted by sympathetic block alone.

PMID: 17173603

Rating: 4c

Hasenbring M, Ulrich HW, Hartmann M, Soyka D. The efficacy of a risk factor-based cognitive behavioral intervention and electromyographic biofeedback in patients with acute sciatic pain. An attempt to prevent chronicity. Spine. 1999 Dec 1;24(23):2525-35.

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STUDY DESIGN: An investigation of the efficacy of an individually scheduled, risk factor-based cognitive behavioral therapy and a standardized electromyographic biofeedback intervention in the prevention of chronicity in patients with acute sciatica and psychosocial risk factors for chronicity. OBJECTIVES: To investigate the possibility of enhancing pain relief and preventing chronicity in patients with acute sciatica, based on a screening for psychosocial high-risk factors of chronification. SUMMARY OF BACKGROUND DATA: Psychological interventions were evaluated mainly in patients with chronic low back pain. Numerous randomized trials have demonstrated their efficacy, whereas the amount of pain relief was found to be marginal. METHODS: Subjective and behavioral outcome parameters were compared with the respective parameters in age-, gender-, and diagnosis-matched high- and low-risk patients. No additional behavioral treatment for in-patient medical therapy was offered to the patients. Outcome of these patients also was compared with that of a group of refusers of behavioral therapy. Psychological, functional, and behavioral variables were measured before and after treatment and at 3-, 6-, 12- and 18-month follow-up visits. Changes over time, group differences, and possible group x time interactions were analyzed by analysis of variance and nonparameteric comparisons. RESULTS: Data analysis showed a statistically and clinically significant, beneficial effect of both behavioral interventions. However, risk factor-based cognitive behavioral therapy was superior to electromyographic biofeedback intervention with respect to pain relief and application for early retirement. The cognitive behavioral therapy showed a similar good outcome (e.g., 90% showed a clinical significant pain reduction) as the low-risk patients (83% pain reduction). High risk patients and refusers of therapy showed a poor outcome in pain (33% and 20% pain reduction, respectively), disability, and work performance. CONCLUSIONS: Individually scheduled, risk factor-based cognitive behavior therapy could be a beneficial treatment modality, which can be offered, in addition to a medical treatment, to patients with acute sciatica and psychosocial high risk factors for chronicity. It may be an effective way to prevent chronification in these patients.

PMID: 10626316

Rating: 2c

Hassenbusch SJ, Portenoy RK, Cousins M, Buchser E, Deer TR, Du Pen SL, Eisenach J, Follett KA, Hildebrand KR, Krames ES, Levy RM, Palmer PP, Rathmell JP, Rauck RL, Staats PS, Stearns L, Willis KD. Polyanalgesic Consensus Conference 2003: an update on the management of pain by intraspinal drug delivery-- report of an expert panel. J Pain Symptom Manage. 2004 Jun;27(6):540-63.

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Intraspinal drug infusion using fully implantable pump and catheter systems is a safe and effective therapy for selected patients with chronic pain. The options for this approach are increasing, as drugs that are commercially available for systemic administration are adapted to this use and other drugs that

are in development specifically for intraspinal administration become available. In 2000 a Polyanalgesic Consensus Conference was organized to evaluate the existing literature and develop guidelines for drug selection. The major outcome of this effort, an algorithm for drug selection, was based on the best available evidence at the time. Rapid changes have occurred in the science and practice of intraspinal infusion and a Polyanalgesic Consensus Conference 2003 was organized to pursue the following goals: 1) to review the literature on intraspinal drug infusion since 1999, 2) to revise the 2000 drug-selection algorithm, 3) to develop guidelines for optimizing drug dosage and concentration, 4) to create a process for documenting minimum evidence supporting the use of a drug for intraspinal infusion, and 5) to clarify issues pertaining to compounding of drugs. Based on the best available evidence and expert opinion, consensus recommendations were developed in all these areas. The panel's conclusions may provide a foundation for clinical practice and a rational basis for new research.

PMID: 15165652

Rating: 5b

Hassenbusch, S. Intrathecal Clonidine in the Treatment of Intractable Pain: A Phase I/II Study" Pain Medicine. 2002; Volume 3, Number 2: 85-91.

Rating: 2c

Quality: Low. Total Rating: 2.0. Comment: Does not meet inclusion criteria for evidence-based review. [CA DWC]

Hasson D, Arnetz B, Jelveus L, Edelstam B. A randomized clinical trial of the treatment effects of massage compared to relaxation tape recordings on diffuse long-term pain. Psychother Psychosom. 2004 Jan-Feb;73(1):17-24.

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BACKGROUND: Long-term musculoskeletal pain is a common problem in primary health care settings that is difficult to treat. Two common treatments are mental relaxation and massage. Scientific studies show contradictory results. Furthermore, many studies lack long-term follow-up even though it is a chronic disorder. The purpose of this randomized clinical trial was to assess possible effects of massage as compared to listening to relaxation tapes in conditions of 'diffuse' and long-term musculoskeletal pain. METHODS: 129 patients from primary health care suffering from long-term musculoskeletal pain were randomized to either a massage or mental relaxation group, and assessed before, during and after treatment. RESULTS: During treatment there was a significant improvement in the three main outcome measures: self-rated health, mental energy, and muscle pain only in the massage group as compared to the relaxation group. However, at the 3-month post-treatment follow-up, there was a significant

worsening in the outcome measures (time x group effect $p < 0.05$) back to initial rating levels in the massage group as compared to no changes in the relaxation group. CONCLUSION: Massage, but not mental relaxation, is beneficial in attenuating diffuse musculoskeletal symptoms. Beneficial effects were registered only during treatment. This lack of long-term benefits could be due to the short treatment period or treatments such as these do not address the underlying causes of pain. Future studies of long-term pain should include longer treatment periods and post-treatment follow-up. It might also be worthwhile assessing the long-term benefits from booster treatment after the initial intense treatment period. Copyright 2004 S. Karger AG, Basel

PMID: 14665792

Rating: 2b

Heacock C, Bauer MS. Tolerance and dependence risk with the use of carisoprodol. Am Fam Physician. 2004 Apr 1;69(7):1622-3.

Carisoprodol (Soma) is an unscheduled muscle relaxant commonly used in primary care. It is metabolized to meprobamate, a schedule IV drug that has a long history of abuse and exhibits cross-tolerance to barbituates. A small but growing amount of literature is available regarding morbidity associated with the use of carisoprodol, including respiratory compromise1 and vehicle crashes. This case report highlights this potential danger.

Publication Types:
Case Reports
Letter

PMID: 15086035

Rating: 11b

Hedges DW, Brown BL, Shwalb DA, Godfrey K, Larcher AM. The efficacy of selective serotonin reuptake inhibitors in adult social anxiety disorder: a meta-analysis of double-blind, placebo-controlled trials. J Psychopharmacol. 2007; 21:102-11.

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Social anxiety disorder is associated with impairment in social and occupational functioning, significant personal distress and a possible economic burden, resulting in a reduction in quality of life. To understand better the efficacy of selective serotonin reuptake inhibitors in social anxiety disorder, randomized, double-blind, placebo-controlled trials were evaluated. Pubmed and PsychINFO electronic

databases were searched for social anxiety disorder, social phobia, selective serotonin reuptake inhibitors, citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine and sertraline. Fifteen published, randomized, double-blind, placebo-controlled trials of selective serotonin reuptake inhibitors in social anxiety disorder were identified. Design, subject number, drug and dose, trial length, rating instruments, and baseline and end point data were extracted and then verified independently by a second investigator. Effect sizes were calculated from mean changes in drug and placebo groups in the Liebowitz Social Anxiety Scale and the Sheehan Disability Scale, as well as from other scales where available. For the binary data of the Clinical Global Impression of Change scores, Theta log-odds ratios (the effect-size measure appropriate for binary data) were calculated from proportion changes. Effect sizes for the Liebowitz Social Anxiety Scale ranged from -0.029 to 1.214. Effect sizes for the Sheehan Disability Scale ranged from 0.203 to 0.480 for work, 0.237 to 0.786 for social function, and 0.118 to 0.445 for family function. The Theta log-odds ratios for Clinical Global Impression of Change scores ranged from 0.644 to 3.267. Consistent with previous studies, selective serotonin reuptake inhibitors appear more effective than placebo for social anxiety disorder, with improvement extending into social and occupational function.

PMID: 16714326

Rating: 1b

Heit HA, Gourlay DL, Covington EC. The truth about pain management: the interface of pain and addiction. Program and abstracts of the American Academy of Pain Medicine 23rd Annual Meeting; February 7-10, 2007; New Orleans, Louisiana.

It is extremely important for the treating physician to create a transparent record that will allow regulatory agencies to clearly see the thoughtful consideration that went into the decision-making process, and to exhibit a system of careful controls. Treatment agreements are generally regarded as being a standard measure for prescribing opioids. The American Academy of Pain Medicine has useful templates for a patient opioid treatment agreement on the Web site (painmed.org) that may be given to the patient, to serve as both a consent form and an advisory form with the rules and issues involved with controlled substance prescribing. In my own practice, I have a standard form that I have every patient receiving opioid therapy review and sign, and then I give them a copy and I keep the signed copy in their chart. I regard an opioid agreement to be documentation of the boundaries that have been established with each patient, and as a means of documenting their understanding or the risks and requirements associated with continued opioid therapy. They do not serve as a formal contract, but more as a valuable education tool. However, you have to be cautious not to be overly restrictive to avoid creating unintended liability traps. For example, if you have a patient who screens positive for marijuana use in their urine drug screen, should this be a sufficient trigger to withdraw therapy? There is a debate about what to do with this information. It is essential to really think about these issues and establish protocols to deal with the results of urine screens ahead of time, before you start screening. Failure to do so will create possible legal liability.

Rating: 10b

Heit HA, Gourlay DL. Buprenorphine: new tricks with an old molecule for pain management. Clin J Pain. 2008 ;24:93-7. Review.

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It may be used "on label" as an alternative choice to methadone for the treatment of opioid addiction or "off-label" for the treatment of both acute and chronic pain.

PMID: 18209513

Rating: 5b

Helin-Salmivaara A, Huttunen T, Gronroos JM, Klaukka T, Huupponen R. Risk of serious upper gastrointestinal events with concurrent use of NSAIDs and SSRIs: a case-control study in the general population. Eur J Clin Pharmacol. 2007;63:403-8.

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OBJECTIVES: To study the risk of serious upper gastrointestinal (GI) events associated with the concurrent use of selective serotonin re-uptake inhibitors (SSRIs) and different types of non-steroidal anti-inflammatory drugs (NSAIDs). METHODS: This was a nationwide, register-based matched case-control study on non-institutionalized residents of Finland during the period 2000-2004. Patient-cases with serious upper GI events (n = 9191) were drawn from the Hospital Discharge Register, and individually matched controls (n = 41,780) were drawn from the Population Register. Logistic regression was applied in the data analysis, and adjustments were made for various co-morbidities and the use of other drugs associated with the risk of serious upper GI event. RESULTS: The adjusted odds ratio (AOR) of serious upper GI events for SSRI use compared to non-use of SSRIs or NSAIDs was 1.30 [95% confidence interval (95%CI: 1.13-1.50)], and the AOR for concurrent SSRI and NSAID use compared to the non-use of either drug was 4.19 (95%CI: 3.30-5.31). The AOR of upper GI events for the concurrent use of SSRIs with NSAIDs compared to patients using NSAIDs only was 1.57 (95%CI: 1.24-1.99). The respective AOR for traditional, non-selective NSAIDs was 1.77 (95%CI: 1.31-2.38), for semi-selective NSAIDs (nimesulide, nabumetone, meloxicam, and etodolac) 1.30 (95%CI: 0.76-2.24) and for COX-2 selective NSAIDs 1.33 (95%CI: 0.70-2.50). CONCLUSIONS: The concurrent use of SSRIs and NSAIDs is associated with a moderate excess relative risk of a serious upper GI event when compared with NSAID use alone.

PMID: 17347805

Rating; 3a

Helm S, Trescot AM, Colson J, Sehgal N, Silverman S. Opioid antagonists, partial agonists, and agonists/antagonists: the role of office-based detoxification. Pain Physician. 2008;11:225-35. Review.

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BACKGROUND: Buprenorphine is classified as a partial agonist. It has a high affinity, but low efficacy at the mu receptor where it yields a partial effect upon binding. It also, however, possesses kappa receptor antagonist activity making it useful not only as an analgesic, but also in opioid abuse deterrence, detoxification, and maintenance therapies. Naloxone is added to sublingual buprenorphine (Suboxone) to prevent the intravenous abuse of buprenorphine. CONCLUSION: Based on the present evaluation, it appears that opioid antagonists, partial agonists, and antagonists are useful in office-based opioid treatment for addiction.

PMID: 18354714

Rating: 1b

Hindsén M, Zimerson E, Bruze M. Photoallergic contact dermatitis from ketoprofen in southern Sweden. Contact Dermatitis. 2006;54:150-7.

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The non-steroidal anti-inflammatory drug ketoprofen is widely used for topical treatment. In Sweden, ketoprofen has been available for topical application since 1995. Photoallergic contact dermatitis from ketoprofen-containing topical preparations usually includes severe eczematous reactions. Ketoprofen is derived from propionic acid, and it is also a substituted benzophenone and therefore structurally similar to fenofibrate and sunscreen agents based on benzophenones. During the last 2 years, 35 patients have been refereed to our department with suspected photoallergic or allergic reactions after having used ketoprofen-containing gels. Photopatch testing with the photopatch standard series, the ketoprofen-containing gels and their ingredients, fenofibrate, benzophenone-3, benzophenone-10 and benzophenone-4, was performed. Photoallergic reactions to ketoprofen were noted in 35 patients and a simultaneous contact allergy to ketoprofen in 2 patients. Simultaneous photoallergy to fentichlor, tetrachlorosalicylanilide and fenofibrate was registered in 74%, 40% and 73% of the patients, respectively.

PMID: 16524438

Rating: 5b

Hoffman EJ, Mathew SJ. Anxiety disorders: a comprehensive review of pharmacotherapies. Mt Sinai J Med. 2008; 75:248-62.

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This article reviews the evidence from randomized, placebo-controlled trials and meta-analyses of pharmacological treatments of the following anxiety disorders: generalized anxiety disorder, panic disorder, social anxiety disorder, and post-traumatic stress disorder. There is evidence from multiple randomized, placebo-controlled trials to support the use of selective serotonin reuptake inhibitors as first-line pharmacotherapy in these disorders, and a number of the selective serotonin reuptake inhibitors have received US Food and Drug Administration approval for these indications. Serotonin-norepinephrine reuptake inhibitors are now emerging as first-line treatments for these anxiety disorders alongside the selective serotonin reuptake inhibitors and have been US Food and Drug Administration-approved for some of these indications as well. Benzodiazepines are also effective treatments for anxiety disorders, and although this medication class has the advantage of a rapid onset of action, their use is limited by their potential for abuse and lack of antidepressant properties. In addition to reviewing the clinical trials that have investigated the anxiolytic effects of these commonly used medications, we review the evidence for novel uses of other agents, including anticonvulsants and atypical antipsychotics, in anxiety disorders.

PMID: 18704983

Rating: 1a

Holbrook AM, Crowther R, Lotter A, Cheng C, King D. Meta-analysis of benzodiazepine use in the treatment of insomnia. CMAJ. 2000 Jan 25;162(2):225-33.

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OBJECTIVE: To systematically review the benefits and risks associated with the use of benzodiazepines to treat insomnia in adults. DATA SOURCES: MEDLINE and the Cochrane Controlled Trials Registry were searched for English-language articles published from 1966 to December 1998 that described randomized controlled trials of benzodiazepines for the treatment of insomnia. Key words included "benzodiazepines" (exploded), "randomized controlled trial" and "insomnia." Bibliographies of relevant articles were reviewed for additional studies and manufacturers of benzodiazepines were asked to submit additional randomized controlled trial reports not in the literature. STUDY SELECTION: Articles were considered for the meta-analysis if they were

randomized controlled trials involving patients with insomnia and compared a benzodiazepine with placebo or another active agent. Of the 89 trials originally identified, 45 met our criteria, representing a total of 2672 patients. DATA EXTRACTION: Data were extracted regarding the participants, the setting, details of the intervention, the outcomes (including adverse effects) and the methodologic quality of the studies. DATA SYNTHESIS: The meta-analyses of sleep records indicated that, when compared with placebo, benzodiazepines decreased sleep latency by 4.2 minutes (non-significant; 95% confidence interval (CI -0.7 to 9.2) and significantly increased total sleep duration by 61.8 minutes (95% CI 37.4 to 86.2). Patient-reported outcomes were more optimistic for sleep latency; those randomized to benzodiazepine treatment estimated a sleep latency decrease of 14.3 minutes (95% CI 10.6 to 18.0). Although more patients receiving benzodiazepine treatment reported adverse effects, especially daytime drowsiness and dizziness or light-headedness (common odds ratio 1.8, 95% CI 1.4 to 2.4), dropout rates for the benzodiazepine and placebo groups were similar. Cognitive function decline including memory impairment was reported in several of the studies. Zopiclone was not found to be superior to benzodiazepines on any of the outcome measures examined. INTERPRETATION: The use of benzodiazepines in the treatment of insomnia is associated with an increase in sleep duration, but this is countered by a number of adverse effects. Additional studies evaluating the efficacy of nonpharmacological interventions would be valuable.

Rating: 1a

Homik JE, Suarez-Almazor M. An economic approach to health care. Best Pract Res Clin Rheumatol. 2004 Apr;18(2):203-18.

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Economic analyses have the potential to put all of the positive and negative outcomes of an intervention into perspective to aid decision making. The quality of the data upon which the analysis is based has an impact on the resulting quality of the analysis itself. Analysis of cost-effectiveness requires the input of many types of data, and where data are not available, assumptions must be made. There are many instances where the analysis may go wrong, and it is important to remain cognizant of these. The critical parts of the analysis, which have also been identified in quality assessment tools, include the following: design of the study question, sources of probability estimates and cost data, sensitivity analysis, and the interpretation of results. If the readers are able to identify the assumptions of the analysis they are better equipped to judge the validity. We have reviewed economic analyses relating to two hot economic topics in rheumatology. These are the cost-effectiveness of cyclooxygenase-2 (COX-2) inhibitors for 'arthritis' and cost-effectiveness of anti-tumor necrosis factor alpha (anti-TNF) agents for rheumatoid arthritis (RA). The results of the COX-2 analyses vary by review. Some show cost savings, while others calculate a significant cost in order to achieve any change in quality of life. Given the unanswered questions that still exist, it seems reasonable to conclude that COX-2 inhibitors may be cost effective when used in patients at a high risk of GI complications. Unanswered questions remain regarding the

concomitant use of low-dose ASA and proton pump inhibitors and how they may affect the results of these economic analyses. The cost-effectiveness of anti-TNF agents has not been explored in as much detail as that of the COX-2 agents. Two studies have presented cost-effectiveness models that include a hypothetical biologic agent. Two economic analyses report on the cost-effectiveness of etanercept compared with traditional disease-modifying anti-rheumatic drugs (DMARDs) in methotrexate-resistant and methotrexate-naive patients with RA. Both the analyses show that etanercept has a cost-effectiveness ratio of around 40,000 US dollars for every patient who achieves an American College of Rheumatology 20% improvement score (ACR 20) within a 6-month period. A cost-utility analysis was published regarding the use of infliximab in methotrexate resistant RA. It showed a cost-utility ratio of 3400:34,000 Euro per quality adjusted life year (QALY) gained, depending on the country evaluated (Sweden and the UK, respectively). An important finding in all three studies was that indirect costs dominate costs in RA; therefore, they should be included in all future analyses of this disease.

PMID: 15121040

Rating: 5b

Hong CZ, Simons DG. Pathophysiologic and electrophysiologic mechanisms of myofascial trigger points. Arch Phys Med Rehabil. 1998 Jul;79(7):863-72.

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OBJECTIVE: To review recent clinical and basic science studies on myofascial trigger points (MTrPs) to facilitate a better understanding of the mechanism of an MTrP. DATA SOURCES: English literature in the last 15 years regarding scientific investigations on MTrPs in either humans or animals. STUDY SELECTION: Research works, especially electrophysiologic studies, related to the pathophysiology of MTrP. DATA SYNTHESIS: (1) Studies on an animal model have found that a myofascial trigger spot (MTrS) in a taut band of rabbit skeletal muscle fibers is similar to a human MTrP in many aspects. (2) An MTrP or an MTrS contains multiple minute loci that are closely related to nerve fibers and motor endplates. (3) Both referred pain and local twitch response (characteristics of MTrPs) are related to the spinal cord mechanism. (4) The taut band of skeletal muscle fibers (which contains an MTrP or an MTrS in the endplate zone) is probably related to excessive release of acetylcholine in abnormal endplates. CONCLUSION: The pathogenesis of an MTrP appears to be related to integrative mechanisms in the spinal cord in response to sensitized nerve fibers associated with abnormal endplates.

Publication Types:
Review

PMID: 9685106

Rating: 5a

Hoogendoorn WE, Bongers PM, De Vet HC, Ariens GA, Van Mechelen W, Bouter LM. High physical work load and low job satisfaction increase the risk of sickness absence due to low back pain: results of a prospective cohort study. Occupational Environmental Medicine. 2002 May;59(5):323-8.
Abstract:
Objective: To determine whether physical and psychosocial load at work influence sickness absence due to low back pain. Methods: The research was a part of the study on musculoskeletal disorders, absenteeism, stress, and health (SMASH), a 3 year prospective cohort study on risk factors for musculoskeletal disorders. Workers from 21 companies located throughout The Netherlands participated in the part of this study on sickness absence due to low back pain. The study population consisted of 732 workers with no sickness absences of 3 days or longer due to low back pain in the 3 months before the baseline survey and complete data on the reasons for absences during the follow up period. The mean (range) period of follow up in this group was 37 (7-44) months. Physical load at work was assessed by analyses of video recordings. Baseline information on psychosocial work characteristics was obtained by a questionnaire. Data on sickness absence were collected from company records. The main outcome measure was the rate of sickness absences of 3 days or longer due to low back pain during the follow up period. Results: After adjustment of the work related physical and psychosocial factors for each other and for other potential determinants, significant rate ratios ranging from 2.0 to 3.2 were found for trunk flexion, trunk rotation, lifting, and low job satisfaction. A dose-response relation was found for trunk flexion, but not for trunk rotation or lifting. Non-significant rate ratios of about 1.4 were found for low supervisor support and low coworker support. Quantitative job demands, conflicting demands, decision authority, and skill discretion showed no relation with sickness absence due to low back pain. Conclusions: Flexion and rotation of the trunk, lifting, and low job satisfaction are risk factors for sickness absence due to low back pain. Some indications of a relation between low social support, either from supervisors or coworkers, and sickness absence due to low back pain are also present.

Publication Type: Case Control Study, 732 cases

Hord ED, Cohen SP, Cosgrove GR, Ahmed SU, Vallejo R, Chang Y, Stojanovic MP, The predictive value of sympathetic block for the success of spinal cord stimulation, Neurosurgery. 2003 Sep;53(3):626-32; discussion 632-3

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OBJECTIVE: The purpose of this study was to assess the predictive value of response to sympathetic blockade (SB) on the success rate of spinal cord stimulation (SCS) in patients with complex regional pain syndrome. METHODS: We performed a retrospective study on 23 patients with complex regional pain syndrome who underwent both SB and subsequent SCS trials in the past 3 years at the Massachusetts General Hospital Pain Center, Boston, MA, and Walter Reed Army Medical Center,

Washington, DC. Fifteen of these patients underwent permanent placement of an SCS device, and pain relief at 1- and 9-month follow-up was recorded. RESULTS: Among the 23 patients included in the study, those having transient pain relief with SB were more likely to have a positive SCS trial: all 13 with positive SB had good pain relief during the trial, compared with only 3 of the 10 with negative SB (100% versus 30%, P < 0.001). Among the 10 patients with negative SB, 7 noted poor pain relief during the trial despite adequate coverage, and they did not undergo placement of a permanent device. Among the patients who underwent permanent placement of an SCS device, those who received good pain relief with SB were more likely to have greater than 50% pain relief at 1-month follow-up (100% versus 33%, P = 0.029) and 9-month follow-up (87.5% versus 33.3%, P = 0.15). CONCLUSION: We conclude that patients with good response to SB before SCS are more likely to have a positive response during their SCS trial and long-term pain relief after placement of permanent SCS device.

Publication Types:
- Evaluation Studies

PMID: 12943579

Rating: 4c

Hord AH, Rooks MD, Stephens BO, Rogers HG, Fleming LL. Intravenous regional bretylium and lidocaine for treatment of reflex sympathetic dystrophy: a randomized, double-blind study. Anesth Analg. 1992 Jun;74(6):818-21.

Department of Anesthesiology, Emory University School of Medicine, Atlanta, Georgia.

Patients with reflex sympathetic dystrophy, who received transient pain relief from stellate ganglion blocks or lumbar sympathetic blocks and had abnormal isolated cold stress tests, were enrolled in a study to determine the efficacy of intravenous regional bretylium. Each patient received two control treatments (0.5% lidocaine) and two treatments with 0.5% lidocaine and bretylium 1.5 mg/kg in a randomized, double-blind fashion. A standard intravenous regional technique was used with a 300-mm Hg tourniquet pressure for 20 min. Patients kept a daily record of pain relief (0 = no relief, 100% = complete relief). A decrease in pain of more than 30% was considered clinically significant. Therefore, once the patient's pain relief was less than 30%, the next intravenous regional treatment was performed. Bretylium and lidocaine provided more than 30% pain relief for a mean of 20.0 (+/- 17.5) days, whereas lidocaine alone provided relief for only 2.7 (+/- 3.7) days (Mann-Whitney U-test, P less than 0.001). A mean temperature increase in the treated limb of +2.64 +/- 3.41 degrees C above the baseline temperature was noted after bretylium administration, whereas after control treatments the change was -0.086 +/- 1.30 degrees C (Mann-Whitney U-test, P less than 0.02). We conclude that the combination of bretylium and lidocaine is significantly more effective than lidocaine alone when an intravenous block is used to treat reflex sympathetic dystrophy.

PMID: 1595913

Rating: 2c

Humana Coverage Issues, Transcutaneous Electrical Nerve Stimulation (TENS) or Interferential Current Stimulation (ICS), 06/14/04

Transcutaneous electrical nerve stimulation (TENS) and interferential current stimulation (ICS) are the two most common forms of transcutaneous electrical stimulation used for pain management therapy. Both therapies send electrical impulses from a portable, battery-powered pulse generator using skin electrodes placed over the affected tissue.
A one month rental period is used to assess a patient's suitability for on-going treatment of either of the following:
• Acute post-operative or post-traumatic pain, only in the first 30 days after the surgery or injury, or
• Chronic pain of at least three months duration that is not responsive to other methods of pain management
If the TENS or interferential stimulator unit significantly alleviates pain during this trial period continued rental or purchase may be approved.
Replacement electrodes, batteries (must be specifically for use in these type units), and electrode gel are considered as medical supplies.
Members would not be eligible under the Plan for TENS or interferential stimulators:
• For any indication not listed above
• When durable medical equipment is not a covered benefit in the member's contract
CPT© Code: 64550 Application of surface (transcutaneous) neurostimulator
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Rating: 7c

Hunt RH, Choquette D, Craig BN, De Angelis C, Habal F, Fulthorpe G, Stewart JI, Turpie AG, Davis P. Approach to managing musculoskeletal pain: acetaminophen, cyclooxygenase-2 inhibitors, or traditional NSAIDs? Can Fam Physician. 2007;53:1177-84.

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OBJECTIVE: To provide family physicians and pharmacists with practical, evidence- and expertise-based guidance on choosing the safest approach to using analgesics to manage patients with musculoskeletal pain. MAIN MESSAGE: Treatment should begin with an effective analgesic with the best safety profile at the lowest dose and escalate to higher doses and different analgesics as required. Acetaminophen is a safe medication that should be considered first-line therapy.

PMID: 17872814

Rating: 5b

Institute for Clinical Systems Improvement (ICSI). Assessment and management of chronic pain. Bloomington (MN). 2005 Nov.

The recommendations for the assessment and management of chronic pain are presented in the form of two algorithms with 29 components, accompanied by detailed annotations. Algorithms are provided for Assessment and Management. Clinical highlights and selected annotations (numbered to correspond with the algorithm) follow.
Clinical Highlights
1. Chronic pain is separate from acute pain and is a difficult clinical problem to treat
2. Chronic pain is a persistent, life-altering condition. The target is management not elimination.
3. A patient centered, multi-factorial, comprehensive management plan is necessary, that includes addressing biopsychosocial factors. Addressing spiritual and cultural issues is also important. It is important to have a multidisciplinary team approach coordinated by the primary care physician to lead a team including specialty areas of psychology and physical rehabilitation.
4. The goals of treatment are an emphasis on improving function through the development of long term self-management skills including fitness and a healthy lifestyle.

Rating: 6a

Institute for Clinical Systems Improvement (ICSI). Assessment and management of chronic pain (2nd edition). Bloomington (MN). 2007 Mar.

The recommendations for the assessment and management of chronic pain are presented in the form of two algorithms with 29 components, accompanied by detailed annotations. Algorithms are provided for Assessment and Management. Clinical highlights and selected annotations (numbered to correspond with the algorithm) follow.
Clinical Highlights
1. Chronic pain is separate from acute pain and is a difficult clinical problem to treat
2. Chronic pain is a persistent, life-altering condition. The target is management not elimination.
3. A patient centered, multi-factorial, comprehensive care plan is necessary, that includes addressing biopsychosocial factors. Addressing spiritual and cultural issues is also important. It is important to have a multidisciplinary team approach coordinated by the primary care physician to lead a team including specialty areas of psychology and physical rehabilitation.
4. The goals of treatment are an emphasis on improving function through the development of long term self-management skills including fitness and a healthy lifestyle.
5. Medications are not the primary focus of treatment in managing pain.
Skeletal muscle relaxants were found to have limited evidence of effectiveness. They were thought to be useful for short-term management of muscle spasm and pain. Mixed evidence was found for long-term use. Benzodiazepines and Carisoprodol were noted to carry a risk for physical dependence. These latter drugs were not recommended for chronic use. The one medication recommended for longer periods was Tizanidine due to its mechanism of action (alpha-2 sympathomimetic). This drug was noted to be an

adjunct treatment of fibromyalgia. Baclofen was noted to have benefits for treating lancinating, paroxysmal neuropathic pain.

Rating: 6a

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No abstract available. A consensus guideline for diagnosis and treatment of CRPS.

Rating: 5b

Ipser JC, Kariuki CM, Stein DJ. Pharmacotherapy for social anxiety disorder: a systematic review. Expert Rev Neurother. 2008; 8:235-57.

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Social anxiety disorder (SAD) is a prevalent, disabling disorder. We aimed to assess the effects of pharmacotherapy for SAD and to determine whether particular classes of medication are more effective and/or better tolerated than others. A systematic review and meta-analysis was conducted of all published and unpublished placebo-controlled randomized controlled trials (RCTs) undertaken between 1966 and 2007. A rigorous search, which included searching the Cochrane CCDANTR, MEDLINE and PsycINFO electronic databases, yielded a total of 51 RCTs (9914 participants) considered eligible for inclusion in the review. On average, over half of trial participants responded to medication, as assessed with the improvement item of the Clinical Global Impressions scale (55.2%), with approximately four participants having to be treated for an average of 12 weeks before an additional person responded to medication, relative to placebo (number needed to benefit = 4.19). There was substantial variation across medication classes in the number of dropouts due to adverse events, with an average number needed to harm of 14.4. Maintenance and relapse prevention studies confirm the value of longer-term medication in treatment responders. Medication was also effective in reducing SAD symptoms, comorbid depressive symptoms and associated disability. However, evidence for the efficacy of beta-blockers in treating performance anxiety was lacking. Taken together, trials of selective serotonin reuptake inhibitors and serotonin-norepinephrine reuptake inhibitors provide the largest evidence base for agents that are both effective and well tolerated. This review is an updated version of a Cochrane Review in The Cochrane Library, Issue 4, 2004. Cochrane Reviews are regularly updated as new evidence emerges and in response to feedback, and The Cochrane Library should be consulted for the most recent version of the review.

PMID: 18271710

Rating: 1a

Isidori AM, Giannetta E, Gianfrilli D, Greco EA, Bonifacio V, Aversa A, Isidori A, Fabbri A, Lenzi A. Clin Endocrinol (Oxf). 2005 Dec;63(6):601-2. Effects of testosterone on sexual function in men: results of a meta-analysis. Clin Endocrinol (Oxf). 2005;63:381-94.

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OBJECTIVES: The role of androgen decline in the sexual activity of adult males is controversial. To clarify whether sexual function would benefit from testosterone (T) treatment in men with partially or severely reduced serum T levels, we conducted a systematic review and meta-analysis of placebo-controlled studies published in the past 30 years. The aim of this study was to assess and compare the effects of T on the different domains of sexual life. DATA SOURCE: A comprehensive search of all published randomized clinical trials was performed in MEDLINE, the Cochrane Library, EMBASE and Current Contents databases. REVIEW METHODS: Guided by prespecified criteria, software-assisted data abstraction and quality assessed by two independent reviewers, a total of 17 randomized placebo-controlled trials were found to be eligible. For each domain of sexual function we calculated the standardized mean difference relative to T and reported the results of pooled estimates of T treatment using the random effect model of meta-analysis. Heterogeneity, reproducibility and consistency of the findings across studies were explored using sensitivity and meta-regression analysis. RESULTS: Overall, 656 subjects were evaluated: 284 were randomized to T, 284 to placebo (P) and 88 treated in cross-over. The median study length was 3 months (range 1-36 months). Our meta-analysis showed that in men with an average T level at baseline below 12 nmol/l, T treatment moderately improved the number of nocturnal erections, sexual thoughts and motivation, number of successful intercourses, scores of erectile function and overall sexual satisfaction, whereas T had no effect on erectile function in eugonadal men compared to placebo. Heterogeneity was explored by grouping studies according to the characteristics of the study population. A cut-off value of 10 nmol/l for the mean T of the study population failed to predict the effect of treatment, whereas the presence of risk factors for vasculogenic erectile dysfunction (ED), comorbidities and shorter evaluation periods were associated with greater treatment effects in the studies performed in hypogonadal, but not in eugonadal, men. Meta-regression analysis showed that the effects of T on erectile function, but not libido, were inversely related to the mean baseline T concentration. The meta-analysis of available studies indicates that T treatment might be useful for improving vasculogenic ED in selected subjects with low or low-normal T levels. The evidence for a beneficial effect of T treatment on erectile function should be tempered with the caveats that the effect tends to decline over time, is progressively smaller with increasing baseline T levels, and long-term safety data are not available. The present meta-analysis highlights the need, and pitfalls, for large-scale, long-term, randomized controlled trials to formally investigate the efficacy of T replacement in symptomatic middle-aged and elderly men with reduced T levels and ED.

PMID: 16181230

Rating: 1a

Isidori AM, Giannetta E, Greco EA, Gianfrilli D, Bonifacio V, Isidori A, Lenzi A, Fabbri A. Effects of testosterone on body composition, bone metabolism and serum lipid profile in middle-aged men: a meta-analysis. Clin Endocrinol (Oxf). 2005;63:280-93.

Cattedra di Andrologia, Universita 'La Sapienza', Rome, Italy. andrea.isidori@uniroma1.it

OBJECTIVES: Ageing in men is associated with a gradual decline in serum testosterone levels and a concomitant loss of muscle mass, accumulation of central adiposity, impaired mobility and increased risk of bone fractures. Whether androgen treatment might be beneficial in these subjects is still under debate. We have carried out a systematic review of randomized controlled trials (RCTs) evaluating the effects of testosterone (T) administration to middle-aged and ageing men on body composition, muscle strength, bone density, markers of bone metabolism and serum lipid profile. DATA SOURCE: A comprehensive search of all published randomized clinical trials was performed using the MEDLINE, Cochrane Library, EMBASE and Current Contents databases. REVIEW METHODS: Guided by prespecified criteria, software-assisted data abstraction and quality assessed by two independent reviewers, 29 RCTs were found to be eligible. For each investigated variable, we reported the results of pooled estimates of testosterone treatment using the random effect model of meta-analysis. Heterogeneity, reproducibility and consistency of the findings across studies were explored using sensitivity and meta-regression analysis. RESULTS: Overall, 1,083 subjects were evaluated, 625 randomized to T, 427 to placebo and 31 to observation (control group). Weighted mean age was 64.5 years (range 49.9--77.6) and mean serum testosterone was 10.9 nmol/l (range 7.8--19). Testosterone treatment produced: (i) a reduction of 1.6 kg (CI: 2.5--0.6) of total body fat, corresponding to -6.2% (CI: 9.2--3.3) variation of initial body fat, (ii) an increase in fat free mass of 1.6 kg (CI: 0.6--2.6), corresponding to +2.7% (CI: 1.1--4.4) increase over baseline and (iii) no change in body weight. The effects of T on muscle strength were heterogeneous, showing a tendency towards improvement only at the leg/knee extension and handgrip of the dominant arm (pooled effect size=0.3 standard mean difference (SMD), CI: -0.0 to 0.6). Testosterone improved bone mineral density (BMD) at the lumbar spine by +3.7% (CI: 1.0--6.4%) compared to placebo, but not at the femoral neck, and produced a consistent reduction in bone resorption markers (pooled effect size = -0.6 SMD, CI: -1.0 to -0.2). Testosterone also reduced total cholesterol by 0.23 mmol/l (CI: -0.37 to -0.10), especially in men with lower baseline T concentrations, with no change in low density lipoprotein (LDL)-cholesterol. A significant reduction of high density lipoprotein (HDL)-cholesterol was found only in studies with higher mean T-values at baseline (-0.085 mmol/l, CI: -0.017 to -0.003). Sensitivity and meta-regression analysis revealed that the dose/type of T used, in particular the possibility of aromatization, explained the heterogeneity in findings observed on bone density and HDL-cholesterol among studies. CONCLUSION: The present analysis provides an estimate of the average treatment effects of testosterone therapy in middle-aged men. Our findings are sufficiently strong to justify further

interventional studies focused on alternative targets of androgenic treatment carrying more stringent clinical implications, in particular the cardiovascular, metabolic and neurological systems.

PMID: 16117815

Rating: 1a

Jabbari B, Ney J, Sichani A, Monacci W, Foster L, Difazio M. Treatment of refractory, chronic low back pain with botulinum neurotoxin A: an open-label, pilot study. Pain Med. 2006 May-Jun;7(3):260-4.

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OBJECTIVE: To study the short- and long-term effects of botulinum neurotoxin A (BoNT-A, Botox, Allergan Inc.) on refractory chronic low back pain. DESIGN: The effect of botulinum neurotoxin A on chronic low back pain was prospectively studied in 75 patients with repeated treatments over a period of 14 months. Pain intensity (visual analog scale [VAS]), pain frequency (pain days), and perceived functional status (Oswestry scale) were assessed at baseline, 3 weeks, and at 2, 4, 6, 8, 10, 12, and 14 months. BoNT-A was injected into para-spinal muscles at 4-5 levels (between L1 and S1) unilaterally or bilaterally. The dose per site varied from 40 to 50 units. The total dose per session ranged from 200 to 500 units. Reinjections were performed at 4 months only when pain returned. RESULTS: At 3 weeks, 40 patients (53%) and at 2 months, 39 patients (52%) reported significant pain relief. The change in VAS, Oswestry score, and pain days was significant compared with baseline at 2 months after each injection period ($P < 0.005$) and remained so over subsequent treatments. Among initial responders, 91% continued responsiveness over the length of the study. Three patients (4%), after the first treatment, had a mild flulike reaction that lasted 2-5 days. CONCLUSION: Botulinum neurotoxin A may be beneficial in patients with chronic low back pain. A favorable initial response predicts subsequent responsiveness. The treatment is well tolerated, and side effects are mild and transient.

PMID: 16712627

Rating: 4b

Jadad AR, Carroll D, Glynn CJ, McQuay HJ. Intravenous Regional Sympathetic Blockade for Pain Relief in Reflex Sympathetic Dystrophy: A Systematic Review and a Randomized, Double-Blind Crossover Study. J Pain Symptom Manage 1995;10:13-20.

Abstract:

The first aim was a systematic review of intravenous regional sympathetic blocks (IRSBs) in patients with reflex sympathetic dystrophy (RSD). Randomized controlled trials (RCTs) of IRSBs in patients

with RSD were identified by MEDLINE search (1966 to May 1993) and by hand search of 30 journals (1950 to May 1993). Authors of eligible trials were asked for information on additional trials and for unpublished data. Seven RCTs of IRSBs in RSD were found. Four used guanethidine; none showed significant analgesic effect in IRSBs to relieve pain due to RSD. Two reports, one using ketanserin and one bretylium, with 17 patients in total, showed some advantage of IRSBs over control. RCT results were not combined because of the variety of different drugs and outcome measures and because of methodological deficiencies in most of the reports. The second aim was a randomized, double-blind, crossover study to assess the effectiveness of IRSBs with guanethidine. Patients fulfilling diagnostic criteria for RSD and who had reported pain relief after an open IRSB with guanethidine received IRSBs with guanethidine high dose, guanethidine low dose, and normal saline. Pain intensity and relief, adverse effects, mood, duration of analgesia, and global scores were recorded. Sixteen patients with diagnosis of RSD were recruited, but only nine entered the double-blind phase. The trial was stopped prematurely because of the severity of the adverse effects. No significant difference was found between guanethidine and placebo on any of the outcome measures.

Conclusion:
Patients who reported relief from open dose of guanethidine could not distinguish between it and saline.

Publication Type: Systematic Review

Jadad, A., et al. Intravenous Regional Sympathetic Blockade for Pain Relief in Reflex Sympathetic Dystrophy: A Systematic Review and a Randomized, Double-Blind Crossover Study. Journal of Pain Symptom Management. 1995; Volume 10:13-20.

Rating: 1c

Quality: N/A. Total Rating: N/A. Comment: Meta-Analysis Does not meet inclusion criteria for evidence-based review. [CA DWC]
Jamison RN, Kauffman J, Katz NP.Characteristics of methadone maintenance patients with chronic pain. J Pain Symptom Manage. 2000 Jan;19(1):53-62.

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Chronic pain patients who have limited access to opioids may be redirected to methadone maintenance centers for management of their pain. Unfortunately, little information exists on the incidence and characteristics of methadone maintenance patients with chronic pain. The aim of this study was to survey individuals at methadone maintenance centers in order to determine the prevalence of chronic pain and to explore differences between patients with and without pain in this treatment setting. Of 248 participants interviewed at three centers, 152 (61.3%) reported chronic pain. Compared with patients without pain, those with pain reported significantly more health problems (P < 0.001), more psychiatric

disturbance (P < 0.05), more prescription and nonprescription medication use (P < 0.001), and greater belief that they were undertreated (P < 0.001); 44% of those with pain believed that opioids prescribed for their pain had led to an addiction problem. Most of the methadone maintenance patients stated that they had always required some substance (alcohol or opioids) to feel normal. These results raise many questions about chronic-pain treatment policies and resources for persons with a history of substance abuse. Further investigations are needed to define the needs of this population and to improve their access to effective pain management.

PMID: 10687327

Rating: 4a

Jensen MP, Ehde DM, Hoffman AJ, Patterson DR, Czerniecki JM, Robinson LR. Cognitions, coping and social environment predict adjustment to phantom limb pain. Pain. 2002 Jan;95(1-2):133-42.

Abstract:

Biopsychosocial models of chronic pain hypothesize a role for psychological and environmental factors in adjustment to chronic pain. To test the utility of such models for understanding phantom limb pain, 61 persons with recent amputations were administered measures of average phantom limb pain intensity, pain interference, depression, pain coping use, pain cognitions and appraisals, and social environmental variables 1 month post-amputation, and the measures of pain intensity, pain interference, and depression again 5 months later. Multiple regression analyses showed that the psychosocial predictors made a statistically significant contribution to the concurrent prediction of average phantom limb pain, pain interference, and depression at the initial assessment, and a significant contribution to the prediction of subsequent change in pain interference and depression over the course of 5 months. The results support the utility of studying phantom limb pain from a biopsychosocial perspective, and identify specific biopsychosocial factors (e.g., catastrophizing cognitions, social support, solicitous responses from family members, and resting as a coping response) that may play an important role in adjustment to phantom limb pain.

Publication Type: Case Control, 61 cases

Jensen TS, Backonja MM, Hernández Jiménez S, Tesfaye S, Valensi P, Ziegler D. New perspectives on the management of diabetic peripheral neuropathic pain. Diab Vasc Dis Res. 2006;3:108-19.

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Peripheral neuropathy affects about 30% of people with diabetes mellitus. Between 16% and 26% of diabetes patients experience chronic pain. This may be referred to as diabetic neuropathic pain (DNP) or diabetic peripheral neuropathic pain (DPNP). Minimum requirements for diagnosis of DPNP should include assessment of pain and symptoms and neurological examination, with the accent on sensory examination. Given that depression and other co-morbidities are commonly associated with this condition, a broad approach to management is essential. Lifestyle intervention and optimisation of glycaemic control are recommended as initial steps in management. An evidence-based treatment algorithm for DPNP has been proposed, recommending initial use of either a tricyclic antidepressant, selective serotonin noradrenaline re-uptake inhibitor or alpha-2-delta agonist, depending on patient co-morbidities and contra-indications. Addition of an opioid agonist may be required in the event of inadequate pain control. Irrespective of which treatment is offered, only about one third of patients are likely to achieve more than 50% pain relief. Further research to improve the diagnosis and management of DPNP is needed.

PMID: 17058631

Rating: 5b

Jick H, Kaye JA, Jick SS. Antidepressants and the risk of suicidal behaviors. JAMA. 2004 Jul 21;292(3):338-43.

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The relation between use of antidepressants, especially selective serotonin reuptake inhibitors (SSRIs), and suicidal ideation and behaviors has received considerable public attention recently. This was a matched case-control study of patients treated in UK general practices using the UK General Practice Research Database for 1993-1999 with a base population of 159,810 users of the 4 antidepressant drugs. The study concluded, "The risk of suicidal behavior after starting antidepressant treatment is similar among users of amitriptyline, fluoxetine, and paroxetine compared with the risk among users of dothiepin. The risk of suicidal behavior is increased in the first month after starting antidepressants, especially during the first 1 to 9 days. A possible small increase in risk (bordering statistical significance) among those starting the newest antidepressant, paroxetine, is of a magnitude that could readily be due to uncontrolled confounding by severity of depression. Based on limited information, we also conclude that there is no substantial difference in effect of the 4 drugs on people aged 10 to 19 years."

PMID: 15265848

Rating: 4a

Johnsen SP, Larsson H, Tarone RE, McLaughlin JK, Norgard B, Friis S, Sorensen HT. Risk of hospitalization for myocardial infarction among users of rofecoxib, celecoxib, and other NSAIDs: a population-based case-control study. Arch Intern Med. 2005 May 9;165(9):978-84.

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BACKGROUND: It remains uncertain if the excess cardiovascular risk of rofecoxib and celecoxib reported in clinical trials is present in routine practice and whether the use of other nonaspirin nonsteroidal anti-inflammatory drugs (NSAIDs) also carries an increased cardiovascular risk. We performed a population-based case-control study to examine the risk of myocardial infarction (MI) among users of various categories of nonaspirin NSAIDs. METHODS: Using data from hospital discharge registries in the counties of North Jutland, Viborg, and Aarhus, Denmark, and the Danish Civil Registration System, we identified 10,280 cases of first-time hospitalization for MI and 102,797 sex- and age-matched non-MI population controls. All prescriptions for nonaspirin NSAIDs filled before the date of admission for MI were identified using population-based prescription databases. Relative risk estimates for MI were adjusted for a history of cardiovascular disease, hypertension, diabetes mellitus, chronic bronchitis or emphysema, alcoholism, liver cirrhosis, upper gastrointestinal bleeding, rheumatoid arthritis, systemic lupus erythematosus and the use of high-dose aspirin, platelet inhibitors, insulin or oral hypoglycemic drugs, antihypertensive drugs, lipid-lowering drugs, oral anticoagulants, nitrates, penicillamine, gold, oral glucocorticoids, and hormone therapy before the date of admission for MI. RESULTS: Current users of rofecoxib had an elevated risk estimate for hospitalization for MI compared with nonusers of any category of nonaspirin NSAIDs (adjusted relative risk [ARR], 1.80; 95% confidence interval [CI], 1.47-2.21). Increased risk estimates were also found among current users of celecoxib (ARR, 1.25; 95% CI, 0.97-1.62), other cyclooxygenase-2 selective inhibitors (ARR, 1.45; 95% CI, 1.09-1.93), naproxen (ARR, 1.50; 95% CI, 0.99-2.29), and other conventional nonaspirin NSAIDs (ARR, 1.68; 95% CI, 1.52-1.85). The highest ARRs were found among new users of all examined drug categories. CONCLUSIONS: Current and new users of all classes of nonaspirin NSAIDs had elevated relative risk estimates for MI. Although the increased risk estimates may partly reflect unmeasured bias, they indicate the need for further examination of the cardiovascular safety of all nonaspirin NSAIDs.
PMID: 15883235

Rating: 4a

Johnson M, Martinson M. Efficacy of electrical nerve stimulation for chronic musculoskeletal pain: A meta-analysis of randomized controlled trials. Pain. 2007 Jul;130(1-2):157-65. Epub 2007 Mar 23.

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Previous studies and meta-analyses of the efficacy of electrical nerve stimulation (ENS) for the treatment of chronic pain of multiple etiologies have produced mixed results. The objective of the present study was to determine whether ENS is an effective treatment for chronic musculoskeletal pain by using statistical techniques that permit accumulation of a sample size with adequate power. Randomized, controlled trials published between January 1976 and November 2006 were obtained from the National Libraries of Medicine, EMBASE, and the Cochrane Library. Prospective, placebo-controlled studies using any modality of ENS to treat chronic musculoskeletal pain in any anatomical location were included. The main outcome measure was pain at rest. The use of statistical methods to enhance data extraction and a random-effects meta-analysis to accommodate heterogeneity of ENS therapies permitted an adequate number of well designed trials of ENS to be included in the meta-analysis. A total of 38 studies in 29 papers, which included 335 placebo, 474 ENS, and 418 cross-over (both placebo and at least one ENS treatment) patients, met the selection criteria. The overall results showed a significant decrease in pain with ENS therapy using a random-effects model ($p<0.0005$). These results indicate that ENS is an effective treatment modality for chronic musculoskeletal pain and that previous, equivocal results may have been due to underpowered studies.

PMID: 17383095

Rating: 1c

This meta-analysis came to the conclusion that electrical nerve stimulation (ENS) provided a significant decrease in chronic pain. ENS of most types was applied to any anatomic location of chronic musculoskeletal pain (back, knee, hip, neck) for any length of treatment. Of the 38 studies used in the analysis, 35 favored ENS over placebo. All locations were included as "mechanism, rather than anatomic location of pain, is likely to be a critical factor for therapy." This study was funded by Empi, Inc. and performed by an independent contractor, Princeton Reimbursement Group. This group provides consulting services to medical technology companies to address reimbursement issues.
The authors collected randomized controlled trials from 1976-2006 of any type of electrical nerve stimulation used in any anatomic location for neuromuscular pain. This pretty much violates all of the rules of meta-analysis.

Johnson RE, Fudala PJ, Payne R. Buprenorphine: considerations for pain management. J Pain Symptom Manage. 2005;29:297-326. Review.

Department of Psychiatry and Behavioral Sciences, Behavioral Pharmacology Research Unit, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA.

Unlike full mu-opioid agonists, at higher doses, buprenorphine's physiological and subjective effects, including euphoria, reach a plateau. Buprenorphine has been used for the treatment of acute and chronic pain, as a supplement to anesthesia, and for behavioral and psychiatric disorders including treatment for opioid addiction. Prolonged use of buprenorphine can result in physical dependence. However,

withdrawal symptoms appear to be mild to moderate in intensity compared with those of full mu agonists. Overdoses have primarily involved buprenorphine taken in combination with other central nervous system depressants.

PMID: 15781180

Rating 5a

Julka IS, Alvaro M, Kumar D. Beneficial effects of electrical stimulation on neuropathic symptoms in diabetes patients. J Foot Ankle Surg. 1998 May-Jun;37(3):191-4.

Department of Medicine, Los Angeles County University of Southern California Medical Center, University of Southern California School of Medicine 90033, USA.

Transcutaneous electrical nerve stimulation is utilized for relieving pain in the diabetes peripheral neuropathy. Previous studies were short-term and did not document sustained beneficial effects. In this study, the authors evaluated long-term effectiveness of electrotherapy administered by proprietary equipment, an H-wave machine. A detailed questionnaire concerning patients' symptoms prior to and following electrotherapy was mailed to the users of H-wave machine. The responses of 34 individuals who had diabetes mellitus were analyzed (age 74.1 +/- 1.6 SEM years, body mass index 28.5 +/- 0.8 kg/m2, duration of diabetes 15.8 +/- 2.0 years and duration of neuropathic symptoms 8.0 +/- 1.8 years). Telephone interviews were conducted with 20 additional diabetes patients selected randomly from the persons who did not return the questionnaire. Forty-one (76%) patients reported a 44.0 +/- 4.0% subjective improvement in their neuropathic pain. The overall improvement in pain was also significant on an analog scale of 10 ($p < .01$), and correlated well with the percent amelioration data ($r2 = .65$). These data suggest an effectiveness of electrotherapy in managing neuropathic pain as an adjunct to the analgesics. It appears to provide continued benefit as the responders have used this nonpharmacological treatment modality for an average period of 1.7 +/- 0.3 years.

PMID: 9638542

Rating: 3c

Kahan M, Srivastava A, Wilson L, Gourlay D, Midmer D. Misuse of and dependence on opioids: study of chronic pain patients. Can Fam Physician. 2006;52:1081-7.

OBJECTIVE: To review the evidence on identifying and managing misuse of and dependence on opioids among primary care patients with chronic pain. QUALITY OF EVIDENCE: MEDLINE was searched using such terms as "opioid misuse" and "addiction." The few studies on the prevalence of opioid dependence in primary care populations were based on retrospective chart reviews (level II evidence). Most recommendations regarding identification and management of opioid misuse in primary

care are based on expert opinion (level III evidence). MAIN MESSAGE: Physicians should ask all patients receiving opioid therapy about current, past, and family history of addiction. Physicians should take "universal precautions" that include careful prescribing and ongoing vigilance for signs of misuse. Patients suspected of opioid misuse can be treated with a time-limited trial of structured opioid therapy if they are not acquiring opioids from other sources. The trial should consist of daily to weekly dispensing, regular urine testing, and tapering of doses of opioids. If the trial fails or is not indicated, patients should be referred for methadone or buprenorphine treatment. CONCLUSION: Misuse of and dependence on opioids can be identified and managed successfully in primary care.

PMID: 17279218

Rating 5b

Kalauokalani D, Sherman K, Cherkin D. Acupuncture for Chronic Low Back Pain: Diagnosis and Treatment Patterns Among Acupuncturists Evaluating the Same Patient. South Med J 2001; 94(5):486-492.

CONCLUSIONS: "Seven acupuncturists agreed considerably in the diagnoses for the same patient with chronic low back pain, but treatment recommendations varied substantially"

Publication Type: Case Control Study, 7 cases

Kalauokalani D, Cherkin DC, Sherman KJ, Koepsell TD, Deyo RA. Lessons from a trial of acupuncture and massage for low back pain: patient expectations and treatment effects. Spine. 2001 Jul 1;26(13):1418-24.

Washington University Pain Center, St.Louis, MO, USA.

STUDY DESIGN: A subanalysis of data derived from a randomized clinical trial was performed. OBJECTIVE: To evaluate the association of a patient's expectation for benefit from a specific treatment with improved functional outcome. SUMMARY OF BACKGROUND DATA: Psychosocial factors, ambiguous diagnoses, and lack of a clearly superior treatment have complicated the management of patients with chronic low back pain. The authors hypothesized that patient expectation for benefit from a specific treatment is associated with improved functional outcomes when that treatment is administered. METHODS: In a randomized trial, 135 patients with chronic low back pain who received acupuncture or massage were studied. Before randomization, study participants were asked to describe their expectations regarding the helpfulness of each treatment on a scale of 0 to 10. The primary outcome was level of function at 10 weeks as measured by the modified Roland Disability scale. RESULTS: After adjustment for baseline characteristics, improved function was observed for 86% of the participants with higher expectations for the treatment they received, as compared with 68% of those with lower expectations (P = 0.01). Furthermore, patients who expected greater benefit from massage than from

acupuncture were more likely to experience better outcomes with massage than with acupuncture, and vice versa (P = 0.03). CONCLUSIONS: The results of this study suggest that patient expectations may influence clinical outcome independently of the treatment itself. In contrast, general optimism about treatment, divorced from a specific treatment, is not strongly associated with outcome. These results may have important implications for clinical trial design and recruitment, and may help to explain the apparent success of some conventional and alternative therapies in trials that do not control for patient expectations. The findings also may be important for therapy choices made in the clinical setting.

Publication Types:
Clinical Trial
Randomized Controlled Trial

PMID: 11458142

Rating: 2b

Kalso E, Edwards JE, Moore RA, McQuay HJ. Opioids in chronic non-cancer pain: systematic review of efficacy and safety. Pain. 2004;112:372-80.

Pain Clinic, Department of Anaesthesia and Intensive Care Medicine, Helsinki University Central Hospital, P.O. Box 340, FIN 00029 HUS, Finland. eija.kalso@helsinki.fi

Opioids are used increasingly for chronic non-cancer pain. Controversy exists about their effectiveness and safety with long-term use. We analysed available randomised, placebo-controlled trials of WHO step 3 opioids for efficacy and safety in chronic non-cancer pain. The Oxford Pain Relief Database (1950-1994) and Medline, EMBASE and the Cochrane Library were searched until September 2003. Inclusion criteria were randomised comparisons of WHO step 3 opioids with placebo in chronic non-cancer pain. Double-blind studies reporting on pain intensity outcomes using validated pain scales were included. Fifteen randomised placebo-controlled trials were included. Four investigations with 120 patients studied intravenous opioid testing. Eleven studies (1025 patients) compared oral opioids with placebo for four days to eight weeks. Six of the 15 included trials had an open label follow-up of 6-24 months. The mean decrease in pain intensity in most studies was at least 30% with opioids and was comparable in neuropathic and musculoskeletal pain. About 80% of patients experienced at least one adverse event, with constipation (41%), nausea (32%) and somnolence (29%) being most common. Only 44% of 388 patients on open label treatments were still on opioids after therapy for between 7 and 24 months. The short-term efficacy of opioids was good in both neuropathic and musculoskeletal pain conditions. However, only a minority of patients in these studies went on to long-term management with opioids. The small number of selected patients and the short follow-ups do not allow conclusions concerning problems such as tolerance and addiction.

PMID: 15561393

Rating: 5b

Kapczinski F, Lima MS, Souza JS, Schmitt R. Antidepressants for generalized anxiety disorder. Cochrane Database Syst Rev. 2003;(2):CD003592.

Department of Psychiatry, Federal University of Rio Grande do Sul - UFRGS, Departamento de Medicinal Legal e Psiquiatria - HCPA - UFRGS, Rua Ramiro Barcelos, 2350, Porto Alegre, RS, Brazil, 90035-003. kapcz@terra.com.br

BACKGROUND: Pharmacological treatments have been successfully used to treat Generalized Anxiety Disorder (GAD). The mainstay for the pharmacological treatment of GAD in past decades has been the use of benzodiazepine and non benzodiazepine anxiolytics. Data emerging over the last two decades have shown that antidepressants may be equally effective to anxiolytics for treating GAD. The use of antidepressants for treating GAD may be advantageous, due to the fact that GAD presents a high co morbidity ratio with major depressive disorder (62%) and dysthymia (37%). OBJECTIVES: To assess the efficacy and acceptability of antidepressants for treating generalized anxiety disorder. SEARCH STRATEGY: Cochrane Collaboration Depression, Anxiety and Neurosis Controlled Trials Register - CCDANCTR (up to May 2002), Anxiety Neurosis (up to May 2002) and Cochrane Controlled Trials Register (CENTRAL/CCTR) (up to May 2002), MEDLINE (1966 to May 2002), LILACS (1982 to May 2002); reference searching; personal communication; conference abstracts and book chapters on the treatment of generalized anxiety disorder. SELECTION CRITERIA: Randomised controlled trials were included. Exclusion criteria were: non randomised studies; studies which included patients with generalized anxiety disorder and another Axis I co-morbidity. DATA COLLECTION AND ANALYSIS: The data from studies were extracted independently by two reviewers and relative risks, weighted mean difference and number needed to treat were estimated. People who died or dropped out were regarded as having had no improvement. MAIN RESULTS: Antidepressants (imipramine, venlafaxine and paroxetine) were found to be superior to placebo in treating GAD. The calculated NNT for antidepressants in GAD is 5.15. Dropout rates did not differ between antidepressants. Only one study presented data on imipramine and trazodone. Imipramine was chosen as the reference drug and, therefore, data on trazodone could not be included in the meta analysis. Only one study was conducted among children and adolescents (Rynn 2001). The latter study showed very promising results of sertraline in children and adolescents with GAD, which warrants its replication in larger samples. REVIEWER'S CONCLUSIONS: The available evidence suggests that antidepressants are superior to placebo in treating GAD. There is evidence from one trial suggesting that paroxetine and imipramine have a similar efficacy and tolerability. There is also evidence from placebo-controlled trials suggesting that these drugs are well tolerated by GAD patients. Further trials of antidepressants for GAD will help to demonstrate which antidepressants should be used for which patients.

PMID: 12804478

Rating: 1c

Kapural L, Narouze SN, Janicki TI, Mekhail N. Spinal cord stimulation is an effective treatment for the chronic intractable visceral pelvic pain. Pain Med. 2006 Sep-Oct;7(5):440-3.

Pain Management Department, The Cleveland Clinic Foundation, Cleveland, Ohio, USA. Kapural@ccf.org

OBJECTIVE: Recent studies have demonstrated significant involvement of dorsal column pathways in transmission of visceral pelvic pain. Spinal cord stimulation (SCS) suppresses visceral response to colon distension in an animal model and therefore may be an effective therapy for chronic pelvic pain of visceral origin. We are reporting on the value of neurostimulation for chronic visceral pelvic pain in six female patients with the diagnosis of long-standing pelvic pain (history of endometriosis, multiple surgical explorations, and dyspareunia). DESIGN AND SETTINGS: Case-series report. All patients received repeated hypogastric blocks (in an average of 5.3 blocks) with a significant pain relief for a period ranging from 1 to 6 weeks. Three received neurolytic hypogastric block with the pain relief of 3, 8, and 12 months, respectively. Following psychological evaluation and clearance by our Multidisciplinary Committee on Implantable Devices, they all underwent SCS trial for 7-14 days. All patients received SCS systems with dual leads (Compact or Quad leads, Medtronic Inc., Minneapolis, MN, USA). RESULTS: The average follow-up was 30.6 months. Median visual analog scale pain score decreased from 8 to 3. All patients had more than 50% of the pain relief. Pain Disability Index changed from an average of 57.7 +/- 12 to 19.5 +/- 7. Opiate use decreased from an average 22.5 mg to 6.6 mg of morphine sulfate milligram equivalents per day. CONCLUSION: It appears that SCS may have a significant therapeutic potential for treatment of visceral pelvic pain.

PMID: 17014604

Rating: 4c

Karjalainen K, Malmivaara A, van Tulder M, et al. Multidisciplinary Biopsychosocial Rehabilitation of Subacute Low Back Pain in Working-Age Adults: A Systematic Review Within the Framework of the Cochrane Collaboration Back Review Group. Spine 2001;26(3):262-269.

Abstract:

STUDY DESIGN: A systematic review of randomized controlled trials was performed. OBJECTIVE: To evaluate the effectiveness of multidisciplinary biopsychosocial rehabilitation for subacute low back pain among working-age adults. SUMMARY OF BACKGROUND DATA: Multidisciplinary biopsychosocial rehabilitation programs are widely applied for patients with chronic low back pain. The multidisciplinary biopsychosocial approach for prolonged low back pain could be considered to prevent chronicity. Work site visits and a close relationship with occupational health care might produce results

in terms of patients working ability. METHODS: Reviewed randomized controlled trials as well as controlled trials were identified from electronic bibliographic databases, reference checking, and consultation with experts in the rehabilitation field. Four blinded reviewers selected the trials. Two rehabilitation specialists evaluated the clinical relevance. Two other blinded reviewers extracted the data and assessed the main results along with the methodologic quality of the studies. A qualitative analysis was performed to evaluate the level evidence. RESULTS: Of 1808 references, only 2 relevant studies were included. Both were considered to be methodologically low-quality randomized controlled trials. The clinical relevance of the studies was sufficient. The level of scientific evidence was moderate, showing that multidisciplinary rehabilitation involving work site visit or more comprehensive occupational health care intervention helps patients return to work faster, makes sick leaves less, and alleviates subjective disability. CONCLUSIONS: There is moderate evidence showing that multidisciplinary rehabilitation for subacute low back pain is effective, and that work site visit increases the effectiveness, but because the analyzed studies had some methodologic shortcomings, an obvious need still exists for high-quality trials in this field.

Publication Type: Systematic Review

Karjalainen K, Malmivaara A, van Tulder M, Roine R, Jauhiainen M, Hurri H, Koes B. Multidisciplinary biopsychosocial rehabilitation for neck and shoulder pain among working age adults. Cochrane Database Syst Rev. 2003;(2):CD002194.

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BACKGROUND: Multidisciplinary biopsychosocial rehabilitation programs for neck and shoulder pain require substantial staff and financial resources. Despite questionable scientific evidence of their effectiveness, they are widely used. Neck and shoulder complaints are common among working age adults and they are often associated with physical work load and stress. Pain in the neck and shoulder area cause biopsychosocial difficulties for the patient, especially if disability due to pain is prolonged. To help patients with biopsychosocial problems, or to prevent their development, multidisciplinary biopsychosocial programs are used for rehabilitation for patients with neck and shoulder pain. Nevertheless, multidisciplinary treatment programmes are often laborious and rather long processes and require good collaboration between the patient, the rehabilitation team and the work place. OBJECTIVES: The objective of this systematic review was to determine the effectiveness of multidisciplinary biopsychosocial rehabilitation for neck and shoulder pain among working age adults. SEARCH STRATEGY: The reviewed studies for this review were electronically identified from MEDLINE, EMBASE, PsycLIT, CENTRAL, Medic, the Science Citation Index, reference checking and consulting experts in the rehabilitation field. The original search was planned and performed for more broad area of musculoskeletal disorders. Trials on neck and shoulder pain were separated afterwards. The literature search was updated in November 2002 by electronically searching MEDLINE and EMBASE. SELECTION CRITERIA: From all references identified in our original search, we

selected randomized controlled trials (RCTs) and non-randomized controlled clinical trials (CCTs). Trials had to assess the effectiveness of biopsychosocial rehabilitation for working age adults suffering from neck and shoulder pain. The rehabilitation program was required to be multidisciplinary, i.e., it had to consist of a physician's consultation plus either a psychological, social or vocational intervention, or a combination of these. DATA COLLECTION AND ANALYSIS: Four reviewers blinded to journal and author selected the trials that met the specified inclusion criteria. Two experts in the field of rehabilitation evaluated the clinical relevance and applicability of the findings of the selected studies for actual clinical use. Two other reviewers blinded to journal and author extracted the data and assessed the main results and the methodological quality of the studies, using standardized forms. Finally, a qualitative analysis was performed to evaluate the level of scientific evidence for the effectiveness of multidisciplinary biopsychosocial rehabilitation. MAIN RESULTS: After screening 1808 abstracts, and the references of 65 reviews, we found only two relevant studies that satisfied our criteria. No more studies were found for this update. One of the studies was considered to be a methodologically low quality RCT and the other one was a methodologically low quality CCT. The clinical relevance of included studies was satisfactory. There was limited scientific evidence for the effectiveness of multidisciplinary biopsychosocial rehabilitation for neck and shoulder pain. REVIEWER'S CONCLUSIONS: We conclude that there appears to be little scientific evidence for the effectiveness of multidisciplinary biopsychosocial rehabilitation compared with other rehabilitation facilities for neck and shoulder pain. Multidisciplinary rehabilitation is a commonly used intervention for chronic neck and shoulder complaints, therefore we see an urgent need for high quality trials in this field.

PMID: 12804428

Rating: 1c

Katz NP. MorphiDex (MS-DM) Double-Blind, Multiple-Dose Studies in Chronic Pain Patients. J Pain Symptom Manage 2000;19:S37-S41.

Brigham & Women's Hospital, Pain and Management Center, Boston, MA 02115, USA.

Abstract:
Preclinical and double-blind single-dose placebo-controlled studies demonstrated that MorphiDex (MS:DM), a 1:1 ratio of morphine sulfate (MS) to dextromethorphan hydrobromide (DM), provides significantly greater analgesia than an equal dose of immediate release MS, with a faster onset, and a duration of > or = 8 h. The analgesic effect of MS:DM compared to MS was evaluated in 2 double-blind, multiple-dose studies in 321 patients with cancer and other chronic pain: a crossover study that consisted of two 2-wk periods and a 4-wk parallel study. As specified in the study protocols, patients took sufficient MS or MS:DM to achieve satisfactory pain control. In the crossover study, the MS:DM group required half as much morphine as the MS group to achieve satisfactory pain control (80 mg and 162 mg, respectively). The interval between doses and the time from the last dose of the day to the first

dose of the next day were significantly longer for MS:DM compared to MS. In the parallel study, MS:DM also provided pain control at a significantly lower dose. After four weeks of treatment, the mean daily dose of MS increased, while there was little change in the MS:DM mean daily dose (P = 0.025) to maintain satisfactory pain control. More patients preferred MS:DM to run-in MS than preferred MS to run-in MS (P = 0.026). The addition of DM to MS did not increase the incidence of adverse events, which were those commonly associated with opioid use. These studies confirm that MS:DM provides satisfactory pain relief but at a significantly lower morphine daily dose.
Publication Type: Case Control, 321 cases
PMID: 10687338

Katz J, Pennella-Vaughan J, Hetzel RD, Kanazi GE, Dworkin RH. A randomized, placebo-controlled trial of bupropion sustained release in chronic low back pain. J Pain. 2005 Oct;6(10):656-61.

Department of Anesthesiology, University of Rochester School of Medicine and Dentistry, Rochester, New York 14642, USA.

Clinical trials of the efficacy of antidepressant drugs in patients with chronic low back pain have had mixed results, possibly because of the different mechanisms of action of the drugs that have been studied. Because bupropion has a mechanism of action that differs from other antidepressants and has shown efficacy in neuropathic pain, a randomized, placebo-controlled, 2-period crossover trial was conducted to evaluate its efficacy in subjects with chronic low back pain. The primary efficacy variable was mean daily diary pain intensity ratings, and secondary pain intensity and relief outcomes included weekly pain intensity ratings, the McGill Pain Questionnaire (MPQ) Present Pain Intensity scale, pain relief ratings, and satisfaction with pain relief ratings. Adverse events were also assessed throughout the trial. Analyses were performed of an intention-to-treat sample of 44 patients, only 3 of whom met criteria for neuropathic low back pain. Daily and weekly pain intensity ratings, the MPQ Present Pain Intensity scale, and pain relief ratings were not significantly different following treatment with bupropion sustained release (SR) vs. placebo. These results suggest that bupropion SR was not significantly better than placebo in the treatment of patients with non-neuropathic chronic low back pain. PERSPECTIVE: Antidepressant medications that have both noradrenergic and serotonergic effects appear to have greater efficacy in patients with chronic low back pain than those with only serotonergic activity. We studied bupropion because it inhibits the reuptake of both norepinephrine and dopamine, but found no evidence of efficacy in patients with non-neuropathic chronic low back pain.

PMID: 16202958

Rating: 2c

Kavar B, Rosenfeld JV, Hutchinson A, The efficacy of spinal cord stimulation for chronic pain, Clin Neurosci. 2000 Sep;7(5):409-13.

Department of Neurosurgery, Neuroscience Centre, Royal Melbourne Hospital, Melbourne, Australia.

A prospective study was undertaken to evaluate the efficacy of spinal cord stimulation (SCS) in the management of chronic pain syndrome. The study included all patients who underwent this procedure at the Royal Melbourne Hospital and the Melbourne Private Hospital over a period of two years. A total of 29 patients were managed by the end of June 1996. These patients were carefully screened by a neurosurgeon (JVR) and a psychiatrist. Of these, 26 patients had a follow up evaluation at the end of August 1996. From the group of 29 patients, four patients failed to obtain any relief during the trial phase of the procedure and thus did not have the stimulator implanted permanently. From the 25 patients who proceeded to have the stimulator implanted, 11 patients had a variable beneficial response, three patients found it to be of marginal benefit, six had no benefit, three patients initially had a good response but subsequently gained no benefit whilst two patients were uncertain of its benefit. It thus appears that SCS was of benefit in 50% of our carefully selected patients with chronic pain syndromes. Copyright 2000 Harcourt Publishers Ltd.

PMID: 10942661
Rating: 3c

Keefe FJ; Bonk V. Psychosocial assessment of pain in patients having rheumatic diseases. Rheumatic Diseases Clinics of North America. 01-Feb-1999; 25(1): 81-103.
Department of Psychology, Ohio University, Athens, USA.
Abstract:
A variety of reliable and valid psychosocial assessment instruments have been developed. Many of these instruments are brief and easily incorporated into clinical practice settings. Measures of coping, self-efficacy, helplessness, and cognitive distortion are especially useful in understanding the pain experience in rheumatic disease populations. Information gleaned from psychosocial assessments is increasingly being used to guide pain treatment efforts. Recent research, suggests that treatment outcomes can be improved if one tailors psychosocial pain management protocols to address the particular problems identified by comprehensive psychosocial assessments. Considered overall, psychosocial assessment methods have much to offer the clinician working with patients having persistent pain. The current status of this field is promising, and as psychosocial assessment methods become even more fully integrated into clinical practice, they are likely to yield even greater insights into the pain experience of patients with rheumatic diseases.
Major Subjects:
- Arthritis, Rheumatoid / * psychology
- Pain Measurement / * psychology
- Social Support

Publication Type: Review
PMID: 10083960

Keefe FJ, Kashikar-Zuck S, Robinson E, et al. Pain Coping Strategies that Predict Patients' and Spouses' Ratings of Patients' Self-efficacy. Pain 1997;73:191-199.
Duke University Medical School, Durham, NC 27710, USA.
Abstract:
This study examined the relationship of pain coping strategies to osteoarthritis patients' ratings of self-efficacy and to spouses' ratings of the patients' self-efficacy. Subjects, 130 individuals having osteoarthritis of the knees and persistent knee pain, completed a pain coping strategies measure (the Coping Strategies Questionnaire), a measure of self-efficacy (the Arthritis Self-Efficacy Scale), and a measure of pain (the McGill Pain Questionnaire). Two sets of regression analyses were conducted, one examining the degree to which pain coping strategies predicted patients' self-efficacy ratings, and the other examining the degree to which coping strategies predicted spouses' ratings of the patients' self-efficacy. Several pain coping strategies were found to predict a significant proportion of variance in patients' ratings of self-efficacy: (i) ignoring pain sensations was related to higher self-efficacy for pain; (ii) coping self statements were related to higher self-efficacy for controlling other arthritis symptoms (e.g., fatigue or mood symptoms: and (iii) catastrophizing was related to lower self-efficacy for pain, and self-efficacy for other arthritis symptoms. Pain coping strategies were also found to predict a significant proportion of variance in spouses' ratings of the patients' self-efficacy. Specifically: (i) diverting attention was related to lower spousal ratings of self-efficacy for pain; (ii) praying or hoping was related to lower spousal ratings of self-efficacy for function; and (iii) catastrophizing was related to lower spousal ratings of self-efficacy for control of fatigue or mood symptoms. The findings regarding coping strategies were particularly interesting in that they were obtained even after controlling for pain intensity and demographic variables. The pain coping strategies identified are potentially important targets for cognitive-behavioral assessment and treatment efforts. Interventions designed to increase the use of adaptive pain coping strategies and decrease the use of maladaptive pain coping strategies could enhance self-efficacy, reduce pain, and improve the physical and psychological functioning of individuals having osteoarthritis.
Publication Type: Case Control, 130 cases
PMID: 9415505

Keefe FJ, Block AR, Williams RB Jr, Surwit RS. Behavioral treatment of chronic low back pain: clinical outcome and individual differences in pain relief. Pain. 1981 Oct;11(2):221-31.

The response of 111 chronic low back pain patients to a comprehensive behavioral treatment program emphasizing relaxation procedures is examined. Over the course of treatment, significant reductions were obtained on measures of subjective tension, EMG activity, and pain. Many patients also decreased their intake of analgesic/narcotic agents and reported an increase in activity level. In order to examine individual differences in pain relief, the 28 patients who had the greatest decreases in pain were compared to those who had the least decreases in pain. Patients who had the best outcome in terms of pain relief were significantly more likely to show improvements in other outcome measures. In addition, these patients rated their pain initially as more severe, had continuous pain for fewer years, and were less likely to be on disability or to have had multiple surgical procedures. These results are discussed in

the light of recent data from other behavioral treatment studies with chronic low back pain patients and implications for behavioral assessment and treatment are discussed.

PMID: 6459557

Rating: 4b

Keel PJ, Wittig R, Deutschmann R, Diethelm U, Knüsel O, Löschmann C, Matathia R, Rudolf T, Spring H. Effectiveness of in-patient rehabilitation for sub-chronic and chronic low back pain by an integrative group treatment program (Swiss Multicentre Study). Scand J Rehabil Med. 1998 Dec;30(4):211-9.

University Psychiatric Out-Patient Service, Basel, Switzerland.

In this multicentre intervention study, we compared an integrated group treatment program which combines psychological and education methods into a more active training approach, with the traditional individual approach of physiotherapy and physical procedures for sub-chronic and chronic low back pain. Our 411 patients had a 4-week inpatient treatment: 243 patients in an experimental program and 168 in a traditional program. Outcomes of 283 patients were assessed 3 months and 1 year after entry. The dropout rate was 31.1%. Both conditions demonstrated favourable initial effects on functional and psychological parameters, but the integrated approach showed better long-term results for work rehabilitation than the traditional approach. The most successful patients (n = 58) were younger and had a higher educational level in comparison to the unsuccessful subgroup (n = 71). The main conclusion is that an integrated approach promoting self control and behaviour change through educational measures achieves better long-term results than the traditional individual physiotherapy approach.

PMID: 9825385

Rating: 3b

Keitel W, Frerick H, Kuhn U, Schmidt U, Kuhlmann M, Bredehorst A. Capsicum pain plaster in chronic non-specific low back pain. Arzneimittelforschung. 2001 Nov;51(11):896-903.

Klinik fur Rheumatologie, Vogelsang, Germany.

Topically applied capsaicin (CAS 404-86-4) induces the release of substance P, a neurotransmitter, from sensory C-fibres. In addition, there is a specific blockade of transport and de-novo synthesis of substance P. As a result, repeated applications of capsaicin bring about a long lasting desensitisation to pain (increase of pain threshold). The desensitising effect is fully reversible. The confirmed pharmacodynamic actions and a number of double-blind clinical studies indicate that local capsicum preparations are very suitable for the treatment of neuropathic pain or musculoskeletal disorders, with or without inflammatory components. In a double-blind, randomised parallel-group study a capsicum

plaster was compared with a placebo for 3 weeks in 154 patients with non-specific back pain. Inclusion criteria were a history of back pain for a minimum period of 3 months and a degree of pain of 5 or more on an eleven grade visual analogue scale. The principal target variable consisted of the score of 3 combined pain scales. Secondary efficacy measures were tests of mobility, a disability index (in the context of Arhus low back rating scale) and global assessments by physicians and patients. For patients to be rated as responders their total pain score at the final examination after 3 weeks of treatment had to show a reduction by at least 30% of the baseline value. The study unequivocally achieved the target criterion with a rate of responders in the capsicum group of 60.8% against 42.1% in the placebo group (p = 0.0219). The sum of the 3 separate pain scales decreased more markedly in the capsicum group than in the placebo group (38.5% compared to 28.0%; p = 0.002). Relatively slight improvements of the impaired mobility and the functional status are explained by the characteristics of the disorder treated. The efficacy ratings by observers and patients was definitely in favour of capsicum. Adverse effects--mostly harmless and resolving spontaneously--were reported by 15 patients in the capsicum group and by 9 in the placebo group. The tolerance ratings by investigators and patients were superior to the placebo product. This, however, partly is due to the local pharmacological actions of the drug. As in comparably positive randomised studies with capsaicin cream in patients with osteoarthritis or fibromyalgia it was shown that a capsicum plaster preparation can also be used to advantage in chronic non-specific back pain.

Publication Types:
- Clinical Trial
- Randomized Controlled Trial

PMID: 11765591

Rating: 2b

Kemler MA, Reulen JP, Barendse GA, van Kleef M, de Vet HC, van den Wildenberg FA, Impact of spinal cord stimulation on sensory characteristics in complex regional pain syndrome type I: a randomized trial, Anesthesiology. 2001 Jul;95(1):72-80.

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BACKGROUND: A randomized trial was performed to assess the effect of spinal cord stimulation (SCS) on detection and pain thresholds for pressure, warmth, and cold and on the extent of mechanical hyperalgesia in patients with chronic complex regional pain syndrome type I. METHODS: Fifty-four chronic complex regional pain syndrome type I patients were randomized to receive both SCS and physical therapy (SCS+PT; n = 36), or to receive only physical therapy (PT; n = 18). Twenty-four SCS+PT patients responded positively to trial stimulation and underwent SCS implantation. During a 12-month follow-up period, six quantitative sensory testing sessions were performed. The main analysis compared 24 SCS patients with 29 nonimplanted patients--one PT patient was excluded. RESULTS:

SCS showed no effect on detection thresholds for warmth and cold or on pain thresholds for any sensation. The pressure detection threshold initially increased by SCS, but after 3 months, pressure detection thresholds returned to normal. Mechanical hyperalgesia, both dynamic and static, was reduced slightly with SCS. CONCLUSIONS: Although SCS has previously been shown to cause a significant pain reduction in complex regional pain syndrome type I, the treatment has no long-term effect on detection and pain thresholds for pressure, warmth, or cold. The treatment seems to have only minimal influence on mechanical hyperalgesia.

Publication Types:
- Clinical Trial
- Randomized Controlled Trial

PMID: 11465587

Rating: 2b

Kemler MA, Barendse GA, van Kleef M, de Vet HC, Rijks CP, Furnee CA, van den Wildenberg FA, Spinal cord stimulation in patients with chronic reflex sympathetic dystrophy, N Engl J Med. 2000 Aug 31;343(9):618-24.

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BACKGROUND: Chronic reflex sympathetic dystrophy (also called the complex regional pain syndrome) is a painful, disabling disorder for which there is no proven treatment. In observational studies, spinal cord stimulation has reduced the pain associated with the disorder. METHODS: We performed a randomized trial involving patients who had had reflex sympathetic dystrophy for at least six months. Thirty-six patients were assigned to receive treatment with spinal cord stimulation plus physical therapy, and 18 were assigned to receive physical therapy alone. The spinal cord stimulator was implanted only if a test stimulation was successful. We assessed the intensity of pain (on a visual-analogue scale from 0 cm [no pain] to 10 cm [very severe pain]), the global perceived effect (on a scale from 1 [worst ever] to 7 [best ever]), functional status, and the health-related quality of life. RESULTS: The test stimulation of the spinal cord was successful in 24 patients; the other 12 patients did not receive implanted stimulators. In an intention-to-treat analysis, the group assigned to receive spinal cord stimulation plus physical therapy had a mean reduction of 2.4 cm in the intensity of pain at six months, as compared with an increase of 0.2 cm in the group assigned to receive physical therapy alone ($P<0.001$ for the comparison between the two groups). In addition, the proportion of patients with a score of 6 ("much improved") for the global perceived effect was much higher in the spinal cord stimulation group than in the control group (39 percent vs. 6 percent, $P=0.01$). There was no clinically important improvement in functional status. The health-related quality of life improved only in the 24 patients who actually underwent implantation of a spinal cord stimulator. Six of the 24 patients had complications that required additional procedures, including removal of the device in 1 patient. CONCLUSIONS: In

carefully selected patients with chronic reflex sympathetic dystrophy, electrical stimulation of the spinal cord can reduce pain and improve the health-related quality of life.

Publication Types:
- Clinical Trial
- Randomized Controlled Trial

PMID: 10965008

Rating: 2c

Kemler MA, Furnee CA, Economic evaluation of spinal cord stimulation for chronic reflex sympathetic dystrophy, Neurology. 2002 Oct 22;59(8):1203-9

Department of Surgery, Maastricht University Hospital, Maastricht, The Netherlands. kemlerm@mzh.nl

OBJECTIVE: To evaluate the economic aspects of treatment of chronic reflex sympathetic dystrophy (RSD) with spinal cord stimulation (SCS), using outcomes and costs of care before and after the start of treatment. METHODS: Fifty-four patients with chronic RSD were randomized to receive either SCS together with physical therapy (SCS+PT; n = 36) or physical therapy alone (PT; n = 18). Twenty-four SCS+PT patients responded positively to trial stimulation and underwent SCS implantation. During 12 months of follow-up, costs (routine RSD costs, SCS costs, out-of-pocket costs) and effects (pain relief by visual analogue scale, health-related quality of life [HRQL] improvement by EQ-5D) were assessed in both groups. Analyses were carried out up to 1 year and up to the expected time of death. RESULTS: SCS was both more effective and less costly than the standard treatment protocol. As a result of high initial costs of SCS, in the first year, the treatment per patient is $4,000 more than control therapy. However, in the lifetime analysis, SCS per patient is $60,000 cheaper than control therapy. In addition, at 12 months, SCS resulted in pain relief (SCS+PT [-2.7] vs PT [0.4] [p < 0.001]) and improved HRQL (SCS+PT [0.22] vs PT [0.03] [p = 0.004]). CONCLUSIONS: The authors found SCS to be both more effective and less expensive as compared with the standard treatment protocol for chronic RSD.

Publication Types:
- Clinical Trial
- Randomized Controlled Trial

PMID: 12391348

Rating: 2c

Kemler MA, Barendse GA, van Kleef M, de Vet HC, Rijks CP, Furnee CA, van den Wildenberg FA. Spinal cord stimulation in patients with chronic reflex sympathetic dystrophy. N Engl J Med. 2000 Aug 31;343(9):618-24.

Department of Surgery, Maastricht University Hospital, The Netherlands. mkeml@shee.azm.nl

BACKGROUND: Chronic reflex sympathetic dystrophy (also called the complex regional pain syndrome) is a painful, disabling disorder for which there is no proven treatment. In observational studies, spinal cord stimulation has reduced the pain associated with the disorder. METHODS: We performed a randomized trial involving patients who had had reflex sympathetic dystrophy for at least six months. Thirty-six patients were assigned to receive treatment with spinal cord stimulation plus physical therapy, and 18 were assigned to receive physical therapy alone. The spinal cord stimulator was implanted only if a test stimulation was successful. We assessed the intensity of pain (on a visual-analogue scale from 0 cm [no pain] to 10 cm [very severe pain]), the global perceived effect (on a scale from 1 [worst ever] to 7 [best ever]), functional status, and the health-related quality of life. RESULTS: The test stimulation of the spinal cord was successful in 24 patients; the other 12 patients did not receive implanted stimulators. In an intention-to-treat analysis, the group assigned to receive spinal cord stimulation plus physical therapy had a mean reduction of 2.4 cm in the intensity of pain at six months, as compared with an increase of 0.2 cm in the group assigned to receive physical therapy alone ($P<0.001$ for the comparison between the two groups). In addition, the proportion of patients with a score of 6 ("much improved") for the global perceived effect was much higher in the spinal cord stimulation group than in the control group (39 percent vs. 6 percent, $P=0.01$). There was no clinically important improvement in functional status. The health-related quality of life improved only in the 24 patients who actually underwent implantation of a spinal cord stimulator. Six of the 24 patients had complications that required additional procedures, including removal of the device in 1 patient. CONCLUSIONS: In carefully selected patients with chronic reflex sympathetic dystrophy, electrical stimulation of the spinal cord can reduce pain and improve the health-related quality of life.

Publication Types:
Clinical Trial
Randomized Controlled Trial

PMID: 10965008

Rating: 2c

Kemler MA, de Vet HC, Barendse GA, van den Wildenberg FA, van Kleef M. Spinal cord stimulation for chronic reflex sympathetic dystrophy--five-year follow-up. N Engl J Med. 2006 Jun 1;354(22):2394-6.

A letter to the editor, not peer reviewed. In analyzing outcomes there were some issues of intention to treat, i.e., patients randomized to SCS but who never received it due to failure of an individual trial prior to implant.

PMID: 16738284

Rating: 11b

Kemler MA, De Vet HC, Barendse GA, Van Den Wildenberg FA, Van Kleef M. The effect of spinal cord stimulation in patients with chronic reflex sympathetic dystrophy: two years' follow-up of the randomized controlled trial. Ann Neurol. 2004 Jan;55(1):13-8.

Department of Plastic Surgery, Medical Center Leeuwarden, Leeuwarden. Marius.Kemler@ZNB.nl

Chronic reflex sympathetic dystrophy is a painful, disabling disorder for which no treatment with proven effect is available. We performed a randomized trial in a 2 to 1 ratio of patients, in which 36 patients were treated with spinal cord stimulation and physical therapy (SCS+PT), and 18 patients received solely PT. Twenty-four SCS+PT patients were given a permanent spinal cord stimulation system after successful test stimulation; the remaining 12 patients received no permanent system. We assessed pain intensity, global perceived effect, functional status, and health-related quality of life. Patients were examined before randomization, before implantation, and also at 1, 3, 6, 12, and 24 months thereafter. At 2 years, three patients were excluded from the analysis. The intention-to-treat analysis showed improvements in the SCS+PT group concerning pain intensity (-2.1 vs 0.0 cm; $p < 0.001$) and global perceived effect (43% vs 6% "much improved"; $p = 0.001$). There was no clinically important improvement of functional status. Health-related quality of life improved only in the group receiving spinal cord stimulation. After careful selection and successful test stimulation, spinal cord stimulation results in a long-term pain reduction and health-related quality of life improvement in chronic reflex sympathetic dystrophy.

PMID: 14705107

Rating: 2b

Kemler MA, de Vet HC, Barendse GA, van den Wildenberg FA, van Kleef M. Effect of spinal cord stimulation for chronic complex regional pain syndrome Type I: five-year final follow-up of patients in a randomized controlled trial. J Neurosurg. 2008 Feb;108(2):292-8.

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OBJECT: Chronic complex regional pain syndrome-Type I (CRPS-I) is a painful, disabling disorder for which no treatment with proven effect is available. In the present randomized controlled trial, the authors assessed the effectiveness of spinal cord stimulation (SCS) in reducing pain due to CRPS-I at the 5-year follow-up. METHODS: The authors performed a randomized trial in a 2:1 ratio in which 36 patients with CRPS-I were allocated to receive SCS and physical therapy (PT) and 18 patients to receive PT alone. Twenty-four patients who received SCS+PT also underwent placement of a permanent spinal cord stimulator after successful test stimulation; the remaining 12 patients did not receive a permanent stimulator. The authors assessed pain intensity, global perceived effect, treatment satisfaction, and health-related quality of life. Patients were examined before randomization, before implantation, and every year until 5 years thereafter. Ten patients were excluded from the final analysis. RESULTS: At 5 years posttreatment, SCS+PT produced results similar to those following PT for pain relief and all other measured variables. In a subgroup analysis, the results with regard to global perceived effect (p=0.02) and pain relief (p=0.06) in 20 patients with an implant exceeded those in 13 patients who received PT. CONCLUSIONS: Despite the diminishing effectiveness of SCS over time, 95% of patients with an implant would repeat the treatment for the same result.

PMID: 18240925

Rating: 2b

The main analysis showed that change in pain intensity was not significantly different between the SCS plus phyisician therapy group and the phyisician therapy alone group (p=0.25). In the subgroup analysis of implanted SCS patients, the change in pain intensity between the two groups approached statistical significance in favor of SCS (p=0.06). Further, implanted SCS patients reported high satisfaction with therapy, 95% reported they would undergo treatment again for the same result, and had an average pain VAS score nearly two points lower than PT-only patients (Kemler, 2008) demonstrating that implanted SCS patients continue to have clinically meaningful pain relief, beyond that experienced by patients treated with physical therapy alone. A thorough understanding of these results including the merits of intention-to-treat and as-treated forms of analysis as they relate to this therapy should be undertaken prior to definitive conclusions being made.

Kerns RD, Thorn BE, Dixon KE. Psychological treatments for persistent pain: An introduction. J Clin Psychol. 2006 Aug 25; [Epub ahead of print]

VA Connecticut Healthcare System, VA Central Office and Yale University.

Psychological treatments for persistent pain have been demonstrated to be effective alternatives or adjuncts to more traditional methods for promoting optimal pain management. The primary goal of this issue is to provide the clinician with updated information on the state of the art of a variety of psychological treatments for persistent pain. Specifically emphasized are important issues that add to the complexity of effective pain management and practical recommendations for clinicians to use in

enhancing the outcomes of these various treatment approaches. This introductory article provides a brief review of the empirical literature supporting the utility of psychological treatments for persistent pain, describes the content of this issue, and highlights several of the common themes highlighted by our panel of expert contributors. (c) 2006 Wiley Periodicals, Inc. J Clin Psychol: In Session.

PMID: 16937343

Rating: 5a

Kessler RC, Chiu WT, Demler O, Walters EE. Prevalence, severity, and comorbidity of twelve-month DSM-IV disorders in the National Comorbidity Survey Replication (NCS-R). Archives of General Psychiatry, 2005;62:617-27.

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BACKGROUND: Little is known about the general population prevalence or severity of DSM-IV mental disorders. OBJECTIVE: To estimate 12-month prevalence, severity, and comorbidity of DSM-IV anxiety, mood, impulse control, and substance disorders in the recently completed US National Comorbidity Survey Replication. DESIGN AND SETTING: Nationally representative face-to-face household survey conducted between February 2001 and April 2003 using a fully structured diagnostic interview, the World Health Organization World Mental Health Survey Initiative version of the Composite International Diagnostic Interview. PARTICIPANTS: Nine thousand two hundred eighty-two English-speaking respondents 18 years and older. MAIN OUTCOME MEASURES: Twelve-month DSM-IV disorders. RESULTS: Twelve-month prevalence estimates were anxiety, 18.1%; mood, 9.5%; impulse control, 8.9%; substance, 3.8%; and any disorder, 26.2%. Of 12-month cases, 22.3% were classified as serious; 37.3%, moderate; and 40.4%, mild. Fifty-five percent carried only a single diagnosis; 22%, 2 diagnoses; and 23%, 3 or more diagnoses. Latent class analysis detected 7 multivariate disorder classes, including 3 highly comorbid classes representing 7% of the population. CONCLUSION: Although mental disorders are widespread, serious cases are concentrated among a relatively small proportion of cases with high comorbidity.

PMID: 15939839

Rating: 4a

Khaliq W, Alam S, Puri N. Topical lidocaine for the treatment of postherpetic neuralgia. Cochrane Database Syst Rev. 2007; 18:CD004846.

BACKGROUND: The cause of postherpetic neuralgia is damage to peripheral neurons, dorsal root ganglia, and the dorsal horn of the spinal cord, secondary to herpes zoster infection (shingles). In

postherpetic neuralgia, peripheral neurons discharge spontaneously and have lowered activation thresholds, and exhibit an exaggerated response to stimuli. Topical lidocaine dampens peripheral nociceptor sensitisation and central nervous system hyperexcitability, and may benefit patients with postherpetic neuralgia. OBJECTIVES: To examine the efficacy and safety of topical lidocaine in the treatment of postherpetic neuralgia. SEARCH STRATEGY: We searched the Cochrane Pain, Palliative and Supportive Care Group Trials Register, The Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, and LILACS, SIGLE for conference proceedings, Citation Index, the reference lists of all eligible trials, key textbooks, and previous systematic reviews. We also wrote to authors of all identified trials. SELECTION CRITERIA: Randomised or quasi-randomised trials comparing all topical applications of lidocaine, including gels and patches in patients of all ages with postherpetic neuralgia (pain persisting at the site of shingles at least one month after the onset of the acute rash). DATA COLLECTION AND ANALYSIS: Two review authors extracted data, and a third checked them. We obtained some missing data from the US Food and Drugs Administration. MAIN RESULTS: Three trials involving 182 topical lidocaine treated participants and 132 control participants were included. Two trials gave data on pain relief, and the remaining study provided data on secondary outcome measures. The largest trial published as an abstract compared topical lidocaine patch to a placebo patch and accounted for 150 of the 314 patients (48%).A meta-analysis combining two of the three studies identified a significant difference between the topical lidocaine and control groups for the primary outcome measure: a mean improvement in pain relief according to a pain relief scale. Topical lidocaine relieved pain better than placebo (P = 0.003).There was a statistical difference between the groups for the secondary outcome measure of mean VAS score reduction (P = 0.03), but this was only for a single small trial. There were a similar number of adverse skin reactions in both treatment and placebo groups.The highest recorded blood lidocaine concentration varied between 59 ng/ml and 431 ng/ml between trials. The latter figure is high and the authors of the study suggest that the sample had been contaminated during the assay procedure. AUTHORS' CONCLUSIONS: There is insufficient evidence to recommend topical lidocaine as a first-line agent in the treatment of postherpetic neuralgia with allodynia. Further research should be undertaken on the efficacy of topical lidocaine for other chronic neuropathic pain disorders, and also to compare different classes of drugs (e.g. topical anaesthetics versus anti-epileptics).

PMID: 17443559

Rating: 1c

Khoromi S, Cui L, Nackers L, Max MB. Morphine, nortriptyline and their combination vs. placebo in patients with chronic lumbar root pain. Pain. 2007;130:66-75.

Section on Developmental Genetic Epidemiology, National Institute of Mental Health, Department of Health and Human Services, Bethesda, MD 20892-3720, USA. khoromisu@mail.nih.gov

Although lumbar radicular pain is the most common chronic neuropathic pain syndrome, there have been few randomized studies of drug treatments. We compared the efficacy of morphine (15-90 mg), nortriptyline (25-100 mg), their combination, and a benztropine "active placebo" (0.25-1 mg) in patients with chronic sciatica. Each period consisted of 5 weeks of dose escalation, 2 weeks of maintenance at the highest tolerated doses, and 2 weeks of dose tapering. The primary outcome was the mean daily leg pain score on a 0-10 scale during the maintenance period. Secondary outcomes included a 6-point ordinal global pain relief scale, the Beck Depression Inventory (BDI), the Oswestry Back Pain Disability Index (ODI) and the SF-36. In the 28 out of 61 patients who completed the study, none of the treatments produced significant reductions in average leg pain or other leg or back pain scores. Pain reduction, relative to placebo treatment was, 14% for nortriptyline (95% CI=[-2%, 30%]), 7% for morphine (95% CI=[-8%, 22%]), and 7% for the combination treatment (95% CI=[-4%, 18%]). Mean doses were: nortriptyline alone, 84+/-24.44 (SD) mg/day; morphine alone, 62+/-29 mg/day; and combination, morphine, 49+/-27 mg/day plus nortriptyline, 55 mg+/-33.18 mg/day. Over half of the study completers reported some adverse effect with morphine, nortriptyline or their combination. Within the limitations of the modest sample size and high dropout rate, these results suggest that nortriptyline, morphine and their combination may have limited effectiveness in the treatment of chronic sciatica.

PMID: 17182183

Rating: 4c

Kirkpatrick A. Reflex Sympathetic Dystrophy / Complex Regional Pain Syndrome. Clinical Practice Guidelines – Second Edition. 10-15-2000.

The best way to describe RSD/CRPS is in terms of an injury to a nerve or soft tissue (e.g. broken bone) that does not follow the normal healing path. The development of RSD/CRPS does not appear to depend on the magnitude of the injury (e.g. a sliver in the finger can trigger the disease). In fact, the injury may be so slight that the patient may not recall ever having received an injury. For reasons we do not understand, the sympathetic nervous system seems to assume an abnormal function after an injury. There is no single laboratory test to diagnose RSD/CRPS. Therefore, the physician must assess and document both subjective complaints (medical history) and, if present, objective findings (physical examination), in order to support the diagnosis. There is a natural tendency to rush to the diagnosis of RSD/CRPS with minimal objective findings because early diagnosis is critical. If undiagnosed and untreated, RSD/CRPS can spread to all extremities, making the rehabilitation process a much more difficult one. If diagnosed early, physicians can use mobilization of the affected extremity (physical therapy) and sympathetic nerve blocks to cure or mitigate the disease. If untreated, RSD/CRPS can become extremely expensive due to permanent deformities and chronic pain. There are no studies showing that RSD/CRPS affects the patient's life span. The potential exists for long-term financial consequences. At an advanced state of the illness, patients may have significant psychosocial and psychiatric problems, they may have dependency on narcotics and may be completely incapacitated by the disease. The treatment of patients with advanced RSD is a challenging and time-consuming task.

Publication Type: Review

Klarskov K, Johnson KL, Benson LM, Cragun JD, Gleich GJ, Wrona M, Jiang XR, Dryhurst G, Naylor S. Structural characterization of a case-implicated contaminant, "Peak X," in commercial preparations of 5-hydroxytryptophan. J Rheumatol. 2003;30:89-95.

Biomedical Mass Spectrometry and Functional Proteomics Facility, Mayo Clinic, Rochester, Minnesota, USA.

OBJECTIVE: To determine the chemical structure of a contaminant, X1, previously found in eosinophilia myalgia syndrome case-implicated 5-hydroxytryptophan (5-OHTrp), and also present in over-the-counter (OTC) commercially available 5-OHTrp. METHODS: Case-implicated 5-OHTrp as well as 6 OTC samples were subjected to accurate mass HPLC-mass spectrometry and HPLC-electrochemical detection, and reacted with reduced glutathione. Peak X1 was subsequently subjected to HPLC-tandem mass spectrometry (MS/MS), as well as the resulting nucleophilic glutathione product. All these data were compared with analysis carried out under identical conditions on authentic 4,5-tryptophan-dione (Trp-4,5D). RESULTS: Based on accurate mass, tandem mass spectrometric analysis, and comparision with authentic standard compound analysis, X1 was determined to be 4,5-tryptophan-dione, a putative neurotoxin. The presence of X1 in OTC samples varied from 0.5 to 10.3% of the amount of Trp-4,5D present in case-implicated 5-OHTrp. CONCLUSION: Peak X1 was identified as the putative neurotoxin Trp-4,5D. It was found in case-implicated 5-OHTrp as well as 6 OTC samples. This gives some cause for concern in terms of the safety of such commercial preparations of 5-OHTrp.

PMID: 12508395

Rating: 4c

Knotkova H, Pappagallo M. Adjuvant analgesics. Med Clin North Am. 2007;91:113-24.

Department of Pain Medicine and Palliative Care, 353 E 17th Street, Gilman Hall, Unit 4C, Beth Israel Medical Center, New York, NY 10003, USA. HKnotkov@chpnet.org

Chronic pain, whether arising from viscera, bone, or any other tissue or structure, is, more often than commonly thought, the result of a mixture of pain mechanisms, and therefore there is no simple formula available to manage chronic complex pain states. Box 1 summarizes a pharmacological algorithm for difficult-to-treat chronic pain, which merely introduces the medication aspect of the treatment. In effect, any comprehensive algorithm should call for an interdisciplinary approach that would include rehabilitation, as well as psychosocial, and when indicated, interventional techniques. Box 1 Analgesic algorithm for difficult-to-treat pain syndromes. Pharmacological Interventions. Moderate to severe pain/functional impairment; pain with a score of >4 on the brief pain inventory. 1. Gabapentinoid

(gabapentin, pregabalin)+/-Opioid/opioid rotation or 2. Antidepressant (TCA, duloxetine, venlafaxine)+/-Opioid/opioid rotation or 3. Gabapentinoid+antidepressant+Opioid/opioid rotation; in addition, may consider trials of one or more of the following adjuvants when clinically appropriate: Topical therapies for cutaneous allodynia/hyperalgesia. Anti-inflammatory drugs (corticosteroids for acute inflammatory neuropathic pain)IV bisphosphonates for cancer bone pain or CRPS/RSDNon-gabapentinoid AEDs such as carbamazepine or oxcarbazepine or lamotrigine+/-baclofen for intermittent lancinating pain due to cranial neuralgiasNMDA antagonists Mexiletine On a compassionate basis, according to the patient's clinical condition and pain mechanism, the physician may want to consider an empirical trial of one or more of the emergent topical, oral or parenteral/intrathecal therapies as discussed in the text. If SMP, consider topical clonidine and sympatholytic interventions; if clinically feasible, trials of topical therapies, eg, lidocaine 5% patch, may be considered for a variety of pain states and features.The major rationale for introducing adjuvants is to better balance efficacy and adverse effects. The following scenarios should prompt the use of adjuvants in clinical practice: The toxic limit of a primary analgesic has been reached. The therapeutic benefit of a primary analgesic has plateaued, eg, treatment has reached its true efficacy limit or pharmachodynamic tolerance has developed. The primary analgesic is contraindicated, eg, substance abuse, aberrant behavior, organ failure, allergy, and so forth. Subjective and qualitative symptoms demand broader coverage. Patients often convey that different medications will impart distinct analgesic benefits. Presence of disabling nonpainful complaints and need to manage symptoms such as insomnia, depression, anxiety, and fatigue that all cause worsening of the patient's quality of life and function.Physicians have also been drawn to the adjuvants secondary to new realities of clinical practice. Moreover, aversion to addiction and diversion remains a potent force that shapes prescribing profiles.

PMID: 17164107

Rating: 5b

Koke AJ, Schouten JS, Lamerichs-Geelen MJ, Lipsch JS, Waltje EM, van Kleef M, Patijn J. Pain reducing effect of three types of transcutaneous electrical nerve stimulation in patients with chronic pain: a randomized crossover trial. Pain. 2004;108:36-42.

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Transcutaneous electrical nerve stimulation (TENS) is a frequently applied therapy in chronic pain although evidence for effectiveness is inconclusive. Several types of TENS, based on different combinations of frequency, pulse duration and intensity, exist. The precise mechanism of action and the relevance of combinations of stimulus parameters are still unclear. To compare the effectiveness of three types of TENS we conducted a randomized, single blinded crossover trial. Patients received two times a 2-week period of daily TENS treatment, separated by a washout period of 2 weeks. In total, 180 chronic pain patients were randomized into three groups. In group 1, high frequency, low intensity TENS (HFT)

was compared with high frequency, high intensity TENS (HIT). In groups 2 and 3, HFT and HIT were compared with a control TENS (COT). The order of applying the different modalities of TENS in each group was also randomized. Primary outcome was the patient's overall assessment of effectiveness and pain reduction (VAS). No differences were found in patient's assessment or pain reducing effect between the three groups, indicating no superiority of one type of TENS. In total, 56% continued TENS after the 2-week treatment period. At 6 months, 42% of all patients still used TENS. We concluded that there were no differences in effectiveness for the three types of TENS used in this study. Because no placebo group was included, no definite conclusions on effectiveness of TENS in general in the treatment of chronic pain could be made.

PMID: 15109505

Rating: 2c

Kool J, Bachmann S, Oesch P, Knuesel O, Ambergen T, de Bie R, van den Brandt P. Function-centered rehabilitation increases work days in patients with nonacute nonspecific low back pain: 1-year results from a randomized controlled trial. Arch Phys Med Rehabil. 2007 Sep;88(9):1089-94.

Department of Rheumatology, Rehabilitation Centre Valens, Valens, Switzerland.

OBJECTIVE: To compare the effect of function-centered treatment (FCT) and pain-centered treatment (PCT) on the number of work days, permanent disability, and the unemployment rate. DESIGN: Randomized controlled trial. SETTING: Inpatient rehabilitation center. PARTICIPANTS: Patients (N=174; 79% male; mean age, 42y) with previous sick leave of 6 weeks or more. INTERVENTIONS: FCT (4h/d for 3wk) emphasized activity despite pain by using work simulation, strength, endurance, and cardiovascular training. PCT (2.5h/d for 3wk) emphasized pain reduction and included passive and active mobilization, stretching, strength training, and a 4-hour mini back school with education and exercise. Analysis was by intention to treat. MAIN OUTCOME MEASURES: Work days, return to work, rate of patients receiving financial compensation for permanent disability, and unemployment rate. Effect sizes (Cohen d) were defined as small (0.2-0.5), moderate (0.5-0.8), and large (>0.8). RESULTS: After 1 year, the FCT group had significantly more work days (mean, 118; median, 39.5; interquartile range [IQR], 0-198) than the PCT group (mean, 74; median, 0; IQR, 0-160; Mann-Whitney U test, P=.011). The odds ratio of returning to work in the FCT group relative to the PCT group was 2.1 (95% confidence interval, 1.1-3.9). The differences in unemployment rates and in the numbers of patients receiving compensation for permanent disability were not significant. CONCLUSIONS: FCT is more effective than PCT for increasing work days.

PMID: 17826451

Rating: 2b

Kool JP, Oesch PR, Bachmann S, Knuesel O, Dierkes JG, Russo M, de Bie RA, van den Brandt PA. Increasing days at work using function-centered rehabilitation in nonacute nonspecific low back pain: a randomized controlled trial. Arch Phys Med Rehabil. 2005 May;86(5):857-64.

Department of Rheumatology, Rehabilitation Center Valens, Valens, Switzerland.

OBJECTIVE: To evaluate the effect of function-centered compared with pain-centered inpatient rehabilitation in patients whose absence from work is due to chronic nonspecific low back pain (LBP). DESIGN: Single-blinded randomized controlled trial with follow-up assessments immediately after treatment and at 3 months. SETTING: Center for work rehabilitation in Switzerland. PARTICIPANTS: Patients with more than 6 weeks of work absence due to chronic nonspecific LBP (N=174; 137 men, 37 women; mean age +/- standard deviation, 42+/-8 y; mean sick leave before study, 6.5 mo). INTERVENTIONS: Function-centered treatment (FCT) (4h/d, 6d/wk, for 3 wk) consisted of work simulation, strength, endurance, and cardiovascular training. Pain-centered treatment (PCT) (2.5h/d, 6d/wk, for 3 wk) used a mini back school, individually selected passive and active mobilization, stretching, and low-intensity strength training. MAIN OUTCOME MEASURES: The number of days at work in 3 months after treatment, self-efficacy, lifting capacity, pain, mobility, strength, and global perceived effect. Effect sizes (ESs) (Cohen d) were defined as small (ES range, 0.2-0.5), moderate (ES range, 0.5-0.8), and large (ES, >0.8). RESULTS: Groups were comparable at baseline. Moderate ESs for the FCT group versus PCT group were found for days at work (25.9 d vs 15.8d, ES=.36, P =.029), self-efficacy (5.9 points vs -7.4 points, ES=.55, P =.003), and lifting capacity (2.3 kg vs 0.2 kg, ES=.54, P =.004). CONCLUSIONS: Function-centered rehabilitation increases the number of work days, self-efficacy, and lifting capacity in patients with nonacute nonspecific LBP.

PMID: 15895328

Rating: 2b

Koppert W, Ihmsen H, Körber N, Wehrfritz A, Sittl R, Schmelz M, Schüttler J. Different profiles of buprenorphine-induced analgesia and antihyperalgesia in a human pain model. Pain. 2005;118:15-22.

Department of Anaesthesiology, University Hospital Erlangen, Krankenhausstrasse 12, D-91054 Erlangen, Germany. koppert@kfa.imed.uni-erlangen.de

In contrast to pure mu-receptor agonists, buprenorphine exerts a lasting antihyperalgesic effect in our model. It will be of major clinical interest whether this difference will translate into improved treatment of pain states dominated by central sensitization.

PMID: 16154698

Rating: 2c

Kress HG. Clinical update on the pharmacology, efficacy and safety of transdermal buprenorphine. Eur J Pain. 2008 Jun 20. [Epub ahead of print]

Department of Special Anaesthesia and Pain Therapy, Medical University of Vienna, Waehringer Guertel 18-20, A-1090 Vienna, Austria.

Contrary to previous concerns, however, no analgesic ceiling effect and no antagonism of combined pure mu-opioid receptor agonists is seen within the therapeutic dose range. Moreover, buprenorphine exerts an antihyperalgesic effect, which is due-at least in part-to antagonistic activity at kappa-opioid receptors. Buprenorphine pharmacokinetics are not altered by advanced age or renal dysfunction. In addition, the risk of respiratory depression is lower than with other opioids including morphine, hydromorphone, methadone and fentanyl. Unlike morphine and fentanyl, there is no immunosuppressive activity with buprenorphine at therapeutic analgesic doses. Finally, the comparably low incidence of CNS adverse events and constipation, and the possibility of use in severe renal dysfunction without a need for dose adjustment make buprenorphine well suited for chronic pain management in at-risk patients, such as diabetics, elderly or renally impaired individuals including those requiring haemodialysis.

PMID: 18567516

Rating: 5a

Kressin NR, Reisine S, Spiro A 3rd, Jones JA. Is negative affectivity associated with oral quality of life? Community Dental Oral Epidemiol. 2001 Dec;29(6):412-23.
Center for Health Quality, Outcomes and Economic Research, VAMC, 200 Springs Rd., Building 70, Bedford, MA 01730, USA. Nkressin@bu.edu
Abstract:
OBJECTIVES: The personality trait of negative affectivity (NA) is associated with reports of worse physical health, more symptoms and worse health-related quality of life but its associations with oral quality of life (OQOL) are unexplored. In this study we examined the association of NA with OQOL. METHODS: We drew on data from two samples of older men: The VA Dental Longitudinal Study (DLS; n=177) and the Veterans Health Study (VHS; n=514), which included three measures of oral quality of life: the Oral Health-Related Quality of Life Measure (OHQOL), the Oral Health Impact Profile (OHIP), and the Geriatric Oral Health Assessment Instrument (GOHAI). For each OQOL measure, and the GOHAI and OHIP subscales, two regression models were estimated to examine the marginal change in variance due to NA: the first model included age, number of teeth, and self-rated oral health, and the second added NA. RESULTS: In both bivariate and multivariate analyses, higher NA was consistently associated with worse scores on the OQOL measures. In the regression analyses, NA explained an additional.01 to 18% of the variance in OQOL, explaining the most variance in the OHIP and the least in the OHQOL. The addition of NA explained more variance in the more subjective,

psychologically oriented GOHAI and OHIP subscales than it did in the more objective, physical function oriented subscales. CONCLUSIONS: Psychosocial factors such as personality are significantly associated with quality of life ratings. Such associations should be taken into account when OQOL measurements are used and interpreted
Publication Type: Case Control Study, 691 cases
PMID: 11784284

Krummel T, Dimitrov Y, Moulin B, Hannedouche T. Drug points: Acute renal failure induced by topical ketoprofen. BMJ. 2000;320:93.

Department of Nephrology, H¿opitaux Universitaires, Strasbourg, France.
PMID: 10625264

Case study of renal failure.

Rating: 5c

Kuffner EK, Green JL, Bogdan GM, Knox PC, Palmer RB, Heard K, Slattery JT, Dart RC. The effect of acetaminophen (four grams a day for three consecutive days) on hepatic tests in alcoholic patients--a multicenter randomized study. BMC Med. 2007;5:13.

Rocky Mountain Poison & Drug Center, Denver Health, Denver, CO, USA. ekuffner@mccus.jnj.com

BACKGROUND: The highest risk period for alcoholic patients is immediately after discontinuation of alcohol intake. CONCLUSION: Alcoholic patients treated with the maximum recommended daily dose of acetaminophen for 3 consecutive days did not develop increases in serum transaminase or other measures of liver injury. Treatment of pain or fever for 3 days with acetaminophen appears safe in newly-abstinent alcoholic patients, such as those presenting for acute medical care.

PMID: 17537264

Rating; 2a

Kumar K, Kelly M, Pirlot T. Continuous Intrathecal Morphine Treatment for Chronic Pain of Nonmalignant Etiology: Long-Term Benefits and Efficacy. Surg Neurol 2001;55:79-88.

Department of Surgery, Section of Neurosurgery, Regina General Hospital, University of Saskatchewan, Regina, Saskatchewan, Canada.

BACKGROUND: To analyze, prospectively, the long-term effects of continuous intrathecal morphine infusion therapy in 16 patients with chronic nonmalignant pain syndromes.METHODS: Twenty-five

patients with severe, chronic, nonmalignant pain that had proven refractory to conservative management were considered candidates for trial of intrathecal spinal morphine. Sixteen patients achieved more than 50% pain relief after a trial period of intrathecal morphine infusion. They were implanted with fully implantable and programmable pumps through which morphine was delivered intrathecally on a continuous basis. These patients were followed prospectively and underwent careful evaluation of their functional and mental status, and pain intensity measurements using standardized techniques before treatment and every 6 months thereafter in the follow-up period. The follow-up period ranged from 13 months to 49 months (mean 29.14 months +/- 12.44 months) for the patients who had implanted morphine pumps.RESULTS: The mean morphine dosage initially administered was 1.11 mg/day (range 0.2--6.5 mg/day); after 6 months, it was 3.1 mg/day (range 0.4--8.75 mg/day). In long-term observation, no patient had a constant dosage history. The patients who received intrathecal morphine for longer than 2 years all showed an increase in morphine dosage to more than 10 mg/day. The best long-term results were seen with deafferentation pain and mixed pain, with 75% and 61% pain reduction (visual analog scale), respectively. Nociceptive pain patients had best pain relief initially (78% pain reduction) but it tended to decrease over the follow-up period to 57% pain reduction at final follow-up. The average pain reduction for all groups after 6 months was 67.5% and at last follow-up, it was 57.5%. Ten patients were satisfied with the delivery system and eleven reported improvement in their quality of life. In two patients, morphine was not able to adequately control the pain without producing undesirable side effects requiring the addition of clonidine to their infusion medication. In this series, 12 patients were considered successes and 4 patients were considered failures. In two patients, the intrathecal opioid therapy was unable to produce satisfactory pain relief and in the other two patients the pumps had to be explanted because of intolerable side effects. CONCLUSIONS: In our experience, the administration of intrathecal opioid medications for nonmalignant pain is justified in carefully selected patients.

PMID: 11301086

Rating: 3c

Kumar K, Malik S, Demeria D, Treatment of chronic pain with spinal cord stimulation versus alternative therapies: cost-effectiveness analysis, Neurosurgery. 2002 Jul;51(1):106-15; discussion 115-6.

Department of Surgery, Regina General Hospital, University of Saskatchewan, Canada. K.Kumar@sk.sympatico.ca

OBJECTIVE: There is limited available research measuring the cost-effectiveness of spinal cord stimulation (SCS), compared with best medical treatment/conventional pain therapy (CPT). The purpose of this study was to tabulate the actual costs (in Canadian dollars) for a consecutive series of patients treated with SCS in a constant health care delivery environment and to compare the costs with those for a control group treated in the same controlled environment. METHODS: We present a consecutive series of 104 patients with failed back syndrome. Within this group, 60 patients underwent SCS

electrode implantation, whereas 44 patients were designated as control subjects. We monitored these patients for a 5-year period and tabulated the actual costs incurred in diagnostic imaging, professional fees paid to physicians, implantation (including the costs for hardware), nursing visits for maintenance of the stimulators, physiotherapy, chiropractic treatments, massage therapy, and hospitalization for treatment of breakthrough pain. From these data, the cumulative costs for each group were calculated for a 5-year period. An analysis of Oswestry questionnaire results was also performed, to evaluate the effects of treatment on the quality of life. RESULTS: The actual mean cumulative cost for SCS therapy for a 5-year period was $29,123/patient, compared with $38,029 for CPT. The cost of treatment for the SCS group was greater than that for the CPT group in the first 2.5 years. The costs of treating patients with SCS became less than those for CPT after that period and remained so during the rest of the follow-up period. In addition, 15% of SCS-treated patients were able to return to employment, because of superior pain control and lower drug intake. No patients in the control group were able to return to employment of any kind. CONCLUSION: SCS is cost-effective in the long term, despite the initial high costs of the implantable devices.

Publication Types:
- Clinical Trial

PMID: 12182407

Rating: 3b

Kumar K, Hunter G, Demeria DD. Treatment of chronic pain by using intrathecal drug therapy compared with conventional pain therapies: a cost-effectiveness analysis. J Neurosurg. 2002 Oct;97(4):803-10.

Department of Surgery, Section of Neurosurgery, Regina General Hospital, University of Saskatchewan, Regina, Saskatchewan, Canada. kkumar@reginahealth.sk.ca

OBJECT: The object of this study was to compare the cost-effectiveness of intrathecal drug therapy (IDT) with that of conventional pain therapy (CPT) in patients suffering from chronic low back pain caused by failed back syndrome. In this study, the authors tabulated actual costs, in Canadian dollars, in a consecutive series of patients undergoing IDT within the Canadian health care system and have compared them with costs in a control group in the same environment. The influence of these treatments on the quality of life (QOL) was also analyzed. METHODS: The authors report on a series of 67 patients suffering from failed back syndrome, 23 of whom underwent implantation of a programmable drug delivery pump and 44 of whom acted as controls. Patients were followed for a 5-year period during which the investigators tabulated the actual costs incurred for diagnostic imaging, professional fees, implantation costs including hardware, nursing visits for maintenance of the pumps, alternative therapies, and hospitalization costs for breakthrough pain. From this data, cumulative costs for each group were calculated for a 5-year period. Patient responses on the Oswestry Pain Questionnaire were

analyzed to assess the impact of treatment on QOL. The actual cumulative costs for IDT during a 5-year period were $29,410, as opposed to $38,000 for CPT. High initial costs of equipment required for IDT were recovered by 28 months. After this time point, managing patients with CPT became the more expensive treatment option for the remainder of the follow-up period. The Oswestry Disability Index showed a 27% improvement for patients in the IDT group, compared with a 12% improvement in the control group. CONCLUSIONS: In patients who respond to this treatment, IDT is cost effective in the long term despite high initial costs of implantable devices.

Publication Types:
- Clinical Trial
- Randomized Controlled Trial

PMID: 12405366

Rating: 3b

Kumar K, Hunter G, Demeria D. Spinal cord stimulation in treatment of chronic benign pain: challenges in treatment planning and present status, a 22-year experience. Neurosurgery. 2006 Mar;58(3):481-96; discussion 481-96.

Section of Neurosurgery, Department of Surgery, University of Saskatchewan, Regina General Hospital, Regina, Canada. krishna.kumar@rqhealth.ca

OBJECTIVE: To present an in-depth analysis of clinical predictors of outcome including age, sex, etiology of pain, type of electrodes used, duration of pain, duration of treatment, development of tolerance, employment status, activities of daily living, psychological status, and quality of life. Suggestions for treatment of low back pain with a predominant axial component are addressed. We analyzed the complications and proposed remedial measures to improve the effectiveness of this modality. METHODS: Study group consists of 410 patients (252 men, 58 women) with a mean age of 54 years and a mean follow-up period of 97.6 months. All patients were gated through a multidisciplinary pain clinic. The study was conducted over 22 years. RESULTS: The early success rate was 80% (328 patients), whereas the long-term success rate of internalized patients was 74.1% (243 patients) after the mean follow-up period of 97.6 months. Hardware-related complications included displaced or fractured electrodes, infection, and hardware malfunction. Etiologies demonstrating efficacy included failed back syndrome, peripheral vascular disease, angina pain, complex regional pain syndrome I and II, peripheral neuropathy, lower limb pain caused by multiple sclerosis. Age, sex, laterality of pain or number of surgeries before implant did not play a role in predicting outcome. The percentage of pain relief was inversely related to the time interval between pain onset and time of implantation. Radicular pain with axial component responded better to dual Pisces electrode or Specify-Lead implantation. CONCLUSION: Spinal cord stimulation can provide significant long-term pain relief with improved quality of life and employment. Results of this study will be effective in better

defining prognostic factors and reducing complications leading to higher success rates with spinal cord stimulation.

Publication Type:
Clinical Trial

PMID: 16528188

Rating: 4a

Kumar D, Marshall HJ. Diabetic peripheral neuropathy: amelioration of pain with transcutaneous electrostimulation. Diabetes Care. 1997 Nov;20(11):1702-5.

Department of Medicine, Los Angeles County University of Southern California Medical Center 90033, USA.

OBJECTIVE: To evaluate the efficacy of transcutaneous electrotherapy for chronic painful peripheral neuropathy in patients with type 2 diabetes. RESEARCH DESIGN AND METHODS: Thirty-one patients with symptoms and signs of peripheral neuropathy were randomized to the electrotherapy or sham treatment (control) group. The electrostimulation was given by a portable unit (H-Wave machine) than generated a biphasic, exponentially decaying waveform (pulse width 4 ms, 25-35 V, > or = 2 Hz). Patients treated each of their lower extremities for 30 min daily for 4 weeks at home. Nine patients from the sham-treatment group participated for a second period, during which all of them received the active electrotherapy. Patient's degree of pain and discomfort was graded on a scale of 0 to 5. RESULTS: In the sham-treated group (n = 13), the neuropathic symptoms improved in five (38%) patients, and the pain score declined from 2.92 +/- 0.13 to 2.38 +/- 0.26 (P < 0.04), suggesting a procedure-related placebo effect. In the electrotherapy group (n = 18), symptomatic improvement was seen in 15 (83%) cases, 3 of which were completely asymptomatic; the pain score declined from 3.17 +/- 0.12 to 1.44 +/- 0.25 (P < 0.01) and the posttreatment pain scores were considerably lower (P < 0.03), indicating a substantial treatment effect over and above any placebo influence. Patients in the electrotherapy group reported greater reduction in symptoms (52 +/- 7% vs. 27 +/- 10% in control subjects, P < 0.05) on an analog scale. Moreover, the electrotherapy decreased pain scores (from 3.0 +/- 0.62 to 1.56 +/- 0.32, P < 0.02) in nine patients who had received sham treatment earlier. CONCLUSIONS: A form of transcutaneous electrotherapy ameliorated the pain and discomfort associated with peripheral neuropathy. This novel modality offers a potential non-pharmacological treatment option.

PMID: 9353612

Rating: 2c

Kumar D, Alvaro MS, Julka IS, Marshall HJ. Diabetic peripheral neuropathy. Effectiveness of electrotherapy and amitriptyline for symptomatic relief. Diabetes Care. 1998 Aug;21(8):1322-5.

Department of Medicine, Los Angeles County University of Southern California Medical Center 90033, USA.

OBJECTIVE: To evaluate the efficacy of combining electrotherapy with amitriptyline for the management of chronic painful peripheral neuropathy in patients with type 2 diabetes. RESEARCH DESIGN AND METHODS: Patients (n = 26) with peripheral neuropathy were treated with amitriptyline. After 4 weeks, those patients (n = 23) who failed to respond to amitriptyline or who only had partial relief were randomized between a sham treatment group (control) or an electrotherapy group. Transcutaneous electrotherapy was given for 12 weeks by a portable unit (H-wave machine) that generated a biphasic exponentially decaying waveform (pulse width 4 ms, 25-35 V, > or = 2 Hz). The degree of pain and discomfort was graded on a scale of 0-5. An analog scale was used to record the overall change in symptoms. RESULTS: Amitriptyline produced some degree of symptomatic relief in 15 (60%) of the 26 patients by the 4th week; pain scores decreased from 3.8 +/- 0.1 to 2.9 +/- 0.2 (P < 0.1) and the overall reduction in pain was 26 +/- 5% on an analog scale. In the amitriptyline plus sham treatment group (n = 9), pain scores declined from 2.8 +/- 0.3 to 1.9 +/- 0.5 (P < 0.03) and the overall reduction in pain was 55 +/- 12%, suggesting a procedure-related placebo effect. In the group receiving combined electrotherapy and amitriptyline (n = 14), symptomatic improvement occurred in 12 (85%) patients. Five (36%) of the patients in this group became asymptomatic. Pain scores declined from 3.2 +/- 0.2 to 1.4 +/- 0.4 (P < 0.01) and the overall reduction in pain was 66 +/- 10%. The degree of reduction in pain scores and the incremental relief (above the amitriptyline effect) were significantly greater (P < 0.03) with electrotherapy as compared with sham treatment. The outcomes indicate a substantial beneficial effect of electrotherapy over and above any placebo influence. CONCLUSIONS: Our clinical observations suggest that transcutaneous electrotherapy is effective in reducing the pain associated with peripheral neuropathy. This form of therapy may be a useful adjunctive modality when it is combined with a pharmacological agent, such as amitriptyline, to augment symptomatic relief.

PMID: 9702441

Rating: 2c

Kumar K, Taylor RS, Jacques L, Eldabe S, Meglio M, Molet J, Thomson S, O'callaghan J, Eisenberg E, Milbouw G, Buchser E, Fortini G, Richardson J, North RB. Spinal cord stimulation versus conventional medical management for neuropathic pain: A multicentre randomised controlled trial in patients with failed back surgery syndrome. Pain. 2007 Sep 8; [Epub ahead of print]

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Patients with neuropathic pain secondary to failed back surgery syndrome (FBSS) typically experience persistent pain, disability, and reduced quality of life. We hypothesised that spinal cord stimulation (SCS) is an effective therapy in addition to conventional medical management (CMM) in this patient population. We randomised 100 FBSS patients with predominant leg pain of neuropathic radicular origin to receive spinal cord stimulation plus conventional medical management (SCS group) or conventional medical management alone (CMM group) for at least 6 months. The primary outcome was the proportion of patients achieving 50% or more pain relief in the legs. Secondary outcomes were improvement in back and leg pain, health-related quality of life, functional capacity, use of pain medication and non-drug pain treatment, level of patient satisfaction, and incidence of complications and adverse effects. Crossover after the 6-months visit was permitted, and all patients were followed up to 1 year. In the intention-to-treat analysis at 6 months, 24 SCS patients (48%) and 4 CMM patients (9%) ($p<0.001$) achieved the primary outcome. Compared with the CMM group, the SCS group experienced improved leg and back pain relief, quality of life, and functional capacity, as well as greater treatment satisfaction (p0.05 for all comparisons). Between 6 and 12 months, 5 SCS patients crossed to CMM, and 32 CMM patients crossed to SCS. At 12 months, 27 SCS patients (32%) had experienced device-related complications. In selected patients with FBSS, SCS provides better pain relief and improves health-related quality of life and functional capacity compared with CMM alone.

PMID: 17845835

Rating: 2b

Kumar K, Demeria D. The role of opioids in the treatment of chronic nonmalignant pain in the elderly. Annals of Long-Term Care. 2003;11:34-40.

A review of opioid treatment in the elderly as well as adjuvant therapy.

Rating: 5c

Kvarnström A, Karlsten R, Quiding H, Emanuelsson BM, Gordh T. The effectiveness of intravenous ketamine and lidocaine on peripheral neuropathic pain. Acta Anaesthesiol Scand. 2003 Aug;47(7):868-77.

Department of Anesthesiology and Intensive Care, Uppsala University Hospital, Uppsala, Sweden. ann.kvarnstrom@thorax.uas.lul.se

BACKGROUND: Neuropathic pain is often severe and resistant to pharmacological treatment. The aims of the present study were to assess the analgesic effect of ketamine and lidocaine and to investigate if measurement of different variables of sensibility could be used to identify responders. We also wanted to study if treatment resulted in changes of sensibility. METHODS: Twelve patients with long-lasting peripheral neuropathic pain of traumatic origin were included. The effects of ketamine hydrochloride

(Ketalar, Parke Davis) 0.4 mg/kg and lidocaine hydrochloride (Xylocain, Astra) 2.5 mg/kg were investigated. Saline was used as placebo. The intensity of continuous pain was measured by a visual analogue scale (VAS). Warm and cold perception as well as heat and cold pain thresholds were assessed. Sensibility to touch was also tested. Systemic plasma concentrations of lidocaine and ketamine were assessed. RESULTS: The mean reduction in VAS-scores was 55%, 34% and 22% for ketamine, lidocaine and placebo, respectively. A significant difference was registered between ketamine and placebo (P = 0.009). Response to treatment (50% reduction in VAS-score during infusion) was recorded in 7/12 in the ketamine, 4/12 in the lidocaine and 2/12 in the placebo group. Quantitative sensory testing (QST) of thermal sensitivity and sensory tests for mechanical stimuli could not separate responders from non-responders and neither were the results from these assessments changed by the infusion of the drugs. Lidocaine and particularly ketamine were associated with frequent side-effects, the most common being somnolence and dizziness. CONCLUSION: Ketamine showed a significant analgesic effect. The clinical usefulness is, however, limited by disturbing side-effects.

PMID: 12859309

Rating 2c

Kvarnström A, Karlsten R, Quiding H, Gordh T. The analgesic effect of intravenous ketamine and lidocaine on pain after spinal cord injury. Acta Anaesthesiol Scand. 2004 Apr;48(4):498-506.

Department of Anaesthesiology and Intensive Care, University Hospital, Uppsala, Sweden. ann.kvarnstrom@thorax.uas.lul.se

METHODS: Ten patients with spinal cord injury and neuropathic pain below the level of injury were included. The analgesic effect of ketamine 0.4 mg kg(-1) and lidocaine 2.5 mg kg(-1) was investigated. Saline was used as placebo. The drugs were infused over 40 min. A randomized, double-blind, three-period, three-treatment, cross-over design was used. Systemic plasma concentrations of ketamine and lidocaine were assessed. Pain rating was performed using a visual analogue scale (VAS). Sensory function was assessed with a combination of traditional sensory tests and quantitative measurement of temperature thresholds. RESULTS: Response to treatment, defined as 50% reduction in VAS-score during infusion, was recorded in 5/10 in the ketamine, 1/10 in the lidocaine and 0/10 in the placebo groups. Neither ketamine nor lidocaine changed temperature thresholds or assessments of mechanical; dynamic and static sensibility. Nor could these sensory assessments predict response to treatment in this setting. Lidocaine and particularly ketamine were associated with frequent side-effects. CONCLUSION: Ketamine but not lidocaine showed a significant analgesic effect in patients with neuropathic pain after spinal cord injury. The pain relief was not associated with altered temperature thresholds or other changes of sensory function.

PMID: 15025615

[Sample size too small for ODG.]
LaChapelle DL, Hadjistavropoulos HD, McCreary DR, Asmundson GJ. Contributions of pain-related adjustment and perceptions of control to coping strategy use among cervical sprain patients. Eur J Pain 2001;5(4):405-13.

Clinical Research and Development Program, Regina Health District and Department of Psychology, University of Regina, Regina, Saskatchewan, Canada.

Coping is a cyclical process in which an individual evaluates stressful events, chooses and implements coping strategies, re-evaluates the outcome of the coping effort and modifies the strategy if necessary. The intent of the present study was to evaluate the extent to which pain-related adjustment (i.e. pain severity, pain interference, negative affect) and perceptions of control are associated with the implementation of particular coping strategies. Participants were 136 patients assessed at an interdisciplinary pain clinic for cervical sprain injuries. As part of a routine assessment, participants completed a questionnaire package regarding background, pain severity, pain interference, negative affect, perceived control and use of particular coping strategies. Results of hierarchical multiple regression analyses revealed that pain interference, after controlling for all other variables, was associated with greater use of less physically demanding strategies (i.e. resting, guarding, asking for assistance, seeking social support and coping self-statements). Negative affect, on the other hand, after controlling for other variables, was associated with reduced use of task persistence. Finally, perceived control, independent of other variables, was associated with greater use of cognitive and social coping strategies (i.e. asking for assistance, seeking social support and coping self-statements). The results of the study shed light on the complex relationship between use of particular coping strategies and situational variables of pain-related adjustment and perceived control. Implications for clinicians who assist patients via implementation or modification of particular coping techniques are discussed.
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Publication Type: Case Control Study, 136 cases
PMID: 11743706

Laine L, Curtis SP, Cryer B, Kaur A, Cannon CP; MEDAL Steering Committee. Assessment of upper gastrointestinal safety of etoricoxib and diclofenac in patients with osteoarthritis and rheumatoid arthritis in the Multinational Etoricoxib and Diclofenac Arthritis Long-term (MEDAL) programme: a randomised comparison. Lancet. 2007; 369:465-73.

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BACKGROUND: Upper gastrointestinal safety of cyclo-oxygenase (COX)-2 selective inhibitors versus traditional non-steroidal anti-inflammatory drugs (NSAIDs) has not been assessed in trials that simulate standard clinical practice. Our aim was to assess the effects of these drugs on gastrointestinal outcomes

in a population that includes patients taking gastrointestinal protective therapy. METHODS: A prespecified pooled intent-to-treat analysis of three double-blind randomised comparisons of etoricoxib (60 or 90 mg daily) and diclofenac (150 mg daily) in 34 701 patients with osteoarthritis or rheumatoid arthritis was done for upper gastrointestinal clinical events (bleeding, perforation, obstruction, or ulcer) and the subset of complicated events (perforation, obstruction, witnessed ulcer bleeding, or significant bleeding). We also assessed such outcomes in patients who were taking concomitant proton pump inhibitors (PPIs) or low-dose aspirin. These trials are registered with , with the numbers , , and . FINDINGS: Overall upper gastrointestinal clinical events were significantly less common with etoricoxib than with diclofenac (hazard ratio [HR] 0.69, 95% CI 0.57-0.83; p=0.0001). There were significantly fewer uncomplicated gastrointestinal events with etoricoxib than there were with diclofenac (0.57, 0.45-0.74; p<0.0001); there was no difference in complicated events (0.91, 0.67-1.24; p=0.561). PPIs were used concomitantly for at least 75% of the study period by 13 862 (40%) and low-dose aspirin by 11 418 (33%) patients; treatment effects did not differ significantly in these individuals. INTERPRETATION: There were significantly fewer upper gastrointestinal clinical events with the COX-2 selective inhibitor etoricoxib than with the traditional NSAID diclofenac due to a decrease in uncomplicated events, but not in the more serious complicated events. The reduction in uncomplicated events with etoricoxib is maintained in patients treated with PPIs and is also observed with regular low-dose aspirin use.

PMID: 17292766

Rating: 3a

Laine L. GI risk and risk factors of NSAIDs. J Cardiovasc Pharmacol. 2006;47 Suppl 1:S60-6.

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Nonsteroidal anti-inflammatory drugs (NSAIDs) are the most widely used drugs in the United States. Ulcers are found at endoscopy in 15% to 30% of patients using NSAIDs regularly. The annual incidence of upper gastrointestinal (GI) complications such as bleeding with regular NSAID use is approximately 1.0% to 1.5%, whereas the annual rate of upper GI clinical events (complicated plus symptomatic uncomplicated ulcers) is approximately 2.5% to 4.5%. Upper GI symptoms such as dyspepsia also occur in many patients taking NSAIDs--at a relative risk of about 1.5 to 2 compared with that in patients without NSAID use. Important risk factors for upper GI clinical events include older age, prior history of upper GI events, use of corticosteroids or anticoagulants, and high-dose or multiple NSAIDs (including NSAID plus low-dose aspirin). Lower GI clinical events such as bleeding may also occur with NSAIDs, although they are less common and less well studied than upper GI events. The decision to employ a protective strategy to decrease NSAID-associated GI clinical events is based on risk stratification. Strategies employed include the use of non-NSAID analgesics, use of lowest effective dose of NSAID, use of medical cotherapy (eg, proton pump inhibitor, misoprostol), or use of coxibs.

PMID: 16785831

Rating: 5c

Laine L, White WB, Rostom A, Hochberg M. COX-2 Selective Inhibitors in the Treatment of Osteoarthritis. Semin Arthritis Rheum. 2008 Jan 3 [Epub ahead of print].

Professor of Medicine, Division of Gastrointestinal and Liver Diseases, Keck School of Medicine, University of Southern California, Los Angeles, CA.

OBJECTIVES: To assess the efficacy of cyclooxygenase-2 selective inhibitors (coxibs) in osteoarthritis (OA) and their gastrointestinal, cardiovascular, renovascular, and hepatic side effects compared with traditional nonsteroidal antiinflammatory drugs (NSAIDs) and acetaminophen. METHODS: Bibliographic database searches for randomized controlled trials, meta-analyses, and literature reviews. RESULTS: Coxibs are comparable to traditional NSAIDs, providing moderate benefit for OA patients in pain and function versus placebo. NSAIDs, including coxibs, are superior to acetaminophen for OA, particularly in patients with moderate to severe pain. Coxibs decrease gastroduodenal ulcers (74% relative risk reduction) and ulcer complications (61% reduction) versus traditional NSAIDs. Meta-analysis of randomized trials indicates that coxibs increase the risk of myocardial infarctions approximately twofold versus placebo and versus naproxen, but do not increase the risk versus nonnaproxen NSAIDs. NSAIDs, including coxibs, commonly cause fluid retention and increase blood pressure and uncommonly induce congestive heart failure or significant renal dysfunction; risk factors include advanced age, hypertension, and heart or kidney disease. NSAIDs are a rare cause of clinical hepatotoxicity (<1 liver-related death per 100,000 NSAID users in clinical studies). Increased rates of aminotransferase elevations occur with rofecoxib (2%) and high-dose lumiracoxib (3%), and postmarketing cases of clinical liver injury with lumiracoxib have been reported recently. CONCLUSIONS: Coxibs are as effective as traditional NSAIDs and superior to acetaminophen for the treatment of OA. Coxibs cause fewer gastrointestinal complications than traditional NSAIDs. Coxibs increase cardiovascular risk versus placebo and naproxen-but probably not versus nonnaproxen NSAIDs. Blood pressure commonly increases after initiation of selective or nonselective NSAIDs, especially in hypertensive patients.

PMID: 18177922

Rating: 1b

Lake AE 3rd. Screening and behavioral management: medication overuse headache--the complex case. Headache. 2008;48:26-31.

Michigan Head Pain and Neurological Institute, Ann Arbor, MI 48104, USA.

The new appendix criteria for a broader concept of chronic migraine from the International Headache Society no longer require headache resolution or return to the previous headache pattern to confirm the diagnosis of medication overuse headache (MOH). MOH can be subdivided into simple (Type I) and complex (Type II). Complex cases may involve long-term use of daily opioids or combination analgesics, multisourcing, multiple psychiatric comorbidities, and/or a history of relapse. Daily use of opioids for other medical conditions, psychiatric comorbidity including borderline personality disorder, prior history of other substance dependence or abuse, and family history of substance disorders are risk factors for MOH. Relapse for analgesic overusers can be as high as 71% at 4-year follow-up. A case illustration spans 20 years from initial presentation through multiple periods of recovery and relapse to illustrate issues in the screening and management of complex MOH patients.

PMID: 18184282

Rating 5c

Lanas A, Hunt R. Prevention of anti-inflammatory drug-induced gastrointestinal damage: benefits and risks of therapeutic strategies. Ann Med. 2006;38:415-28.

Instituto Aragones de Ciencias de la Salud, Service of Gastroenterology, University Hospital, Zaragoza, Spain.

Patients who take non-steroidal anti-inflammatory drugs (NSAIDs) may develop serious gastrointestinal (GI) side effects in both the upper and lower GI tract. Those at risk should be considered for prevention with misoprostol, proton pump inhibitor (PPI) or COX-2 selective inhibitor (coxib) therapy. A coxib or an NSAID+PPI combination is considered to have comparable GI safety profiles, but evidence from direct comparison is limited. PPIs are effective in the prevention of upper GI events in endoscopy trials and in a few, small, outcome trials in patients at risk. Coxibs have been evaluated in endoscopic ulcer studies and clinical outcome trials, and shown to significantly reduce the risk of upper GI ulcer and complications. Moreover, unlike PPIs, coxibs significantly reduce toxicity in the lower GI tract compared with NSAIDs. Coxibs and possibly some NSAIDs also increase the risk of developing serious cardiovascular events, an effect which may depend on the drug, dose and duration of therapy. It is not known whether concomitant low-dose aspirin use, which occurs in more than 20% of patients, will reduce the incidence of cardiovascular events, although concomitant aspirin increases the risk of developing serious GI events in patients taking either an NSAID or a coxib. Such patients may require additional PPI co-therapy. Current prevention strategies with an NSAID+PPI, misoprostol or a coxib must be considered in the individual patient with GI and cardiovascular risk factors. A PPI+coxib is indicated in those at highest risk (e.g. previous ulcer bleeding). PPI therapy must be considered for the treatment and prevention of NSAID-induced dyspepsia.

PMID: 17008305

Rating: 5b

Landau CJ, Carr WD, Razzetti AJ, Sessler NE, Munera C, Ripa SR. Buprenorphine transdermal delivery system in adults with persistent noncancer-related pain syndromes who require opioid therapy: a multicenter, 5-week run-in and randomized, double-blind maintenance-of-analgesia study. Clin Ther. 2007 Oct;29(10):2179-93.

Purdue Pharma, L.P., Stamford, Connecticut 06901-3431, USA.

OBJECTIVE: This study compared the efficacy and safety profile of buprenorphine transdermal delivery system (BTDS) and placebo in subjects with persistent noncancer-related pain who required opioid analgesics. METHODS: This was a multicenter, double-blind, parallel-group study in adult subjects (age >/=18 years) with at least a 2-month history of noncancer-related pain for which they received oral opioid combination agents. The study employed a maintenance-of-analgesia, or randomized-withdrawal, design. During a 7- to 21-day open-label run-in phase, all subjects received BTDS, titrated as needed. Subjects who achieved stable pain control and were able to tolerate BTDS in the run-in phase were randomly assigned to continue BTDS at the dose achieved during the run-in phase or to receive placebo for up to 14 days. Acetaminophen 500-mg tablets were provided as escape (rescue) medication. Subjects completed the study on day 14 or when they met predefined criteria for ineffective treatment: requiring >1 g of acetaminophen as escape medication on any day of the double-blind evaluation phase, requiring a change in study drug dose, having difficulty keeping the patch affixed, or discontinuing because of ineffective treatment without meeting any of the first 3 criteria. The primary efficacy variable was the proportion of subjects with ineffective treatment. Secondary efficacy variables were the time to ineffective treatment; the proportion of subjects who reached ineffective treatment or discontinued for any reason other than ineffective treatment; and the amount of escape medication used. Assessment of the safety profile was based on adverse events and changes in vital signs and physical and laboratory findings. RESULTS: Five hundred eighty-eight subjects entered the open-label run-in phase, and 267 (129 BTDS, 138 placebo) were subsequently randomized to doubleblind treatment. Demographic characteristics were similar between the double-blind BTDS and placebo groups (61.2% and 63.8% female, respectively; 99.2% and 98.6% white; mean [SD] age, 56.2 [13.3] and 59.2 [11.5] years). In the primary efficacy analysis, the proportion of subjects with ineffective treatment was lower with BTDS than with placebo (51.2% vs 65.0%; 95% CI, 1.09-2.95); the odds of ineffective treatment were 1.79 times greater for placebo relative to BTDS (P = 0.022). In the secondary efficacy analyses, the median time from the first dose of double-blind study drug to ineffective treatment was significantly longer with BTDS than with placebo (median, 10 vs 3 days; P = 0.011). The proportion of subjects who reached ineffective treatment or discontinued for reasons other than ineffective treatment was lower in the BTDS group compared with the placebo group (55.0% vs 67.9%); the odds of ineffective treatment or discontinuation for a reason other than ineffective treatment was 1.76 times greater with placebo compared with BTDS (P = 0.028). The mean amount of escape medication used was significantly lower in the BTDS group than in the placebo group (1.7 vs 2.2 acetaminophen tablets per day; P = 0.015). The

most common adverse events in the open-label run-in or double-blind phase occurring at a higher incidence with BTDS than with placebo were pruritus at the patch application site (9.3% vs 5.1%, respectively), headache (3.9% vs 2.2%), and somnolence (2.3% vs 0.7%). CONCLUSION: In this population of adult subjects with persistent noncancer-related pain who required opioid therapy, BTDS use was associated with analgesic efficacy and was generally well tolerated. Results of this study were presented in part at the annual meeting of the American Pain Society, March 30-April 2, 2005, Boston, Massachusetts.

PMID: 18042474

Rating: 2b

Lang JD Jr. Pain. A prelude. Critical Care Clinics. 01-Jan-1999; 15(1): 1-16.
Department of Anesthesiology, University of Alabama at Birmingham, USA.
Abstract:
Although pain is a common fear to most, our overall ability to recognize pain, and assess and intervene with appropriate therapies is mediocre at best. However, if made a priority, substantial gains can be made in improving patient satisfaction with pain control and in rectifying deficits in the knowledge of health-care professionals. This goal is not easily obtained and generally requires time, patience, and a multidisciplinary team approach. Pain can induce numerous metabolic and neuroendocrine responses. While seemingly homeostatic, these changes can have significant physiologic and sometimes adverse consequences. Anesthesia and analgesia, especially by way of neural blockade, can alleviate some of the changes and sometimes improve unwanted consequences. While at times these techniques have not significantly altered outcome, at other times significant benefits have been observed. More sophisticated techniques and pharmacotherapies are being developed and introduced with increased frequency, but alone they will probably have only minimal impact on overall morbidity and mortality. The integration of a multimodal approach seems logical in the critical care setting, with analgesia as the cornerstone.
Major Subjects:
- Critical Illness
- Pain / physiopathology / prevention & control / psychology

Publication Type: Review
PMID: 9929783

Lee DC. Sedative Hypnotic Agents. In: Goldfrank's Toxicological Emergencies, 7th ed. 2002. McGraw-Hill.

A complete "how-to" poison management resource, delivers information on virtually all aspects of medical toxicology. Organized into four sections, Toxicologic Emergencies comprehensively covers: General principles and techniques: how to manage the poisoned or overdosed patient, what techniques effectively eliminate toxins, which imaging studies are most useful in toxicologic emergencies, how to identify nontoxic exposures, and more, The biomedical and molecular basis of medical toxicology: how

toxins affect neurotransmission, clear explanations of the principles and mathematics behind pharmacokinetics, how toxins disrupt metabolic processes, causes of metabolic alkalosis, and much more, The organ system approach to medical toxicology: how toxins affect vital signs, body temperature, blood pressure, and organs and systems throughout the body, Medical toxicology from a clinical perspective: a close-up look at more than 70 categories of toxins, featuring informative case studies as well as signs and symptoms, diagnostic testing, pathophysiology, and in-depth patient management guideline.

Rating: 9b

Leichsenring F, Rabung S. Effectiveness of long-term psychodynamic psychotherapy: a meta-analysis. JAMA. 2008 Oct 1;300(13):1551-65.

Department of Psychosomatics and Psychotherapy, University of Giessen, Ludwigstrasse 76, 35392 Giessen, Germany. falk.leichsenring@psycho.med.uni-giessen.de

CONTEXT: The place of long-term psychodynamic psychotherapy (LTPP) within psychiatry is controversial. Convincing outcome research for LTPP has been lacking. Only studies that used individual psychodynamic psychotherapy lasting for at least a year, or 50 sessions; had a prospective design; and reported reliable outcome measures were included. Twenty-three studies involving a total of 1053 patients were included. RESULTS: According to comparative analyses of controlled trials, LTPP showed significantly higher outcomes in overall effectiveness, target problems, and personality functioning than shorter forms of psychotherapy. With regard to overall effectiveness, a between-group effect size of 1.8 (95% confidence interval [CI], 0.7-3.4) indicated that after treatment with LTPP patients with complex mental disorders on average were better off than 96% of the patients in the comparison groups (P = .002). CONCLUSIONS: There is evidence that LTPP is an effective treatment for complex mental disorders.

PMID: 18827212

Rating: 1a

Levendoglu F, Ogun CO, Ozerbil O, Ogun TC, Ugurlu H, Gabapentin is a first line drug for the treatment of neuropathic pain in spinal cord injury, Spine. 2004 Apr 16;29(7):743-51.

Department of Physical Medicine and Rehabilitation, Selcuk University, Meram School of Medicine, Konya, Turkey.

STUDY DESIGN: Prospective, randomized, double blind, placebo-controlled, crossover clinical trial. OBJECTIVES: To determine the efficacy of gabapentin in the treatment of neuropathic pain related to spinal cord injury. SUMMARY OF BACKGROUND DATA: Neuropathic pain is initiated or caused by

a primary lesion or dysfunction in the nervous system. Neuropathic pain associated with spinal cord injury is quite refractory, and current treatments are not effective. Gabapentin, an anticonvulsant, has become the first choice in the treatment of neuropathic pain. The place of gabapentin in the treatment of spinal cord injury-related neuropathic pain was questioned in only a few recent reports; however, they are retrospectively designed, nonstandardized, and uncontrolled studies, or involve a very small series of patients using less than optimum doses. METHODS: A total of 18-week study period included a 4-week medication/placebo titration period. This was followed by a 4-week stable dosing period when the patients continued to receive maximum tolerated doses, a 2-week washout period, then a crossover of 4 weeks of medication/placebo titration, and another 4 weeks of stable dosing period. Twenty paraplegic patients (female/male: 7/13) with complete spinal cord injury at the thoracic and lumbar level, aged between 20 and 65 years, with neuropathic pain for more than 6 months were recruited for the study. RESULTS: All patients completed the study. Gabapentin reduced the intensity as well as the frequency of pain, relieved all neuropathic pain descriptors except the itchy, sensitive, dull, and cold types, and improved the quality of life ($P < 0.05$). CONCLUSIONS: Gabapentin can be added to the list of first-line medications for the treatment of chronic neuropathic pain in spinal cord injury patients. It is a promising new agent and offers advantages over currently available treatments.

Publication Types:
- Clinical Trial
- Randomized Controlled Trial

PMID: 15087796
Rating: 2b

Lew MF, Adornato BT, Duane DD et al. Botulinum toxin type B: A double-blind, placebo-controlled, safety and efficacy study in cervical dystonia. Neurology 1997;49:701-7.
University of Southern California, Los Angeles 90033-4606, USA.
Conclusion: "BotB is safe, well tolerated, and efficacious in the treatment of cervical dystonia at the doses tested."
Publication Type: RCT, 122 cases
PMID: 9305326

Lexi-Comp Inc. Lexi-Drugs OnlineTM , Hudson, Ohio: Lexi-Comp, Inc. 2008.

Rating: 9a

Li Z, Smith BP, Smith TL, Koman LA. Diagnosis and management of complex regional pain syndrome complicating upper extremity recovery. J Hand Ther. 2005 Apr-Jun;18(2):270-6.

Department of Orthopaedic Surgery, Wake Forest University School of Medicine, Winston-Salem, North Carolina 27157-1070, USA.

Complex regional pain syndrome (CRPS) is a clinical syndrome of pain, autonomic dysfunction, trophic changes, and functional impairment. CRPS is common after hand trauma or surgery. Early diagnosis and intervention is critical for adequate recovery. The diagnosis of CRPS requires a careful history, physical examination, and supporting diagnostic testing. Optimal treatment requires a multidisciplinary approach. A large spectrum of pharmacologic interventions is efficacious in treating CRPS. Surgery may be used to relieve nociceptive foci. Patient-specific hand therapy is very important in reducing swelling, decreasing pain, and improving range of motion.

Publication Types:
Review
Review, Tutorial

PMID: 15891984

Rating: 5b

Lin EH, Katon W, Von Korff M, Tang L, Williams JW Jr, Kroenke K, Hunkeler E, Harpole L, Hegel M, Arean P, Hoffing M, Della Penna R, Langston C, Unutzer J; IMPACT Investigators. Effect of improving depression care on pain and functional outcomes among older adults with arthritis: a randomized controlled trial. JAMA. 2003 Nov 12;290(18):2428-9.

Center for Health Studies, Group Health Cooperative, Seattle, Wash 98101, USA. lin.e@ghc.org

The objective of this study was to, "determine whether enhancing care for depression improves pain and functional outcomes in older adults with depression and arthritis." The design was a randomized controlled trial of 1801 depressed older adults. Interventions included antidepressant medications and/or 6 to 8 sessions of psychotherapy. In addition to reduction in depressive symptoms, the intervention group compared with the usual care group at 12 months had lower mean scores for pain intensity; interference with daily activities due to arthritis; and interference with daily activities due to pain. Overall health and quality of life were also enhanced among intervention patients relative to control patients at 12 months. The conclusion was, "In a large and diverse population of older adults with arthritis (mostly osteoarthritis) and comorbid depression, benefits of improved depression care extended beyond reduced depressive symptoms and included decreased pain as well as improved functional status and quality of life."

Publication Types:
- Clinical Trial
- Comment

- Multicenter Study
- Randomized Controlled Trial

PMID: 14612479

Rating: 2a

Lin J, Zhang W, Jones A, Doherty M. Efficacy of topical non-steroidal anti-inflammatory drugs in the treatment of osteoarthritis: meta-analysis of randomised controlled trials. BMJ. 2004 Aug 7;329(7461):324.

Academic Rheumatology, University of Nottingham, City Hospital, Nottingham NG5 1PB.

OBJECTIVE: To assess the efficacy of topical non-steroidal anti-inflammatory drugs (NSAIDs) in the treatment of osteoarthritis. DATA SOURCES: Medline, Embase, Scientific Citation Index, CINAHL, Cochrane Library, and abstracts from conferences. REVIEW METHODS: Inclusion criterion was randomised controlled trials comparing topical NSAIDs with placebo or oral NSAIDs in osteoarthritis. Effect size was calculated for pain, function, and stiffness. Rate ratio was calculated for dichotomous data such as clinical response rate and adverse event rate. Number needed to treat to obtain the clinical response was estimated. Quality of trial was assessed, and sensitivity analyses were undertaken. RESULTS: Topical NSAIDs were superior to placebo in relieving pain due to osteoarthritis only in the first two weeks of treatment. Effect sizes for weeks 1 and 2 were 0.41 (95% confidence interval, 0.16 to 0.66) and 0.40 (0.15 to 0.65), respectively. No benefit was observed over placebo in weeks 3 and 4. A similar pattern was observed for function, stiffness, and clinical response rate ratio and number needed to treat. Topical NSAIDs were inferior to oral NSAIDs in the first week of treatment and associated with more local side effects such as rash, itch, or burning (rate ratio 5.29, 1.14 to 24.51). CONCLUSION: Randomised controlled trials of short duration only (less than four weeks) have assessed the efficacy of topical NSAIDs in osteoarthritis. After two weeks there was no evidence of efficacy superior to placebo. No trial data support the long term use of topical NSAIDs in osteoarthritis.

Publication Types:
Meta-Analysis

PMID: 15286056

Rating: 1b

Linde K, Streng A, Jurgens S, Hoppe A, Brinkhaus B, Witt C, Wagenpfeil S, Pfaffenrath V, Hammes MG, Weidenhammer W, Willich SN, Melchart D. Acupuncture for patients with migraine: a randomized controlled trial. JAMA. 2005 May 4;293(17):2118-25.

Centre for Complementary Medicine Research, Department of Internal Medicine II, Technische Universitat Munchen, Munich, Germany. Klaus.Linde@lrz.tu-muenchen.de

The objective of this study was to investigate the effectiveness of acupuncture compared with sham acupuncture and with no acupuncture in patients with migraine, and included a three-group, randomized, controlled trial involving 302 patients, with migraine headaches, based on International Headache Society criteria. The interventions were acupuncture, sham acupuncture, or waiting list control. Acupuncture and sham acupuncture were administered by specialized physicians and consisted of 12 sessions per patient over 8 weeks. Patients completed headache diaries from 4 weeks before to 12 weeks after randomization and from week 21 to 24 after randomization. Between baseline and weeks 9 to 12, the mean number of days with headache of moderate or severe intensity decreased by 2.2 days from a baseline of 5.2 days in the acupuncture group compared with a decrease to 2.2 days from a baseline of 5.0 days in the sham acupuncture group, and by 0.8 days from a baseline if 5.4 days in the waiting list group. No difference was detected between the acupuncture and the sham acupuncture groups while there was a difference between the acupuncture group compared with the waiting list group (1.4 days). The proportion of responders (reduction in headache days by at least 50%) was 51% in the acupuncture group, 53% in the sham acupuncture group, and 15% in the waiting list group. The conclusion was, "Acupuncture was no more effective than sham acupuncture in reducing migraine headaches although both interventions were more effective than a waiting list control."

Publication Types:
Clinical Trial
Randomized Controlled Trial

PMID: 15870415

Rating: 2a

Linton SJ. Early identification and intervention in the prevention of musculoskeletal pain. American Journal of Independent Medicine. 2002 May.

Department of Occupational and Environmental Medicine, Orebro University Hospital, Sweden. steven.linton@orebroll.se

A large number of people suffer from upper extremity disorders, but a few apparently consume the majority of the resources. Early interventions are badly needed to prevent the development of persistent disability. Since psychological factors are central in the development of a chronic problem these might be utilized in this endeavor.MethodsA series of studies are described where a screening procedure based on psychological risk factors was employed to help identify people at risk for developing long-term work disability. The utility of a cognitive-behavioral group intervention that focuses on coping strategies as prevention was assessed in three randomized-controlled studies where participants had low, medium,

and high risk, respectively.ResultsThe study with low risk showed no significant difference between the groups, while the studies with medium- and high-risk populations demonstrated significantly lower work disability than control groups receiving treatment as usual.ConclusionsIt appears to be feasible to identify patients with high levels of risk and to subsequently lower the risk for work disability by administering a cognitive-behavioral intervention focusing on psychological aspects of the pain problem. Am. J. Ind. Med. 41:433-442, 2002. Copyright 2002 Wiley-Liss, Inc.
Publication Type: Review, RCT

PMID: 12071495

Linton SJ. Occupational psychological factors increase the risk for back pain: a systematic review. J Occup Rehabil. 2001 Mar;11(1):53-66.

Department of Occupational and Environmental Medicine, Orebro Medical Center, 701 85 Orebro, Sweden. steven.linton@orebroll.se

The purpose of this review was to summarize current knowledge concerning the role of psychological workplace variables in back pain. To this end the literature on psychological factors and back pain was systematically searched and analyzed. Psychological and medical databases and cross-referencing were used to locate 975 studies. To be included in this review, studies had to have a prospective design, include a psychological predictor variable, report on back pain, and be published in English. Twenty-one studies fulfilled the criteria for psychological workplace factors. The results showed a clear association between psychological variables and future back pain. There was strong evidence that job satisfaction, monotonous tasks, work relations, demands, stress, and perceived ability to work were related to future back pain problems. Further, moderate evidence was established for work pace, control, emotional effort at work, and the belief that work is dangerous. There was inconclusive evidence about work content. The attributable fraction indicated that substantial reductions in the number of cases of back pain could be achieved if the exposure to the psychological risk factor was eliminated. Although the methodological quality of the studies varied, they were deemed to provide "best evidence," and the consistency of the findings suggests that they are relatively robust. It is concluded that psychological work factors play a significant role in future back pain problems. However, there is still a lack of knowledge concerning the mechanisms by which these operate. These results suggest that a change in the way we view and deal with back pain is needed. Applying knowledge about psychological factors at work might enhance prevention as well as rehabilitation.

PMID: 11706777

Rating: 1a

Loeser JD. Pain: An Overview. Lancet 1999;353:1607-09.

Department of Neurological Surgery, University of Washington, Seattle 98195, USA.
jdloeser@u.washington.edu
Publication Type: Review

PMID: 10334273

Lorberg B, Youssef NA, Bhagwagar Z. Lamotrigine-associated rash: to rechallenge or not to rechallenge? Int J Neuropsychopharmacol. 2008 Oct 10:1-9. [Epub ahead of print].

Department of Psychiatry, Yale University School of Medicine, CT, USA.

Current guidelines recommend discontinuing lamotrigine in patients who develop rash. In addition, very slow titration of lamotrigine is crucial to the reduction of rash recurrence rate. Several cases that develop benign rash on lamotrigine can be rechallenged without adverse consequences. We believe that lamotrigine rechallenge in bipolar depression is an under-utilized option in our clinical armamentarium, and further studies are needed to guide us in this area.

PMID: 18845017

Lundeberg T. Relief of pain from a phantom limb by peripheral stimulation. J Neurol. 1985;232(2):79-82.

In the present study, 24 patients suffering pain from a phantom limb were given vibratory stimulation or placebo as a pain-relieving measure. During stimulation, a reduction in pain was reported by 75% of the patients as compared to 44% during placebo. Depending on the phantom sensation, the best pain-reducing site was found to be either the area of pain or the antagonistic muscle. In 90% of the patients the best pain-reducing effect was obtained when stimulation was applied with moderate pressure over a large area. The results of the present study suggest that vibratory stimulation may be a valuable symptomatic treatment measure in patients suffering pain from a phantom limb.

PMID: 2410571

Rating: 4c

Lynch SS, Cheng CM, Yee JL.Intrathecal ziconotide for refractory chronic pain. Ann Pharmacother. 2006;40:1293-300.

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lynchs@pharmacy.ucsf.edu

OBJECTIVE: To describe the pharmacology, efficacy, and safety of ziconotide for treatment of severe chronic pain in patients who are candidates for intrathecal therapy. DATA SOURCES: A PubMed/MEDLINE search (1966-June 2006) was conducted using the terms ziconotide, Prialt, and SNX-111. Manufacturer-provided data, the Food and Drug Administration medical review of ziconotide, and abstracts presented at American Pain Society meetings (2001-2006) were also reviewed. STUDY SELECTION AND DATA EXTRACTION: Human studies evaluating the efficacy and safety of ziconotide for the treatment of chronic pain were considered. Animal data were excluded. DATA SYNTHESIS: Ziconotide is the first and only neuronal-type (N-type) calcium-channel blocker. Ziconotide must be administered intrathecally via continuous infusion. A programmable implanted variable-rate microinfusion device, or an external microinfusion device and catheter must be utilized. In double-blind, placebo-controlled studies, ziconotide significantly improved patient perception of pain from baseline to the end of the study periods, which ranged from 11 to 21 days. Patients enrolled in clinical trials were intolerant of or refractory to other treatment modalities. There have been no studies that directly compared ziconotide with other intrathecal or systemic analgesics. Key ziconotide-related adverse events are neuropsychiatric, including depression, cognitive impairment, and hallucinations; depressed levels of consciousness; and elevation of creatine kinase levels. Ziconotide is also associated with a risk of meningitis due to possible contamination of the microinfusion device. CONCLUSIONS: Ziconotide is a therapeutic option for treatment of severe chronic pain in patients who have exhausted all other agents, including intrathecal morphine, and for whom the potential benefit outweighs the risks of serious neuropsychiatric adverse effects and of having an implanted device. Further studies are needed to determine the comparative efficacy of ziconotide and other pain therapies.

PMID: 16849624

Rating: 5a

This article reiterates the warnings on dosage and adverse effects that were outlined by Fisher et al. in 2005.

Lynch ME, Clark AJ, Sawynok J, Sullivan MJ. Topical 2% amitriptyline and 1% ketamine in neuropathic pain syndromes: a randomized, double-blind, placebo-controlled trial. Anesthesiology. 2005;103:140-6.

Pain Management Unit, Queen Elizabeth II Health Sciences Centre, Halifax, Nova Scotia, Canada. mary.lynch@dal.ca

BACKGROUND: A double-blind, randomized, placebo-controlled 3-week study evaluated the efficacy of topical 2% amitriptyline, 1% ketamine, and a combination of both in treating patients with neuropathic pain. METHODS: Ninety-two patients with diabetic neuropathy, postherpetic neuralgia, or postsurgical/posttraumatic neuropathic pain with allodynia, hyperalgesia, or pinprick hypesthesia were

randomly assigned to receive one of four creams (placebo, 2% amitriptyline, 1% ketamine, or 2% amitriptyline-1% ketamine combined). The primary outcome measure was change in average daily pain intensity (baseline week vs. final week) using an 11-point numerical pain rating scale. Secondary outcomes included the McGill Pain Questionnaire, measures of allodynia and hyperalgesia, and patient satisfaction. RESULTS: A reduction in pain scores of 1.1-1.5 units was observed in all groups, and there was no difference between groups. Blood concentrations revealed no significant systemic absorption. Minimal side effects were encountered. CONCLUSION: This randomized, placebo-controlled trial examining topical 2% amitriptyline, 1% ketamine, and a combination in the treatment of neuropathic pain revealed no difference between groups. Optimization of doses may be required, because another study has revealed that higher concentrations of these agents combined do produce significant analgesia.

PMID: 15983466

Rating: 2b

Lyseng-Williamson KA, Perry C. Ziconotide. CNS Drugs. 2006;20(4):331-8

Adis International Limited, Auckland, New Zealand. demail@adis.co.nz

Ziconotide, an intrathecal analgesic for the management of chronic intractable pain, binds with high affinity to N-type calcium channels in neuronal tissue and obstructs neurotransmission. In three pivotal, well designed trials of 5-6 or 21 days' duration, titrated ziconotide was significantly more effective than placebo in treating chronic malignant or nonmalignant pain as assessed by mean percentage improvements from baseline in Visual Analogue Scale Pain Intensity scores. Improvements in secondary endpoints (e.g. proportion of patients who responded or achieved pain relief and the change in opioid use) generally support the efficacy of ziconotide over placebo. Ziconotide maintains its analgesic efficacy in preliminary results from long-term, open-label trials (data available for up to 12 months). Most ziconotide-related adverse events are neurological, mild to moderate in severity, resolve over time and reverse without sequelae on drug discontinuation. Low initial doses of ziconotide and gradual titration to onset of analgesia reduce the incidence and severity of adverse events. No evidence of respiratory depression has been reported with intrathecal ziconotide.

PMID: 16599651

Rating: 5b

Mackey SC, Maeda F. Functional imaging and the neural systems of chronic pain. Neurosurg Clin N Am. 2004 Jul;15(3):269-88.

Division of Pain Management, Department of Anesthesia, Stanford University Medical Center, Palo Alto, CA 94305, USA. smackey@stanford.edu

Pain remains a serious health care problem affecting millions of individuals, costing billions of dollars, and causing an immeasurable amount of human suffering. In designing improved therapies, there is still much to learn about peripheral nociceptor, nerves, and the spinal cord, and brain stem modulatory systems. Nevertheless, it is the brain that presents us with an incredible opportunity to understand the experience we call pain. Functional neuroimaging is helping to unlock the secrets of the sensory and emotional components of pain and its autonomic responses. These techniques are helping us to understand that pain is not a static disease with the pathologic findings localized to the periphery but is instead a highly plastic condition affecting multiple central neural systems. Functional neuroimaging is transforming our understanding of the neurobiology of pain and will be instrumental in helping us to design more rational treatments ultimately aimed at reducing the impact of pain on our patients. It is opening windows into the function of the brain that were previously closed.

PMID: 15246336

Rating: 5b

Mackie K, Huestis MA, Ratcliffe S, Mead AP. Cannabinoids -- a new class of analgesics. Presentation of the 23rd Annual Meeting of the American Academy of Pain Medicine; February 8, 2007; New Orleans, Louisiana.

Cannabinoids have demonstrated significant analgesic properties, but problems with side effects remain. Newer compounds show promise for analgesic efficacy while reducing common side effects of dizziness, euphoria, fatigue, and nausea. An oral mucosal spray (Sativex, GW Pharmaceuticals, cannabis-based medicinal extract - CBME) that contains 2.7 mg of delta-9-tetrahydrocannabinol (THC) and 2.5 mg of cannabidiol (CBD) has been well tolerated in clinical studies. The co-administration of CBD appears to reduce the psychoactive effects of THC, and intoxication is less than with oral THC, according to presenters at AAPM. The CBME compound has been approved in Canada to treat neuropathic pain generated by MS. Several US clinical trials have been performed, and the US Food and Drug Administration has approved phase 3 studies to evaluate CBME oral mucosal spray in patients with cancer. Obstacles remain to achieving full regulatory and legal approval for cannabis-based medicine in the United States. Eleven states have medical marijuana laws providing patients and caregivers a defense against prosecution; however, federal rulings have created gray areas in how far a practitioner may go to help a patient obtain cannabis.

Rating: 10b

Mackin GA, et al. Ethical considerations for neurologists in the management of chronic pain. Neurology. Volume 57 • Number 12 • December 26, 2001.

Conclusion: "Neurologists have a special responsibility to the patient who has pain, which derives from their expertise in the neurologic examination and the interpretation of confirmatory tests, and from the central role played by the nervous system in the perception and mediation of pain."
Publication Type: Review

Maclaren JE, Gross RT, Sperry JA, Boggess JT. Impact of opioid use on outcomes of functional restoration. Clin J Pain. 2006 May;22(4):392-8.

Department of Psychology, West Virginia University, Morgantown, WV, USA.

OBJECTIVES: To examine the effect of opioid use on psychological function, physical functioning, and return-to-work outcomes of a multidisciplinary rehabilitation program (MRP) for chronic pain. METHODS: The participants were 127 patients with on-the-job injuries who had completed an MRP between 2001 and 2003. Opioid use was controlled by the patients' treating physicians (who were not affiliated with the MRP) and was assessed via patient self-report at the time of admission to the program and discharge. Other measures included pretreatment and posttreatment assessments of depression, pain severity, perceived disability, and physical ability (floor-to-waist lifting capacity). Return-to-work outcomes were obtained via follow-up phone calls approximately 6 months posttreatment. RESULTS: Significant improvements from pretreatment to posttreatment were evidenced on all psychological and physical measures for both opioid users and nonusers. Further, there were no significant posttreatment differences between opioid and nonopioid users on psychological, physical, or return-to-work outcomes. DISCUSSION: The role of opioids in the treatment of chronic pain continues to be controversial. Despite a lack of definitive data on their effectiveness, opioids continue to be prescribed, and thus patients using opioids continue to present for multidisciplinary rehabilitation. Although further exploration is warranted, results of the current study suggest that opioid use during rehabilitation does not necessarily preclude treatment success.

PMID: 16691094

Rating: 4b

Note: The mean dose of daily morphine equivalents was 28.63 mg (range 0.53 mg to 150 mg), which may limit the generalizability of the study

Maddox JD, Joranson D. Angarola RT. The use of opioids for the treatment of chronic pain. A consensus statement from the American Academy of Pain Medicine and the American Pain Society. Clin J Pain. 1997 Mar;13(1):6-8.

PMID: 9084947

Principles of good medical practice should guide the prescribing of opioids. AAPM and APS believe that guidelines for prescribing opioids should be an extension of the basic principles of good professional practice. Evaluation of the patient: Evaluation should initially include a pain history and assessment of the impact of pain on the patient, a directed physical examination, a review of previous diagnostic studies, a review of previous interventions, a drug history, and an assessment of coexisting diseases or conditions. Treatment plan: Treatment planning should be tailored to both the individual and the presenting problem. Consideration should be given to different treatment modalities, such as a formal pain rehabilitation program, the use of behavioral strategies, the use of noninvasive techniques, or the use of medications, depending upon the physical and psychosocial impairment related to the pain. If a trial of opioids is selected, the physician should ensure that the patient or the patient's guardian is informed of the risks and benefits of opioid use and the conditions under which opioids will be prescribed. Some practitioners find a written agreement specifying these conditions to be useful. An opioid trial should not be done in the absence of a complete assessment of the pain complaint. Consultation as needed: Consultation with a specialist in pain medicine or with a psychologist may be warranted, depending on the expertise of the practitioner and the complexity of the presenting problem. The management of pain in patients with a history of addiction or a comorbid psychiatric disorder requires special consideration, but does not necessarily contraindicate the use of opioids. Periodic review of treatment efficacy: Review of treatment efficacy should occur periodically to assess the functional status of the patient, continued analgesia, opioid side effects, quality of life, and indications of medication misuse. Periodic reexamination is warranted to assess the nature of the pain complaint and to ensure that opioid therapy is still indicated. Attention should be given to the possibility of a decrease in global function or quality of life as a result of opioid use. Documentation: Documentation is essential for supporting the evaluation, the reason for opioid prescribing, the overall pain management treatment plan, any consultations received, and periodic review of the status of the patient.

Rating: 7b

Mailis A, Furlan A, Sympathectomy for neuropathic pain (Cochrane Review), Cochrane Database Syst Rev. 2003;(2):CD002918

Department of Medicine, Comprehensive Pain Program, 399 Bathurst Street, Fell Pavillion 4B-174, Toronto, Ontario, CANADA, M5T 2S8. angela.mailis@uhn.on.ca

BACKGROUND: Neuropathic pain is defined as pain initiated or caused by a primary lesion or dysfunction in the nervous system. Some examples of this condition are phamtom limb pain, post-stroke pain and complex regional pain syndrome type I (reflex sympathetic dystrophy) and type II (causalgia). Treatment options include drugs, physical treatments, surgery and psychological interventions. The concept that many neuropathic pain syndromes, particularly RSD and causalgia are "sympathetically maintained pains" has historically led to attempts to temporarily or permanently interrupt the sympathetic nervous system. Chemical sympathectomies use alcohol or phenol injections to destroy the sympathetic chain, but this effect is temporary until regeneration of the sympathetic chain occurs.

Surgical ablation can be performed by open removal or electrocoagulation of the sympathetic chain, or minimally invasive procedures using stereotactic thermal or laser interruption. OBJECTIVES: The review aimed to assess the effects of both chemical and surgical sympathectomy for neuropathic pain. Secondary objectives were to compare the effects of sympathectomy with no treatment, placebo or conventional treatment, and to evaluate whether the technique of sympathectomy influences the outcomes of the procedure. SEARCH STRATEGY: We searched MEDLINE and EMBASE up to February 2003 and the latest issue of the Cochrane Library (Issue 1, 2003). We screened references in the retrieved articles, literature reviews and book chapters. We also contacted experts in the field of neuropathic pain. SELECTION CRITERIA: Clinical trials and observational studies assessing the effects of sympathectomy (surgical or chemical) for neuropathic pain of both central or peripheral origin were included. DATA COLLECTION AND ANALYSIS: Two reviewers applied the selection criteria to titles and abstracts. Full articles of potentially eligible trials were obtained and the same reviewers applied the inclusion criteria to the studies. The methodological quality of the studies was evaluated. The studies were also evaluated for clinical relevance according to a classification developed by our group. Statistical pooling was not possible due to heterogeneity of data; instead a narrative description of each included study was performed. MAIN RESULTS: We included four studies. One randomized trial comparing radiofrequency sympatholysis with phenol sympathectomy was rated as low methodological quality and it showed that radiofrequency sympatholysis does not offer advantage over phenol techniques. However, a modified technique produced sympatholysis comparable to that produced by 6% phenol, with less incidence of post-sympathectomy neuralgia. REVIEWER'S CONCLUSIONS: The practice of surgical and chemical sympathectomy is based on poor quality evidence, uncontrolled studies and personal experience. Furthermore, complications of the procedure may be significant, in terms of both worsening the pain or producing a new pain syndrome; and abnormal forms of sweating (compensatory hyperhidrosis and pathological gustatory sweating). Therefore, more clinical trials of sympathectomy are required to establish the overall effectiveness and potential risks of this procedure.

PMID: 12804444

Mailis-Gagnon A, Furlan A, Sandoval J, Taylor R, Spinal cord stimulation for chronic pain, Cochrane Database Syst Rev. 2004;3:CD003783

Department of Medicine, Comprehensive Pain Program, 399 Bathurst Street, Fell Pavillion 4F811, Toronto, Ontario, CANADA, M5T 2S8.

BACKGROUND: Spinal cord stimulation (SCS) is a form of therapy used to treat certain types of chronic pain. It involves an electrical generator that delivers pulses to a targeted spinal cord area. The leads can be implanted by laminectomy or percutaneously and the source of power is supplied by an implanted battery or by an external radio-frequency transmitter. The exact mechanism of action of SCS is poorly understood. OBJECTIVES: To assess the efficacy and effectiveness of spinal cord stimulation in relieving certain kinds of pain, as well as the complications and adverse effects of this procedure.

SEARCH STRATEGY: We searched MEDLINE and EMBASE to September 2003; the Cochrane Central Register of Controlled Trials (CENTRAL) (Issue 3, 2003); textbooks and reference lists in retrieved articles. We also contacted experts in the field of pain and the main manufacturer of the stimulators. SELECTION CRITERIA: We included trials with a control group, either randomized controlled trials (RCTs) or non-randomized controlled clinical trials (CCTs), that assessed spinal cord stimulation for chronic pain. DATA COLLECTION AND ANALYSIS: Two independent reviewers selected the studies, assessed study quality and extracted the data. One of the assessors of methodological quality was blinded to authors, dates and journals. The data were analysed using qualitative methods (best evidence synthesis). MAIN RESULTS: Two RCTs (81 patients in total) met our inclusion criteria. One was judged as being of high quality (score of 3 on Jadad scale) and the other of low quality (score of 1 on Jadad scale). One trial included patients with Complex Regional Pain Syndrome Type I (reflex sympathetic dystrophy) and the other patients with Failed Back Surgery Syndrome. The follow-up periods varied from 6 to 12 months. Both studies reported that SCS was effective, however, meta-analysis was not undertaken because of the small number of patients and the heterogeneity of the study population. REVIEWERS' CONCLUSIONS: Although there is limited evidence in favour of SCS for Failed Back Surgery Syndrome and Complex Regional Pain Syndrome Type I, more trials are needed to confirm whether SCS is an effective treatment for certain types of chronic pain. In addition, there needs to be a debate about trial designs that will provide the best evidence for assessing this type of intervention.

PMID: 15266501

Rating: 1b

Main CJ, Williams AC, Clinical review ABC of psychological medicine Musculoskeletal pain, BMJ 2002;325:534-537 (7 September)

The increasing prevalence of musculoskeletal pain, including back pain, has been described as an epidemic. Pain complaints are usually self limiting, but if they become chronic the consequences are serious. These include the distress of patients and their families and consequences for employers in terms of sickness absence and for society as a whole in terms of welfare benefits and lost productivity. Many causes for musculoskeletal pain have been identified. Psychological and social factors have been shown to play a major role in exacerbating the biological substrate of pain by influencing pain perception and the development of chronic disability. This new understanding has led to a "biopsychosocial" model of back pain.

Maizels M, McCarberg B. Antidepressants and antiepileptic drugs for chronic non-cancer pain. Am Fam Physician. 2005 Feb 1;71(3):483-90.

Department of Family Practice, Kaiser Permanente, Woodland Hills, California 91365, USA. morris.maizels@kp.org

The development of newer classes of antidepressants and second-generation antiepileptic drugs has created unprecedented opportunities for the treatment of chronic pain. These drugs modulate pain transmission by interacting with specific neurotransmitters and ion channels. The actions of antidepressants and antiepileptic drugs differ in neuropathic and non-neuropathic pain, and agents within each medication class have varying degrees of efficacy. Tricyclic antidepressants (e.g., amitriptyline, nortriptyline, desipramine) and certain novel antidepressants (i.e., bupropion, venlafaxine, duloxetine) are effective in the treatment of neuropathic pain. The analgesic effect of these drugs is independent of their antidepressant effect and appears strongest in agents with mixed-receptor or predominantly noradrenergic activity, rather than serotoninergic activity. First-generation antiepileptic drugs (i.e., carbamazepine, phenytoin) and second-generation antiepileptic drugs (e.g., gabapentin, pregabalin) are effective in the treatment of neuropathic pain. The efficacy of antidepressants and antiepileptic drugs in the treatment of neuropathic pain is comparable; tolerability also is comparable, but safety and side effect profiles differ. Tricyclic antidepressants are the most cost-effective agents, but second-generation antiepileptic drugs are associated with fewer safety concerns in elderly patients. Tricyclic antidepressants have documented (although limited) efficacy in the treatment of fibromyalgia and chronic low back pain. Recent evidence suggests that duloxetine and pregabalin have modest efficacy in patients with fibromyalgia.

Publication Types:
Review

PMID: 15712623

Rating: 5a

Malanga G, Wolff E. Evidence-informed management of chronic low back pain with nonsteroidal anti-inflammatory drugs, muscle relaxants, and simple analgesics. Spine J. 2008;8:173-84.

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The management of chronic low back pain (CLBP) has proven to be very challenging in North America, as evidenced by its mounting socioeconomic burden. Choosing amongst available nonsurgical therapies can be overwhelming for many stakeholders, including patients, health providers, policy makers, and third-party payers. Although all parties share a common goal and wish to use limited health-care resources to support interventions most likely to result in clinically meaningful improvements, there is often uncertainty about the most appropriate intervention for a particular patient. To help understand and evaluate the various commonly used nonsurgical approaches to CLBP, the North American Spine Society has sponsored this special focus issue of The Spine Journal, titled Evidence-Informed

Management of Chronic Low Back Pain Without Surgery. Articles in this special focus issue were contributed by leading spine practitioners and researchers, who were invited to summarize the best available evidence for a particular intervention and encouraged to make this information accessible to nonexperts. Each of the articles contains five sections (description, theory, evidence of efficacy, harms, and summary) with common subheadings to facilitate comparison across the 24 different interventions profiled in this special focus issue, blending narrative and systematic review methodology as deemed appropriate by the authors. It is hoped that articles in this special focus issue will be informative and aid in decision making for the many stakeholders evaluating nonsurgical interventions for CLBP.

PMID: 18164465

Rating: 5c

Malanga GA, Gwynn MW, Smith R, Miller D. Tizanidine is effective in the treatment of myofascial pain syndrome. Pain Physician. 2002; 5:422-32.

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Myofascial pain syndrome (MPS) is difficult to treat. The efficacy and safety of tizanidine, an alpha2-adrenergic agent with effects on spasticity and pain, in treating MPS was evaluated. Female subjects (n = 29) with MPS of 9 to > 52 weeks' duration and mean age 37.5 (range 20-51) years, who also had reduced pressure thresholds, were enrolled. Subjects were titrated up to 12 mg of tizanidine over 3 weeks and maintained for 2 weeks. Sleep was assessed via visual analog scale (VAS), pain intensity via short form McGill questionnaire including VAS, disability/level of function, and pressure threshold (tested by algometry) at baseline, weeks 3 and 5, and 1 week after tizanidine was discontinued. Patient and physician global assessments of treatment were reported at week 5. Twenty-four subjects completed the study. Pain intensity and disability decreased significantly from baseline at weeks 3 and 5 and after washout (P < .001). Pressure threshold and sleep improved for all study periods (P < .001). Tizanidine was rated as good to excellent in relieving pain by 89% of subjects and 79% of physicians. No serious adverse events occurred. Tizanidine was effective in the treatment of MPS.

PMID: 16886022

Rating: 4c

Malinoff HL, Barkin RL, Wilson G. Sublingual buprenorphine is effective in the treatment of chronic pain syndrome. Am J Ther. 2005;12:379-84.

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Many patients with chronic pain have less than optimal therapeutic outcomes after prolonged treatment with opiate analgesics. Worsening of pain perception, functional capacity, and mood often result. Medical detoxification is often undertaken in this situation. After a minimum of 12 hours of abstinence from all opiate analgesics, patients were given low doses of sublingual (SL) buprenorphine or buprenorphine/naloxone (Reckitt Benckiser). Maintenance dosing was individualized to treat chronic pain. Daily SL dose of buprenorphine ranged from 4 to 16 mg (mean, 8 mg) in divided doses. Mean duration of treatment is 8.8 months (range, 2.4-16.6 months). At clinic appointments, patients were assessed for pain reports, functional capacity, and mood inventory. Eighty-six percent of patients experienced moderate to substantial relief of pain accompanied by both improved mood and functioning.

PMID: 16148422

Rating: 4b

Manchikanti L, Staats PS, Singh V, Schultz DM, Vilims BD, Jasper JF, Kloth DS, Trescot AM, Hansen HC, Falasca TD, Racz GB, Deer TR, Burton AW, Helm S, Lou L, Bakhit CE, Dunbar EE, Atluri SL, Calodney AK, et al. Evidence-based practice guidelines for interventional techniques in the management of chronic spinal pain. Pain Phys 2003;6:3-81.

MAJOR RECOMMENDATIONS
Comment: This guideline tends to be liberal in recommending unproven techniques.

Diagnostic Interventional Techniques

Facet Joint Diagnostic Blocks

Based on multiple evaluations, the validity, specificity and sensitivity of facet joint nerve blocks are considered strong in the diagnosis of facet joint pain. Based on multiple evaluations, facet or zygapophysial joints have been implicated as the source of chronic spinal pain in 15% to 45% of the heterogenous groups of patients with chronic low back pain, 48% of the patients with thoracic pain, and 54% to 67% of the patients with chronic neck pain. Reported false-positive rates varied from 27% to 63% in cervical spine, 58% in thoracic spine, and 22% to 47% in lumbar spine.

Provocative Discography

Extensive evidence of provocative discography was reviewed on normal volunteers, comparison of discography findings on post mortem specimens, comparison with computed tomography and magnetic resonance imaging, high-intensity zone identification, evidence of discogenic pain or internal disc disruption and false-positives in patients with low back pain or with psychological abnormalities. Based on the cumulative analysis of the literature, the evidence for cervical and thoracic discography is limited. However, the evidence for lumbar discography is strong for discogenic pain provided that lumbar

discography is performed based on the history, physical examination, imaging data, and analysis of other precision diagnostic techniques. There is no evidence to support discography without other non-invasive or less invasive modalities of treatments or other precision diagnostic injections.

Transforaminal Epidural Injections

The current evidence provides moderate evidence of transforaminal epidural injections in the preoperative evaluation of patients with negative or inconclusive imaging studies and clinical findings of nerve root irritation. The present review of the available literature provides limited evidence as to the role of transforaminal epidural injections in the diagnosis of segmental dural-nerve root pain in the absence of disc herniation and negative provocative discography.

Sacroiliac Joint Blocks

Based on the results of controlled diagnostic local anesthetic blocks, prevalence of sacroiliac joint pain has been shown to be present in 10% to 18.5% of patients with low back pain with a false-positive rate of 20%. The evidence for specificity and validity of sacroiliac joint diagnostic injections is moderate.

Therapeutic Interventional Techniques

Facet Joint Pain

Intraarticular Injections. The evidence of intraarticular injections of local anesthetics and steroids from randomized trials, complemented with that of non-randomized trials (prospective and retrospective evaluations) provided moderate evidence of short-term relief and limited evidence of long-term relief of chronic neck and low back pain.
Medial Branch Blocks. Combined evidence of the medial branch blocks from one randomized trial, complimented with two non-randomized trials (one prospective and one retrospective evaluation) provided strong evidence of short-term relief and moderate evidence of long-term relief of pain of facet joint origin.
Medial Branch Neurotomy. Considering the one systematic review, two randomized trials, four prospective evaluations, and three retrospective evaluations, combined evidence of radiofrequency neurotomy of medial branches provided strong evidence of short-term relief and moderate evidence of long-term relief of chronic spinal pain of facet joint origin.

Epidural Injections

Caudal Epidural Injections. The combined evidence of caudal epidural steroid injections with randomized trials and non-randomized trials (prospective and retrospective trials) is strong for short-term relief and moderate for long-term relief.

Interlaminar Epidural Injections. Evidence for the overall effectiveness of interlaminar epidural steroid injections in managing chronic low back pain is moderate for short-term relief and limited for long-term relief.
Transforaminal Epidural Injections. Based on the evaluation of multiple randomized and non-randomized trials, transforaminal epidural injections provided strong evidence for short-term and long-term relief. Their effectiveness in post lumbar laminectomy syndrome and disc extrusions is inconclusive.

Epidural Adhesiolysis

Evidence of effectiveness of percutaneous adhesiolysis, based on randomized and non-randomized evaluations is moderate for short-term and long-term relief with repeat interventions.
Evidence synthesis for spinal endoscopy with prospective evaluations and retrospective evaluations showed moderate evidence for short-term relief and limited evidence for long-term relief.

Intradiscal Therapies

Intradiscal Electrothermal Therapy. Based on this evidence analysis, it appears that intradiscal electrothermal therapy meets the criteria for moderate evidence for short-term relief and limited evidence for long-term relief.
Nucleoplasty. Evidence is limited showing the effectiveness of percutaneous disc decompression (PDD) with nucleoplasty.

Implantable Therapies

Spinal Cord Stimulation. The evidence for spinal cord stimulation in properly selected population with neuropathic pain is moderate for long-term relief.
Implantable Intrathecal Drug Administration System. Based on the available literature, there is moderate evidence indicating the long-term effectiveness of intrathecal infusion systems.

Evaluation

Appropriate history, physical examination, and medical decision making from the initial evaluation of a patient's presenting symptoms are essential. There are numerous acceptable medical methods to evaluate a chronic spinal pain patient. These methods vary from physician to physician and textbook to textbook. Following the guidelines established by the Centers for Medicare and Medicaid Services (CMS) not only would assist a physician in performing a comprehensive and complete evaluation, but also assist them to be in compliance with regulations. The guidelines of CMS provide various criteria for five levels of services. The three crucial components of evaluation and management services are: history, physical examination, and medical decision-making.

Evaluation and Management Algorithm

A suggested algorithm for the Comprehensive Evaluation and Management of Chronic Pain is available in the original guideline document (page 55).

Criteria for Performing Interventional Techniques

The following criteria should be considered carefully in performing interventional techniques:

Complete initial evaluation, including history and physical examination.
Physiological and functional assessment, as necessary and feasible.
Definition of indications and medical necessity:
Suspected organic problem
Nonresponsiveness to less invasive modalities of treatments except in acute situations such as acute disc herniation, herpes zoster and postherpetic neuralgia, reflex sympathetic dystrophy, and intractable pain secondary to carcinoma.
Pain and disability of moderate-to-severe degree.
No evidence of contraindications such as severe spinal stenosis resulting in intraspinal obstruction, infection, or predominantly psychogenic pain.
Responsiveness to prior interventions with improvement in physical and functional status to proceed with repeat blocks or other interventions.
Repeating interventions only upon return of pain and deterioration in functional status.

Delivery of Interventional Technology

Following is the description of frequency of various types of interventional techniques. Safety and effectiveness of multiple types of interventional techniques have been established. These are based on available evidence and consensus to the safety, clinical effectiveness, and cost effectiveness. However, these are not based on evidence synthesis methodology. Descriptions are provided only for some commonly used procedures.

Facet Joint Injections

In the diagnostic phase, a patient may receive injections at intervals of no sooner than 1 week or, preferably, 2 weeks.
In the therapeutic phase (after the stabilization is completed), the suggested frequency would be 2 months or longer between each injection, provided that at least >50% relief is obtained for 6 weeks.
If the neural blockade is applied for different regions, it can be performed at intervals of no sooner than 1 week or preferably 2 weeks for most types of blocks. It is suggested therapeutic frequency remain at 2 months for each region. It is further suggested that all regions be treated at the same time, provided all procedures are performed safely.

In the diagnostic or stabilization phase, the suggested number of injections would be limited to no more than 4 times per year.
In the treatment or therapeutic phase, the interventional procedures should be repeated only as necessary judging by the medical necessity criteria, and it is suggested that these be limited to a maximum of six times for local anesthetic and steroid blocks for a period of 1 year.
Under unusual circumstances with a recurrent injury or cervicogenic headache, blocks may be repeated at intervals of 6 weeks after stabilization in the treatment phase.

Medial Branch Neurolysis

The suggested frequency would be 3 months or longer between each neurolytic procedure, provided that at least >50% relief is obtained for 10 to 12 weeks.
If the neural blockade is applied for different regions, it may be performed at intervals of no sooner than 1 week or, preferably, 2 weeks for most types of blocks. The therapeutic frequency for neurolytic blocks would preferably remain at intervals of at least 3 months for each region. It is further suggested that all regions be treated at the same time, provided all procedures are performed safely.

Epidural Injections

Epidural injections include caudal, interlaminar, and transforaminal.
In the diagnostic phase, a patient may receive injections at intervals of no sooner than 1 week or preferably, 2 weeks, except for blockade in cancer pain or when a continuous administration of local anesthetic is employed for reflex sympathetic dystrophy.
In the therapeutic phase (after the diagnostic phase is completed), the suggested frequency of interventional techniques would be 2 months or longer between each injection, provided that at least >50% relief is obtained for 6 to 8 weeks.
If the neural blockade is applied for different regions, it may be performed at intervals of no sooner than 1 week and preferably 2 weeks for most type of blocks. The therapeutic frequency may remain at intervals at least 2 months for each region. It is further suggested that all regions be treated at the same time, provided all procedures are performed safely.
In the diagnostic phase, it is suggested number of injections would be limited to no more than 2 times except for reflex sympathetic dystrophy, in which case 3 times is reasonable.
In the treatment or therapeutic phase, the interventional procedures should be repeated only as necessary judging by the medical necessity criteria, and it is suggested that these be limited to a maximum of 6 times per year.
Under unusual circumstances with a recurrent injury current injury, carcinoma, or reflex sympathetic dystrophy, blocks may be repeated at intervals of 6 weeks after diagnosis/stabilization in the treatment phase.

Percutaneous Lysis of Adhesions

The number of procedures are preferably limited to:
With a 3-day protocol, 2 interventions per year,
With a 1-day protocol, 4 interventions per year.

Spinal Endoscopy

The procedures are preferably limited to a maximum of 2 per year provided the relief was >50% for >4 months.

Sacroiliac Joint Injections

In the diagnostic or stabilization phase, a patient may receive injections at intervals of no sooner than 1 week or, preferably, 2 weeks.
In the treatment or therapeutic phase (after the stabilization is completed), the suggested frequency would be 2 months or longer between each injection, provided that at least >50% relief is obtained for 6 weeks.
If the neural blockade is applied for different regions, it may be performed at intervals of no sooner than 1 week or, preferably, 2 weeks for most types of blocks. The therapeutic frequency may remain at 2 months for each region. It is further suggested that all regions be treated at the same time, provided all procedures are performed safely.
In the diagnostic or stabilization phase, the suggested number of injections would be limited to no more than 4 times per year.
In the treatment or therapeutic phase, the interventional procedures should be repeated only as necessary judging by the medical necessity criteria, and these should be limited to a maximum of 6 times for local anesthetic and steroid blocks for a period of 1 year.

Rating: 6b

~~Manchikanti L, Singh V, Helm S, Trescot AM, Hirsch JA. A Critical Appraisal of 2007 American College of Occupational and Environmental Medicine (ACOEM) Practice Guidelines for Interventional Pain Management: An Independent Review Utilizing AGREE, AMA, IOM, and Other Criteria. Pain Physician. 2008 May;11(3):291-310~~.

~~Pain Management Center of Paducah, Paducah, KY; Pain Diagnostics Associates, Niagara, WI; Pacific Coast Pain Management Center, Laguna Hills, CA; University of Florida, Gainesville, FL; and Massachusetts General Hospital, Harvard Medical School, Boston, MA.~~

~~BACKGROUND: Today, with the growing interest of the medical community and others in practice guidelines, there is greater emphasis on formal procedures and methods for arriving at a widely scrutinized and endorsed consensus than ever before. Conflicts in terminology and technique are notable for the confusion that guidelines create and for what they reflect about differences in values,~~

~~experiences, and interests among different parties. While public and private development activities continue to multiply, the means for coordinating these efforts to resolve inconsistencies, fill in gaps, track applications and results, and assess the soundness of particular guidelines continue to be limited. In this era of widespread guideline development by private organizations, the American College of Occupational and Environment Medicine (ACOEM) has developed guidelines that evaluate areas of clinical practice well beyond the scope of occupational medicine and yet fail to properly involve physicians expert in these, especially those in the field of interventional pain management. As the field of guidelines suffers from imperfect and incomplete scientific knowledge as well as imperfect and uneven means of applying that knowledge without a single or correct way to develop guidelines, ACOEM guidelines have been alleged to hinder patient care, reduce access to interventional pain management procedures, and transfer patients into a system of disability, Medicare, and Medicaid. OBJECTIVE: To critically appraise occupational medicine practice guidelines for interventional pain management by an independent review utilizing the Appraisal of Guidelines for Research and Evaluation (AGREE), American Medical Association (AMA), Institute of Medicine (IOM), and other commonly utilized criteria. METHODS: Revised chapters of ACOEM guidelines, low back pain and chronic pain, developed in 2007 and 2008 are evaluated, utilizing AGREE, AMA, IOM instruments, and Shaneyfelt et al's criteria, were independently reviewed by 4 appraisers. RESULTS: Critical appraisal utilizing the AGREE instrument found that both chapters scored less than 10% in 3 of the 6 domains, less than 20% in one domain, over 30% in one domain, and over 70% in one domain. Global assessment also scored below 30% with a recommendation from AGREE, "not recommended or suitable for use in practice." Based on AMA key attributes, both chapters of ACOEM guidelines met only one of the 6 key attributes, only 3 of the 8 attributes were met by IOM criteria, and based on the criteria described by Shaneyfelt et al, overall only 28% of criteria were met. CONCLUSION: Both the low back pain and chronic pain chapters of the ACOEM guidelines may not be ideal for clinical use based on the assessment by the AGREE instrument, AMA attributes, and criteria established by Shaneyfelt et al. They also scored low on IOM criteria (37.5%). These guidelines may not be applicable for clinical use.~~

~~PMID: 18523501~~

~~Rating: 5b~~

~~Manchikanti L, Singh V, Derby R, Helm S 2nd, Trescot AM, Staats PS, Prager JP, Hirsch JA. Review of occupational medicine practice guidelines for interventional pain management and potential implications. Pain Physician. 2008 May-Jun;11(3):271-89.~~

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~~In the modern day environment, workers' compensation costs continue to be a challenge, with a need to balance costs, benefits, and quality of medical care. The cost of workers' compensation care affects all stakeholders including workers, employers, providers, regulators, legislators, and insurers.~~

~~Consequently, a continued commitment to quality, accessibility to care, and cost containment will help ensure that workers are afforded accessible, high quality, and cost-effective care. In 2004, workers' compensation programs in all 50 states, the District of Columbia, and federal programs in the United States combined received an income of $87.4 billion while paying out only $56 billion in medical and cash benefits with $31.4 billion or 37% in administrative expenses and profit. Occupational diseases represented only 8% of the workers' compensation claims and 29% of the cost. The American College of Occupational and Environmental Medicine (ACOEM) has published several guidelines; though widely adopted by WCPs, these guidelines evaluate the practice of medicine of multiple specialties without adequate expertise and expert input from the concerned specialties, including interventional pain management. An assessment of the ACOEM guidelines utilizing Appraisal of Guidelines for Research and Evaluation (AGREE) criteria, the criteria developed by the American Medical Association (AMA), the Institute of Medicine (IOM), and other significantly accepted criteria, consistently showed very low scores (< 30%) in most aspects of the these guidelines. The ACOEM recommendations do not appear to have been based on a careful review of the literature, overall quality of evidence, standard of care, or expert consensus. Based on the evaluation utilizing appropriate and current evidence-based medicine (EBM) principles, the evidence ratings for diagnostic techniques of lumbar discography; cervical, thoracic, and lumbar facet joint nerve blocks and sacroiliac joint nerve blocks; therapeutic cervical and lumbar medial branch blocks and radiofrequency neurolysis; cervical interlaminar epidural steroid injections, caudal epidural steroid injections, and lumbar transforaminal epidural injections; caudal percutaneous adhesiolysis; abd spinal cord stimulation were found to be moderate with strong recommendation applying for most patients in most circumstances. The evidence ratings for intradiscal electrothermal therapy (IDET), an automated percutaneous disc decompression and also deserve further scrutiny and analysis. In conclusion, these ACOEM guidelines for interventional pain management have no applicability in modern patient care due to lack of expertise by the developing organization (ACOEM), lack of utilization of appropriate and current EBM principles, and lack of significant involvement of experts in these techniques resulting in a lack of clinical relevance. Thus, they may result in reduced medical quality of care; may severely hinder access to appropriate, medically needed and essential medical care; and finally, they may increase costs for injured workers, third party payors, and the government by transferring the injured worker into a non-productive disability system.~~

~~PMID: 18523500~~

~~Rating: 5b~~

Manicourt DH, Brasseur JP, Boutsen Y, Depreseux G, Devogelaer JP. Role of alendronate in therapy for posttraumatic complex regional pain syndrome type I of the lower extremity. Arthritis Rheum. 2004 Nov;50(11):3690-7.

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OBJECTIVE: To evaluate the effects of the antiresorptive agent alendronate at a daily oral dose of 40 mg in patients with posttraumatic complex regional pain syndrome type I (CRPS I) of the lower extremity. METHODS: Forty patients were enrolled in this 8-week randomized, double-blind, placebo-controlled study of alendronate therapy for CRPS I, a condition associated with regional osteoclastic overactivity. An optional 8-week open extension of alendronate therapy (weeks 12-20) was available after a 4-week period without therapy. Clinical assessments included joint mobility, edema of the lower extremity, tolerance to pressure in the lower extremity, and levels of spontaneous pain. Urinary levels of type I collagen N-telopeptide (NTX) were assessed by enzyme-linked immunosorbent assay. Patients were examined at weeks 4, 8, 12, 16, 20, and 24. Statistical analysis included two-way factorial analysis of variance. RESULTS: In contrast to placebo-treated patients (n = 20), all of the alendronate-treated patients (n = 19) exhibited a marked and sustained improvement in levels of spontaneous pain, pressure tolerance, and joint mobility, as well as a significant reduction in urinary levels of NTX at weeks 4 and 8. The improvement was maintained at week 12. Twelve patients from each treatment group volunteered for the 8-week open trial, and all of them had a positive response to alendronate. CONCLUSION: Our findings support the use of oral alendronate in posttraumatic CRPS I. By reducing local acceleration of bone remodeling, alendronate might relieve pain by effects on nociceptive primary afferents in bone, pain-associated changes in the spinal cord, and possibly also through a central mechanism.

PMID: 15529370

Rating: 2b

Mantyselka PT, Turunen JH, Ahonen RS, Kumpusalo EA. Chronic pain and poor self-rated health. JAMA. 2003 Nov 12;290(18):2435-42.

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The objective of this study was to analyze the association between chronic pain and self-rated health via a questionnaire survey carried out during the spring of 2002 of a sample of 6500 individuals in Finland aged 15 to 74 years, with a response rate of 71% (N = 4542). Chronic pain was defined as pain with a duration of at least 3 months and was graded by frequency: (1) at most once a week; (2) several times a week; and (3) daily or continuously. On the basis of a 5-item questionnaire on self-rated health, individuals were classified as having good, moderate, or poor health. Results reported were, "The prevalence of any chronic pain was 35.1%; that of daily chronic pain, 14.3%. The prevalence of moderate self-rated health was 26.6% and of poor health, 7.6%. For moderate self-rated health among individuals having chronic pain at most once a week compared with individuals having no chronic pain, the adjusted odds were 1.36; several times a week, 2.41; and daily, 3.69. Odds for poor self-rated health

were as follows: having chronic pain at most once a week, 1.16; several times a week, 2.62; and daily, 11.82." The conclusion was, "Chronic pain is independently related to low self-rated health in the general population."

PMID: 14612480

Rating: 4a

Marcus DA . Treatment of nonmalignant chronic pain. American Family Physician. 1-Mar-2000; 61(5): 1331-8, 1345-6.
University of Pittsburgh Medical Center, Pennsylvania, USA.
Abstract:
Nonmalignant, chronic pain is associated with physical, emotional and financial disability. Recent animal studies have shown that remodeling within the central nervous system causes the physical pathogenesis of chronic pain. This central neural plasticity results in persistent pain after correction of pathology, hyperalgesia, allodynia, and the spread of pain to areas other than those involved with the initial pathology. Patient evaluation and management focus on pain symptoms, functional disabilities, contributory comorbid illnesses, and medication use or overuse. Treatment of chronic pain involves a comprehensive approach using medication and functional rehabilitation. Functional rehabilitation includes patient education, the identification and management of contributing illnesses, the determination of reachable treatment goals and regular reassessment.
Major Subjects:
- Pain / drug therapy / etiology / * therapy

Publication Type: Review
PMID: 10735341

Maroon JC, Bost JW, Borden MK, Lorenz KM, Ross NA. Natural antiinflammatory agents for pain relief in athletes. Neurosurg Focus. 2006 Oct 15;21(4):E11.

Department of Neurosurgery, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania, USA.

Most athletes experience musculoskeletal injuries during their sports activity that require rest at a minimum, and occasionally injuries are severe enough to necessitate surgical repair. Neurosurgeons are often consulted for athletically sustained injuries and prescribe medications for the associated pain. The use of both over-the-counter and prescription nonsteroidal medications is frequently recommended, but recent safety concerns must now be considered. The authors discuss the biochemical pathways of nonsteroidal drugs and review the potentially serious side effects of these medications. They also review the use of natural supplements, which may be a safer, and often as effective, alternative treatment for pain relief.

PMID: 17112189

Rating: 5a

Lesser-Known Side Effects of NSAIDs - Reduced Healing
Besides the well-documented gastric side effects of NSAIDs and more recently discovered vascular side effects of selective COX-2 inhibitors, there are other less well-known but just as serious effects of NSAIDs, particularly in sports medicine. In this field of medicine, NSAIDs are still the most commonly used agent for the treatment of pain and inflammation arising from acute soft-tissue injuries, despite the wide recognition that there is no convincing evidence of their effectiveness in the treatment of these injuries. In fact, by blocking the COX- 1 or -2 inflammatory pathway, healing may actually be hampered. Various studies have shown that such agents delay muscle regeneration and that their primary role is actually in relieving pain, which could be done just as well with other medications without the deleterious effect of reduced healing. The use of NSAIDs has been shown to delay and hamper healing in all the soft tissues, including muscles (despite their tremendous blood supply), ligaments, tendons, and cartilage. The mechanism for this effect is as follows: by taking powerful NSAIDs, the patient does not permit the body to mount any—or at best a very limited—inflammatory response, which is generally believed to be necessary as a prelude to healing because it draws the white blood cells into the injured area to start the repair process. Specifically, NSAIDs are believed to wipe out the entire inflammatory proliferative phase of healing (Days 0–4). Although NSAIDs have commonly been used for the treatment of muscle injury, recent research has provided evidence that these drugs have limited effectiveness when it comes to such injuries.
Omega-3 EFAs (Fish Oil)
The use of fish oil (in the form of cod liver oil), an omega- 3 EFA, for the treatment of muscular, skeletal, and discogenic diseases can be traced back to the late 18th century. Unfortunately, because of the rapid onset of rancidity of this polyunsaturated oil when exposed to air and hence its disconcerting odor, cod liver oil fell out of favor.
With recently developed extraction techniques, which are performed under a nitrogen blanket, and with enhanced oxygen-free encapsulation methods, which prevent oxidation, the therapeutic benefits of fish oil can now be realized without the regurgitation and odor of previous products. Research has shown that the omega-3 polyunsaturated fatty acids are some of the most effective natural antiinflammatory agents available. With the discovery that vascular inflammation is the underlying cause of coronary artery disease, fish and fish oil supplements are now recommended by the American Heart Association for the prevention of this disease. Countries in which the highest fish consumption occurs have populations with a lower incidence of neurodegenerative disease and depression. The biological basis for the effectiveness of fish oil in treating arthritis has been well documented, with many positive clinical studies when compared with traditional pharmaceutical antiinflammatory agents.
White Willow Bark
Bark from the white willow tree is one of the oldest herbal remedies for pain and inflammation. Salix alba, or white willow, is the species most commonly used for medicinal purposes. The mechanism of action of white willow bark is similar to that of aspirin in that it is also a nonselective inhibitor of COX-1 and COX-2, thus reducing the inflammatory prostaglandins. Various randomized placebocontrolled

studies comparing white willow bark with nonsteroidal agents have show an efficacy comparable to these agents and aspirin. Salicin from white willow bark is converted to salicylic acid by the liver and is considered to have fewer side effects than aspirin.

Curcumin (Turmeric)

Curcumin is a naturally occurring yellow pigment derived from turmeric (Curcuma longa), a flowering plant in the ginger family. It has traditionally been used as a coloring and flavoring spice in food products. Curcumin has long been used in both Ayurvedic and Chinese medicine as an antiinflammatory agent, a treatment for digestive disorders, and to enhance wound healing. Several clinical trials have demonstrated curcumin's antioxidant, antiinflammatory, and antineoplastic effects. It may be considered a viable natural alternative to nonsteroidal agents for the treatment of inflammation.

Green Tea

Green tea has long been recognized to have cardiovascular and cancer preventative characteristics due to its antioxidant properties. Its use in the treatment of arthritic disease as an antiinflammatory agent has been recognized more recently. The constituents of green tea are polyphenolic compounds called catechins, and epigallocatechin- 3 galate is the most abundant catechin in green tea. From various studies, the molecular basis of the antiinflammatory and chondroprotective effects of green tea is being discovered. A recent review article from Yale University regarding green tea as the Asian paradox summarizes its currently recognized therapeutic effects: as a cardiovascular and neuroprotective agent, an inhibitor of carcinogenesis, and an antiinflammatory agent.

Pycnogenol (Maritime Pine Bark)

Pycnogenol, like white willow bark, is a nutraceutical material that has been used since ancient times. With the mounting evidence of its antiinflammatory effects and its virtual absence of toxicity, pycnogenol may play a larger role in the treatment of the pain from arthritic conditions in athletes as well as in degenerative disease of all kinds. Studies have shown that this agent is 50 to 100 times more potent than vitamin E in neutralizing free radicals and that it helps recycle and prolong the activity of vitamins C and E. Pycnogenol should not be taken by patients who are being treated with immunosuppressants or by those receiving corticosteroid drugs, because it can enhance immune system function and interact with drugs that are supposed to suppress the immune system.

Boswellia Serrata Resin (Frankincense)

The Boswellia species are trees located in India, Ethiopia, Somalia, and the Arabian peninsula that produce a gum resin called olibanum, better known in the western world as frankincense. In one recent study, a statistically significant improvement in arthritis of the knee was shown after 8 weeks of treatment with 333 mg B. serrata extract taken three times a day. The treatment improved function, but radiographically there was no change in the affected joints.

Uncaria Tomentosa (Cat's Claw)

Uncaria tomentosa and U. guianensis are Peruvian herbs derived from woody vines with small clawlike thorns (hence the vernacular name, cat's claw) at the base of the leaf that allows the plant to climb to heights of up to 100 ft. Various studies indicate that this Peruvian herb induces a generalized reduction in proinflammatory mediators.

Capsaicin (Chili Pepper)

Capsicum annum is a small spreading shrub originally cultivated in the tropical regions of the Americas but now is grown throughout the world, including the US. Capsaicin produces highly selective regional anesthesia by causing degeneration of capsaicin-sensitive nociceptive nerve endings, which can produce significant and long-lasting increases in nociceptive thresholds.

Martell BA, O'Connor PG, Kerns RD, Becker WC, Morales KH, Kosten TR, Fiellin DA. Systematic review: opioid treatment for chronic back pain: prevalence, efficacy, and association with addiction. Ann Intern Med. 2007 Jan 16;146(2):116-27.

Yale University School of Medicine, New Haven, Connecticut 06520-8025, USA.

BACKGROUND: The prevalence, efficacy, and risk for addiction for persons receiving opioids for chronic back pain are unclear. PURPOSE: To determine the prevalence of opioid treatment, whether opioid medications are effective, and the prevalence of substance use disorders among patients receiving opioid medications for chronic back pain. DATA SOURCES: English-language studies from MEDLINE (1966-March 2005), EMBASE (1966-March 2005), Cochrane Central Register of Controlled Clinical Trials (to 4th quarter 2004), PsychInfo (1966-March 2005), and retrieved references. STUDY SELECTION: Articles that studied an adult, nonobstetric sample; used oral, topical, or transdermal opioids; and focused on treatment for chronic back pain. DATA EXTRACTION: Two investigators independently extracted data and determined study quality. DATA SYNTHESIS: Opioid prescribing varied by treatment setting (range, 3% to 66%). Meta-analysis of the 4 studies assessing the efficacy of opioids compared with placebo or a nonopioid control did not show reduced pain with opioids (g, -0.199 composite standardized mean difference [95% CI, -0.49 to 0.11]; P = 0.136). Meta-analysis of the 5 studies directly comparing the efficacy of different opioids demonstrated a nonsignificant reduction in pain from baseline (g, -0.93 composite standardized mean difference [CI, -1.89 to -0.03]; P = 0.055). The prevalence of lifetime substance use disorders ranged from 36% to 56%, and the estimates of the prevalence of current substance use disorders were as high as 43%. Aberrant medication-taking behaviors ranged from 5% to 24%. LIMITATIONS: Retrieval and publication biases and poor study quality. No trial evaluating the efficacy of opioids was longer than 16 weeks. CONCLUSIONS: Opioids are commonly prescribed for chronic back pain and may be efficacious for short-term pain relief. Long-term efficacy (> or =16 weeks) is unclear. Substance use disorders are common in patients taking opioids for back pain, and aberrant medication-taking behaviors occur in up to 24% of cases.

PMID: 17227935

Rating: 1b

NEW YORK (Reuters Health) Jan 15 - Findings from a systematic review of published research suggest that opioids often provide no advantage over non-opioids for relieving chronic back pain, but carry a high risk of addiction. Dr. David A. Fiellin, from Yale University in New Haven, Connecticut, and colleagues conducted a search of MEDLINE (1966 to 2005) and other databases to identify studies that

looked at the use of opioids for back pain. Data from 38 studies were included in the analysis. Opioid prescribing rates for back pain varied widely between studies, ranging from 3% to 66%, the investigators report in the Annals of Internal Medicine for January 16. A meta-analysis of data from four studies revealed no significant pain-relieving advantage for opioids over either placebo or nonopioid controls. Similarly, an analysis of data from five studies comparing the relative efficacy of different opioids showed only a nonsignificant drop in pain from baseline. The percentage of subjects with a substance use disorder at some point in their lives ranged from 36% to 56%. Up to 43% of subjects had a current substance use disorder. Between 5% and 24% of subjects showed "aberrant medication-taking behaviors," the investigators note. "The findings in this review suggest that clinicians should reconsider treating chronic back pain with opioid medications, and consider other treatments with similar benefit yet fewer long-term adverse effects," Dr. Fiellin's team states.

The quality of the studies showing the prevalence of substance use disorders among patients receiving opioid medications for chronic back pain were poorly designed. (See page 123 of the article.) Only two used a validated instrument to screen for substance use disorder. The highest quality study found no significant difference in substance use disorders between groups who were prescribed opioids and those who were not.

Martelletti P, Van Suijlekom H. Cervicogenic headache: practical approaches to therapy. CNS Drugs. 2004;18 (12):793-805.

Department of Internal Medicine, 2nd School of Medicine, Headache Centre, University "La Sapienza", Rome, Italy.

Cervicogenic headache is a relatively common and still controversial form of headache arising from structures in the neck. The estimated prevalence of the disorder varies considerably, ranging from 0.7% to 13.8%. Cervicogenic headache is a 'side-locked' or unilateral fixed headache characterised by a non-throbbing pain that starts in the neck and spreads to the ipsilateral oculo-fronto-temporal area. In patients with this disorder, attacks or chronic fluctuating periods of neck/head pain may be provoked/worsened by sustained neck movements or stimulation of ipsilateral tender points. The pathophysiology of cervicogenic headache probably depends on the effects of various local pain-producing or eliciting factors, such as intervertebral dysfunction, cytokines and nitric oxide. Frequent coexistence of a history of head traumas suggests these also play an important role. A reliable diagnosis of cervicogenic headache can be made based on the criteria established in 1998 by the Cervicogenic Headache International Study Group. Positive response after an appropriate nerve block is an essential diagnostic feature of the disorder. Differential diagnoses of cervicogenic headache include hemicrania continua, chronic paroxysmal hemicrania, occipital neuralgia, migraine and tension headache. Various therapies have been used in the management of cervicogenic headache. These range from lowly invasive, drug-based therapies to highly invasive, surgical-based therapies. This review evaluates use of drug therapy with paracetamol and NSAIDs, infliximab and botulinum toxin type A; manual modalities and transcutaneous electrical nerve stimulation therapy; local injection of anaesthetic or corticosteroids; and invasive surgical therapies for the treatment of cervicogenic headache. A curative therapy for

cervicogenic headache will not be developed until increased knowledge of the aetiology and pathophysiology of the condition becomes available. In the meantime, limited evidence suggests that therapy with repeated injections of botulinum toxin type A may be the most safe and efficacious approach. The surgical approach, which includes decompression and radiofrequency lesions of the involved nerve structures, may also provide physicians with further options for refractory cervicogenic headache patients. Unfortunately, the paucity of experimental models for cervicogenic headache and the relative lack of biomolecular markers for the condition mean much is still unclear about cervicogenic headache and the disorder remains inadequately treated.

PMID: 15377169
Rating: 5b

Martin, T., et al. Pharmacology of Opioid and Nonopioid Analgesics in Chronic Pain. The Journal of Pharmacology and Experimental Therapeutics. 2001;Volume 299, Number 3: 811-7.

Rating: 1c

Quality: N/A. Total Rating: N/A. Comment: Does not meet inclusion criteria for evidence-based review. [CA DWC]

Mason L, Moore RA, Edwards JE, McQuay HJ, Derry S, Wiffen PJ. Systematic review of efficacy of topical rubefacients containing salicylates for the treatment of acute and chronic pain. BMJ. 2004 Apr 24;328(7446):995. Epub 2004 Mar 19.

Pain Research and Nuffield Department of Anaesthetics, University of Oxford, Oxford Radcliffe Hospital, Headington, Oxford OX3 7LJ.

OBJECTIVE: To determine the efficacy and safety of topical rubefacients containing salicylates in acute and chronic pain. DATA SOURCES: Electronic databases and manufacturers of salicylates. STUDY SELECTION: Randomised double blind trials comparing topical rubefacients with placebo or another active treatment, in adults with acute or chronic pain, and reporting dichotomous information, around a 50% reduction in pain, and analyses at one week for acute conditions and two weeks for chronic conditions. DATA EXTRACTION: Relative benefit and number needed to treat, analysis of adverse events, and withdrawals. DATA SYNTHESIS: Three double blind placebo controlled trials had information on 182 patients with acute conditions. Topical salicylate was significantly better than placebo (relative benefit 3.6, 95% confidence interval 2.4 to 5.6; number needed to treat 2.1, 1.7 to 2.8). Six double blind placebo controlled trials had information on 429 patients with chronic conditions. Topical salicylate was significantly better than placebo (relative benefit 1.5, 1.3 to 1.9; number needed to treat 5.3, 3.6 to 10.2), but larger, more valid studies were without significant effect. Local adverse events and withdrawals were generally rare in trials that reported them. CONCLUSIONS: Based on limited information, topically applied rubefacients containing salicylates may be efficacious in the

treatment of acute pain. Trials of musculoskeletal and arthritic pain suggested moderate to poor efficacy. Adverse events were rare in studies of acute pain and poorly reported in those of chronic pain. Efficacy estimates for rubefacients are unreliable owing to a lack of good clinical trials.

Publication Types:
- Review
- Review, Academic

PMID: 15033879
Rating: 1c

Mason L, Moore RA, Derry S, Edwards JE, McQuay HJ. Systematic review of topical capsaicin for the treatment of chronic pain. BMJ. 2004 Apr 24;328(7446):991. Epub 2004 Mar 19.

Pain Research and Nuffield Department of Anaesthetics, University of Oxford, Oxford Radcliffe Hospital, Headington, Oxford OX3 7LJ.

OBJECTIVE: To determine the efficacy and safety of topically applied capsaicin for chronic pain from neuropathic or musculoskeletal disorders. DATA SOURCES: Cochrane Library, Medline, Embase, PubMed, an in-house database, and contact with manufacturers of topical capsaicin. STUDY SELECTION: Randomised controlled trials comparing topically applied capsaicin with placebo or another treatment in adults with chronic pain. DATA EXTRACTION: Primary outcome was dichotomous information for the number of patients with about a 50% reduction in pain. Outcomes were extracted at four weeks for musculoskeletal conditions and eight weeks for neuropathic conditions. Secondary outcomes were adverse events and withdrawals due to adverse events. DATA SYNTHESIS: Six double blind placebo controlled trials (656 patients) were pooled for analysis of neuropathic conditions. The relative benefit from topical capsaicin 0.075% compared with placebo was 1.4 (95% confidence interval 1.2 to 1.7) and the number needed to treat was 5.7 (4.0 to 10.0). Three double blind placebo controlled trials (368 patients) were pooled for analysis of musculoskeletal conditions. The relative benefit from topical capsaicin 0.025% or plaster compared with placebo was 1.5 (1.1 to 2.0) and the number needed to treat was 8.1 (4.6 to 34). Around one third of patients experienced local adverse events with capsaicin, which would not have been the case with placebo. CONCLUSIONS: Although topically applied capsaicin has moderate to poor efficacy in the treatment of chronic musculoskeletal or neuropathic pain, it may be useful as an adjunct or sole therapy for a small number of patients who are unresponsive to, or intolerant of, other treatments.

PMID: 15033881

Rating: 1c

Capsaicin, which is derived from chili peppers, causes vasodilation, itching, and burning when applied to the skin. These actions are attributed to binding with nociceptors, which causes a period of enhanced sensitivity followed by a refractory period of reduced sensitivity. Repeated application leads to desensitization and, thus, relief of some forms of chronic pain. Although systemic adverse effects are rare, local irritation, burning, and erythema are common. Mason and colleagues studied the efficacy of topical capsaicin in relieving chronic neuropathic and musculoskeletal pain. They searched electronic databases of publications and clinical trials to identify randomized studies of adults treated with capsaicin three to four times daily for a minimum of three weeks for chronic musculoskeletal pain and a minimum of six weeks for neuropathic pain. Each trial was assessed independently for quality and validity by two reviewers, and disputes were settled by consensus. Clinical success was defined as a 50 percent decrease in pain. The numbers of patients who improved, reported adverse events, and withdrew because of adverse events also were counted. From 38 papers identified, 16 met criteria for inclusion in the meta-analysis. The 1,556 patients had moderate to severe pain (11 trials) or were unresponsive to or intolerant of conventional analgesia (five trials). Three trials prohibited concomitant therapy. Based on three trials involving 368 patients, capsaicin was significantly better than placebo in reducing musculoskeletal pain. The relative benefit was 1.5, and the number needed to treat was eight. Topical capsaicin also significantly improved neuropathic pain at four and eight weeks, with relative benefits of 1.4 compared with placebo and a number needed to treat of 5.5 to 6.5. Overall, about one third of patients reported local adverse reactions. Thirteen percent of capsaicin patients and 3 percent of those treated with placebo withdrew because of adverse events.
The authors conclude that topical capsaicin is superior to placebo in relieving chronic neuropathic and musculoskeletal pain. Local adverse reactions were common but seldom serious. However, local irritation could have led some patients to recognize active treatment and may have caused biased results. Although topical capsaicin has moderate to poor efficacy, it may be particularly useful (alone or in conjunction with other modalities) in patients whose pain has not been controlled successfully with conventional therapy.

Mason L, Edwards JE, Moore RA, McQuay HJ. Single dose oral naproxen and naproxen sodium for acute postoperative pain. The Cochrane Database of Systematic Reviews 2006 Issue 3
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Plain language summary
Naproxen sodium is effective for pain relief in adults who have acute pain after surgery

Acute pain is a problem immediately after surgery and can be poorly managed. This review assessed the evidence from 996 patients in 10 randomised, double blind, placebo-controlled clinical trials of naproxen/naproxen sodium (a non-steroidal anti-inflammatory drug) in adults with acute postoperative pain. We found that naproxen sodium taken by mouth at doses of 550 mg and 440 mg is an effective pain killer for treating pain following surgery. The effects of one dose last, on average, up to seven

hours. No conclusions can be drawn about the adverse effects of naproxen and naproxen sodium because reports of these events were inconsistent.

Rating : 1a

Mason L, Moore RA, Edwards JE, Derry S, McQuay HJ. Topical NSAIDs for chronic musculoskeletal pain: systematic review and meta-analysis. BMC Musculoskelet Disord. 2004;5:28.

Pain Research and Nuffield Department of Anaesthetics, University of Oxford, Oxford Radcliffe Hospital, The Churchill, Headington, Oxford, OX3 7LJ, UK. jayne.edwards@pru.ox.ac.uk

A previous systematic review reported that topical NSAIDs were effective in relieving pain in chronic conditions like osteoarthritis and tendinitis. More trials, a better understanding of trial quality and bias, and a reclassification of certain drugs necessitate a new review. METHODS: Studies were identified by searching electronic databases, and writing to manufacturers. We identified randomised, double blind trials comparing topical NSAID with either placebo or another active treatment, in adults with chronic pain. The primary outcome was a reduction in pain of approximately 50% at two weeks, and secondary outcomes were local and systemic adverse events and adverse event-related withdrawals. Relative benefit and number-needed-to-treat (NNT), and relative harm and number-needed-to-harm (NNH) were calculated, and the effects of trial quality, validity and size, outcome reported, and condition treated, were examined by sensitivity analyses. RESULTS: Twelve new trials were added to 13 trials from a previous review. Fourteen double blind placebo-controlled trials had information from almost 1,500 patients. Topical NSAID was significantly better than placebo with relative benefit 1.9 (95% confidence interval 1.7 to 2.2), NNT 4.6 (95% confidence interval 3.8 to 5.9). Results were not affected by trial quality, validity or size, outcome reported, or condition treated. Three trials with 764 patients comparing a topical with an oral NSAID found no difference in efficacy. Local adverse events (6%), systemic adverse events (3%), or the numbers withdrawing due to an adverse event were the same for topical NSAID and placebo. CONCLUSIONS: Topical NSAIDs were effective and safe in treating chronic musculoskeletal conditions for two weeks. Larger and longer trials are necessary to fully elucidate the place of topical NSAIDs in clinical practice.

PMID: 15317652

Rating: 1c

Mason L, Moore RA, Edwards JE, Derry S, McQuay HJ. Topical NSAIDs for acute pain: a meta-analysis. BMC Fam Pract. 2004;5:10.

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BACKGROUND: A previous systematic review reported that topical NSAIDs were effective in relieving pain in acute conditions like sprains and strains, with differences between individual drugs for efficacy. More trials, a better understanding of trial quality and bias, and a reclassification of certain drugs necessitate a new review. METHODS: Studies were identified by searching electronic databases and writing to manufacturers. We selected randomised double blind trials comparing topical NSAID with either placebo or another active treatment in adults with acute pain, and extracted dichotomous information approximating to a 50% reduction in pain at one week, together with details of adverse events and withdrawals. Relative benefit and number-needed-to-treat (NNT), and relative risk and number-needed-to-harm (NNH) were calculated, with sensitivity analyses where appropriate to investigate differences between individual drugs and aspects of trial design. RESULTS: Twenty-six double blind placebo controlled trials had information from 2,853 patients for evaluation of efficacy. Topical NSAID was significantly better than placebo in 19 of the 26 trials, with a pooled relative benefit of 1.6 (95% confidence interval 1.4 to 1.7), and NNT of 3.8 (95% confidence interval 3.4 to 4.4) compared with placebo for the outcome of half pain relief at seven days. Results were not affected by outcome reported, or condition treated, but smaller trials yielded a larger estimate of efficacy. Indirect comparisons of individual topical NSAIDs showed that ketoprofen was significantly better than all other topical NSAIDs, while indomethacin was barely distinguished from placebo. Three trials, with 433 patients, compared topical with oral NSAID (two trials compared the same drug, one compared different drugs) and found no difference in efficacy. Local adverse events, systemic adverse events, or withdrawals due to an adverse event were rare, and no different between topical NSAID and placebo. CONCLUSIONS: Topical NSAIDs were effective and safe in treating acute painful conditions for one week.

PMID: 15147585

Rating: 1a

Mayer TG. Rehabilitation: what do we do with the chronic patient? Neurologic Clinics. 01-Feb-1999; 17(1): 131-47.
University of Texas Southwestern Medical Center, PRIDE and PRIDE Research Foundation, Dallas, Texas 75235, USA.
Abstract:
Neurologists are often called on to see patients who have low back pain presenting with significant chronicity and disabling pain. Even in situations of chronic low back pain, it has been estimated that a structural diagnosis is made only 60% of the time. Even when a physical diagnosis is made in these cases, it may be irrelevant to the primary causes of persistent pain and disability. This article is designed to point out that, when nonstructural factors are adequately rehabilitated, even in a worst-case occupational injury cohort, remarkable outcomes can be anticipated irrespective of the structural pathology, patient age, or postoperative impairment.
Major Subjects:
- Low Back Pain / etiology / * rehabilitation

Publication Type: Review

PMID: 9855675

Mayer TG, Gatchel RJ, Kishino N, Keeley J, Capra P, Mayer H, Barnett J, Mooney V. Objective assessment of spine function following industrial injury. A prospective study with comparison group and one-year follow-up. Spine. 1985 Jul-Aug;10(6):482-93.

Objective functional capacity measurement techniques were used to guide a treatment program for a group of 66 chronic back pain patients. These patients were compared with a group of 38 chronic patients who were not administered the treatment program. Outcome data were collected by telephone survey at an average 1 year follow-up. In addition, functional capacity measures were collected for treatment group patients on admission and follow-up evaluations. Results demonstrated that the functional capacity measures collected for the treatment group improved in approximately 80% of the patients. These changes were also accompanied by positive changes in psychologic measures. In addition, at 1 year follow-up, the treatment group had approximately twice the rate of patients who returned to work, relative to the comparison group. Additional surgery rates were comparable for both groups (6% in the treatment and 7% in the comparison group), but the frequency of additional health-care professional visits was substantially higher in the comparison group. The findings suggest that quantitative functional capacity measures can give objective evidence of patient physical abilities and degree of effort and can significantly guide the clinician in administering an effective treatment program.

PMID: 2934829

Rating: 3c

Mayer TG, Gatchel RJ, Mayer H, Kishino ND, Keeley J, Mooney V. A prospective two-year study of functional restoration in industrial low back injury. An objective assessment procedure. JAMA. 1987 Oct 2;258(13):1763-7.

One hundred sixteen consecutive patients entered a functional restoration treatment program for chronic low back pain and were compared with 72 patients not treated. A two-year follow-up survey reached more than 85% of both groups; its findings were compared with earlier results of a five-month and one-year follow-up. Analysis demonstrated that 87% of the treatment group was actively working after two years, as compared with only 41% of the nontreatment comparison group. Moreover, about twice as many of the comparison group patients had additional spine surgery relative to the treatment group. The comparison group continued with an approximately five times higher rate of patient visits to health professionals in the second year as the treatment group. Also, treatment group reinjury rates were no higher than those expected in the general population, while nontreatment subjects had a higher incidence

of reinjury. Finally, a small treatment "dropout" group did poorest of all, with results in almost all areas even worse than those of the comparison group patients.

PMID: 2957520

Rating: 3c

Note: The comparison group consisted of patients denied access to the functional restoration program by their insurers. The two groups were significantly different in terms of medications, with those patients in the treatment arm receiving significantly more opioid medications. The analysis at 2 years was performed only on those patients that the researchers were able to contact.

Mayer T, Polatin P, Smith B, Gatchel R, Fardon D, Herring S, Smith C, Donelson R, Wong D; North American Spine Society Committee; Contemporary Concepts Review Committee. Spine rehabilitation: secondary and tertiary nonoperative care. Spine J. 2003 May-Jun;3(3 Suppl):28S-36S.

Department of Orthopedic Surgery, University of Texas Southwestern Medical Center, 5701 Maple Avenue, 100, Dallas, TX 75235, USA. tmayerpestes50@aol.com

PMID: 14589215

A review of secondary and tertiary nonoperative care. Includes recommendations for secondary and tertiary treatment.

Rating: 5c

Mazer M, Perrone J. Acetaminophen-induced nephrotoxicity: pathophysiology, clinical manifestations, and management. J Med Toxicol. 2008;4:2-6.

Department of Emergency Medicine, Univ. of Pennsylvania School of Medicine, Philadelphia, PA.

Renal insufficiency occurs in approximately 1-2% of patients with acetaminophen overdose.

PMID: 18338302

Rating: 5c

McCabe S. Rapid detox: understanding new treatment approaches for the addicted patient. Perspect Psychiatr Care. 2000 Oct-Dec;36(4):113-20.

East Tennessee State University, Johnson City, TN, USA. mccabes@etsu.edu

TOPIC: Despite substantive advances in understanding of genetic and biochemical basis of substance abuse and addiction in the last decade, little information has been translated into alternative treatment models for the addicted patient. Rapid detox, an alternative form of detox treatment, is gaining in both acceptance and popularity. PURPOSE: To increase readers' understanding of the neurobiology of addiction and the mode of action of new detox approaches for patients addicted to opiate drugs. SOURCES: A review of the current literature pertaining to rapid detox. CONCLUSIONS: Rapid detox is a viable alternative for selected patients attempting to detox from opiate agents of abuse. Increasing knowledge of new treatment approaches allows nurses working to assist addicted patients in planning and receiving treatment based on new awareness of the neurobiology of addiction.

PMID: 12035203

Rating: 5b

McCracken LM, Matthews AK, Tang TS, Cuba SL. A comparison of blacks and whites seeking treatment for chronic pain. Clinical Journal of Pain. 2001 Sep;17(3):249-55.

Department of Psychiatry, The University of Chicago, Illinois, USA. lance.mccracken@rnhrd-tr.swest.nhs.uk

CONCLUSIONS: "These results show that blacks and whites with chronic pain experience pain differently. Several factors may underlie these differences, including family situation, health care experiences, or other unmeasured behavioral, environmental, or social influences."

Publication Type: Case Control Study, 264 cases

PMID: 11587117

McDowell BC, McElduff C, Lowe AS, Walsh DM, Baxter GD. The effect of high- and low-frequency H-wave therapy upon skin blood perfusion: evidence of frequency-specific effects. Clin Physiol. 1999 Nov;19(6):450-7.

Rehabilitation Sciences Research Group, School of Health Sciences, University of Ulster at Jordanstown, Newtownabbey, Co. Antrim, BT37 0QB, Northern Ireland, UK.

The current study was designed to assess the putative physiological effects of H-wave therapy (HWT, a mode of therapeutic electro-stimulation) on skin blood flow in humans and to determine the relevance of frequency to any such effects. Laser Doppler flowmetry was used to record changes in blood perfusion on the dominant forearm of healthy human volunteers (n=36), who were each assigned, under randomized double blind conditions, to one of three experimental groups: placebo or HWT at 2 or 60

Hz. HWT stimulation was applied for 20 min, during which time concomitant skin temperature was recorded using three surface skin thermistors. Statistical analysis of perfusion measurement and skin temperature changes pre-, during and for up to 18 min post-HWT stimulation showed a highly significant increase in skin blood flow in the 2 Hz group when compared to placebo and 60 Hz (P<or/ = 0.01). This was associated with a significant increase in skin temperature during the period of stimulation (P<or/ = 0.05). No such differences were observed in the 60 Hz group. These results provide evidence that low-frequency HWT may produce direct localized effects on cutaneous blood flow, a finding relevant for clinicians working in the field of tissue repair.

PMID: 10583337

Rating: 5c

Outcome was skin blood flow, not pain relief. No improvement in symptoms or function were examined by this study.

According to H-Wave: Studies done by McDowell that reference H-Wave or HWT were not done with the FDA cleared and US trademarked H-Wave that we (Electronic Waveform Lab) manufacture. The device they used is not legal in the United States and is completely unrelated to our US H-Wave.

McDowell BC, McCormack K, Walsh DM, Baxter DG, Allen JM. Comparative analgesic effects of H-wave therapy and transcutaneous electrical nerve stimulation on pain threshold in humans. Arch Phys Med Rehabil. 1999 Sep;80(9):1001-4.

Rehabilitation Sciences Research Group, School of Health Sciences, University of Ulster at Jordanstown, Northern Ireland, UK.

OBJECTIVE: To assess the comparative analgesic efficacy of H-wave therapy (HWT) and transcutaneous electrical nerve stimulation (TENS) using a mechanical model of pain threshold measurement. STUDY DESIGN: Forty-eight healthy human volunteers (24 women, 24 men) were recruited and randomly assigned into one of six experimental groups; control, HWT (placebo, 2Hz, or 60Hz), or TENS (placebo or 110Hz). For each subject, mechanical pain threshold (MPT) measurements were recorded at three standardized recording points marked on the dorsal web space of the dominant hand. Two MPT measurements were recorded at each point at the following time intervals: before treatment was initiated (baseline), after each of three consecutive 10-minute periods of stimulation (HWT or TENS), and at four intervals within 30 minutes after stimulation. In the control and placebo groups MPT measurements were recorded at similar time intervals. RESULTS: Difference scores, calculated from patients' baseline values, were analyzed by ANOVA for each of the three recording points. Although results showed a significant increase in MPT levels in all three stimulation groups when compared with their relative placebo (indicating a hypoalgesic effect), no differences were observed between the different modalities or HWT frequencies. Significant hypoalgesia continued for 5

minutes after stimulation. CONCLUSION: The findings showed that HWT and TENS provided localized hypoalgesia during stimulation and for up to 5 minutes after it. No frequency- or modality-specific effects were observed between the groups.

PMID: 10488999

Rating: 2c

A total of 48 subjects were divided into 6 groups, leaving each group presumably with 8 members, and it is not clear that these results would be statistically significant in any case; but the study showed no difference between the effects of TENS and H-wave.

According to the U.S. manufacturer of H-Wave, studies done by McDowell that reference H-Wave or HWT were not done with the FDA cleared and US trademarked H-Wave manufactured by Electronic Waveform Lab.
McGeary DD, Mayer TG, Gatchel RJ. High pain ratings predict treatment failure in chronic occupational musculoskeletal disorders. J Bone Joint Surg Am. 2006 Feb;88(2):317-25.

Productive Rehabilitation Institute of Dallas for Ergonomics (PRIDE) Research Foundation, 5701 Maple Avenue, Dallas, TX 75235, USA.

BACKGROUND: Pain intensity is one of the most widely used measures in the treatment of patients with chronic disabling occupational musculoskeletal disorders. Few studies have comprehensively investigated the relationship of pain intensity at the time of rehabilitation to objective socioeconomic outcomes at one year after treatment. This study evaluated the ability of pain intensity ratings, measured with a visual analog scale, to predict rehabilitation outcomes and to identify patients who are "at risk" for a poor outcome. METHODS: A cohort of 3106 patients with chronic disabling occupational musculoskeletal disorders in a multidisciplinary occupational tertiary rehabilitation program was divided into four groups on the basis of the pain intensity ratings (0 to 3, 4 to 5, 6 to 7, and 8 to 10) before and after rehabilitation. A structured interview to assess the socioeconomic outcomes, including work status, health-care utilization, recurrent injury, and whether there had been resolution of Workers' Compensation or third-party financial disputes, was conducted one year after rehabilitation. RESULTS: High pain intensity before rehabilitation was linearly associated with declining rates of program completion and higher rates of self-reported depression and disability after rehabilitation. Although higher pain ratings both before and after rehabilitation were associated linearly with a declining quality of socioeconomic outcomes, extremely high pain ratings (8 to 10) after rehabilitation were most predictive of poor outcomes. At the post-rehabilitation evaluation, patients with extreme pain were far more likely than those with mild pain to seek surgical treatment (risk ratio = 11.2 [95% confidence interval, 4.3, 29.5]) or to persist in seeking health care from new providers (risk ratio = 3.3 [95% confidence interval, 2.4, 4.5]). They were less likely to either return to work (risk ratio = 3.9 [95% confidence interval, 2.6, 6.0]) or to retain work (risk ratio = 4.2 [95% confidence interval, 2.9, 6.0]).

They were also twice as likely to claim a new injury to the same musculoskeletal site after returning to work and to fail to settle Workers' Compensation or third-party financial disputes. CONCLUSIONS: High pain ratings before rehabilitation are associated with higher rehabilitation dropout rates. The patients with chronic disabling occupational musculoskeletal disorders who reported extreme pain after completing a full course of extended treatment (13% of 2573) were at risk for poor outcomes in terms of lost productivity, high utilization of health care, and cost-shifting of state Workers' Compensation payments to federal resources.

PMID: 16452743

Rating: 3c

McGeary DD, Mayer TG, Gatchel RJ, Anagnostis C. Smoking status and psychosocioeconomic outcomes of functional restoration in patients with chronic spinal disability. Spine J. 2004 Mar-Apr;4(2):170-5.

PRIDE Research Foundation, 5701 Maple Ave., Suite 100, Dallas, TX 75235, USA.

BACKGROUND CONTEXT: Studies have revealed smoking to have a negative impact on spinal surgery. It is assumed that this is the result of the negative impact of nicotine on revascularization of damaged tissue. However, there is a paucity of research on the role of smoking with regard to nonsurgical rehabilitation, but there exists a clear bias for believing that smoking is strongly associated with poor socioeconomic and psychosocial outcome. PURPOSE: This study was designed to examine the relationship between smoking and outcomes in a chronically disabled work-related spinal disorder (CDWRSD) cohort undergoing functional restoration. STUDY DESIGN: A prospective comparison cohort study investigating the effects of smoking status on functional restoration treatment outcomes. PATIENT SAMPLE: A cohort of 1,141 consecutive CDWRSD patients were divided into four groups: Group A, patients who did not smoke (n=710); Group B, patients who smoked less than one cigarette pack/day (n=157); Group C, patients who smoked 1.0 to 1.9 packs/day (n=218); Group D, patients who smoked 2.0 or more packs/day (n=56). OUTCOME MEASURES: Before the start of functional restoration, and upon its completion, patients received a standard psychosocial assessment battery and were assessed on a variety of physical factors. A structured clinical interview examining socioeconomic outcomes was conducted 1 year after the program. METHODS: Patients underwent an intensive functional restoration chronic pain management rehabilitation program consisting of quantitatively directed exercise progression and a multimodal disability management program for CDWRSD. The program consisted of four phases, the most significant of which involved a 3-week full-day intensive phase after preparatory preprogram phases and before a work transition phase. RESULTS: Analysis revealed that the percent of males increased as the smoking level increased (Group A=51.8% vs Group D=73.2%; p<.001). Also, as smoking increased, the level of education significantly decreased. In addition, as smoking level increased, the percent of patients completing the rehabilitation program decreased (from 86.3% to 75%; p=.03). No significant differences in 1-year posttreatment

socioeconomic outcomes of work status, health utilization, recurrent injury or case closure were related to smoking except work retention, which decreased with more smoking (85 to 71%, p<.05). Surprisingly, the physical cumulative score at posttreatment increased as smoking frequency increased (p<.01). This finding indicates that those who smoked more performed at a higher level on physical measures. Those who smoked more frequently before treatment also appeared more depressed (p<.001), but after treatment, these differences disappeared. Self-reported pain intensity differed only after treatment, and posttreatment disability ratings showed a significant linear trend. CONCLUSIONS: Contrary to popular belief, CDWRSD patients who smoke do not differ significantly in socioeconomic or psychosocial outcomes relative to those who do not. Although this study does indicate that those who smoke more evidence lower rehabilitation completion rates, those who completed the program had identical 1-year posttreatment outcomes of socioeconomic importance except in retraining work at year end as those who did not smoke. Smokers had slightly higher posttreatment self-reported pain and disability ratings mixed and limited. Overall, there is evidence for the widely held belief that smoking negatively affects tertiary rehabilitation.

PMID: 15016394

Rating: 3c

McLean W, Boucher E, Brennan M. et al. Is there An Indication for the Use of Barbituate-Containing Analgesic Agents in the Treatment of Pain. Guidelines for Their Safe Use and Withdrawl Management. Canadian Journal of Clin Pharm 2000;(7)4:191-197. http://www.pulsus.com/clin-phi/07_04/mcle_ed.htm (February 20, 2001).

Ottawa Hospital, General Campus, Ottawa, Canada.

Abstract:

No evidence exists to show a clinically important enhancement of analgesic efficacy of BCAs due to the barbiturate constituents. Because BCAs do not have a therapeutic advantage, there is no clinical reason to choose such a combination product when a simpler and often less expensive analgesic formulation (eg, acetaminophen, acetylsalicylic acid, nonsteroidal anti-inflammatory drug or narcotic) or a more specific anti-migraine drug (eg, dihydroergotamine or su matriptan) is available. BCAs should be avoided in elderly people and should not be used in children. Extrapolation from published reports on abuse and withdrawal syndrome with these drugs suggests that BCAs have the potential to produce drug dependence and addictive behaviour, especially with regular use. In BCA overdose, the barbiturate component is only one of the clinically significant contributors to any morbidity, but its presence can complicate the management of additive or synergistic toxicities. Therefore, there is no reason to choose a combination product when a simpler product may be a safer alternative by minimizing the potential for addiction and the occurrence of additive side effects or toxicities. It is further recommended that

prescribers re-evaluate treatment for patients using BCAs. Recommendations for withdrawal are provided, based on estimated consumption.
Publication Type: Guideline, Practice Guideline
PMID: 11118965

McNicholas L. Clinical Guidelines for the Use of Buprenorphine in the Treatment of Opioid Addiction. U.S. Ddept HHS, Substance Abuse and Mental Health Services Administration (SAMSA), Center for Substance Abuse Treatment. 2004.

Buprenorphine's pharmacological and safety profile makes it an attractive treatment for patients addicted to opioids as well as for the medical professionals treating them. Buprenorphine as a medication, and the circumstances under which it can be used, together provide a new means to treat opioid addiction in the United States. Buprenorphine's usefulness stems from its unique pharmacological and safety profile, which encourages treatment adherence and reduces the possibilities for both abuse and overdose.

Rating: 6b

McQuay H. Opioids in Pain Management. Lancet 1999;353:2229-32.

Pain Research, Nuffield Department of Anaesthetics, University of Oxford, Oxford Radcliffe Hospital, The Churchill, Headington, Oxford OX3 7LJ, UK. henry.mcquay@pru.ox.ac.uk

Publication Types:
- Meta-Analysis
- Review
- Review, Tutorial

PMID: 11888235

McQuay HJ, Tramer M, Nye BA, Carroll D, Wiffen PJ, Moore RA. A systematic review of antidepressants in neuropathic pain. Pain. 1996 Dec;68(2-3):217-27.

Nuffield Department of Anaesthetics, University of Oxford, UK.

The objective of this study was to review the effectiveness and safety of antidepressants in neuropathic pain. In a systematic review of randomised controlled trials, the main outcomes were global judgements, pain relief or fall in pain intensity which approximated to more than 50% pain relief, and information about minor and major adverse effects. Dichotomous data for effectiveness and adverse effects were analysed using odds ratio and number needed-to-treat (NNT) methods. Twenty-one placebo-controlled treatments in 17 randomised controlled trials were included, involving 10 antidepressants. In six of 13 diabetic neuropathy studies the odds ratios showed significant benefit compared with placebo. The

combined odds ratio was 3.6 (95% CI 2.5-5.2), with a NNT for benefit of 3 (2.4-4). In two of three postherpetic neuralgia studies the odds ratios showed significant benefit, and the combined odds ratio was 6.8 (3.5-14.3), with a NNT of 2.3 (1.7-3.3). In two atypical facial pain studies the combined odds ratio for benefit was 4.1 (2.3-7.5), with a NNT of 2.8 (2-4.7). Only one of three central pain studies had analysable dichotomous data. The NNT point estimate was 1.7. Comparisons of tricyclic antidepressants did not show any significant difference between them; they were significantly more effective than benzodiazepines in the three comparisons available. Paroxetine and mianserin were less effective than imipramine. For 11 of the 21 placebo-controlled treatments there was dichotomous information on minor adverse effects; combining across pain syndromes the NNT for minor (noted in published report) adverse effects was 3.7 (2.9-5.2). Information on major (drug-related study withdrawal) adverse effects was available from 19 reports; combining across pain syndromes the NNT for major adverse effects was 22 (13.5-58). Antidepressants are effective in relieving neuropathic pain. Compared with placebo, of 100 patients with neuropathic pain who are given antidepressants, 30 will obtain more than 50% pain relief, 30 will have minor adverse reactions and four will have to stop treatment because of major adverse effects. With very similar results for anticonvulsants it is still unclear which drug class should be first choice. Treatment would be improved if we could harness the dramatic improvement seen on placebo in some of the trials.

Publication Types:
Meta-Analysis

PMID: 9121808

Rating: 1b

Medicare National Coverage Determinations Manual. Chapter 1, Part 2. 2006. Available at: http://www.cms.hhs.gov/manuals/downloads/ncd103c1_Part2.pdf

Transcutaneous Electrical Nerve Stimulation (TENS)
This technique involves attachment of a transcutaneous nerve stimulator to the surface of the skin over the peripheral nerve to be stimulated. It is used by the patient on a trial basis and its effectiveness in modulating pain is monitored by the physician, or physical therapist. Generally, the physician or physical therapist is able to determine whether the patient is likely to derive a significant therapeutic benefit from continuous use of a transcutaneous stimulator within a trial period of one month; in a few cases this determination may take longer to make. Document the medical necessity for such services which are furnished beyond the first month.
If TENS significantly alleviates pain, it may be considered as primary treatment; if it produces no relief or greater discomfort than the original pain electrical nerve stimulation therapy is ruled out. However, where TENS produces incomplete relief, further evaluation with percutaneous electrical nerve stimulation may be considered to determine whether an implanted peripheral nerve stimulator would provide significant relief from pain.

Usually, the physician or physical therapist providing the services will furnish the equipment necessary for assessment. Where the physician or physical therapist advises the patient to rent the TENS from a supplier during the trial period rather than supplying it himself/herself, program payment may be made for rental of the TENS as well as for the services of the physician or physical therapist who is evaluating its use. However, the combined program payment which is made for the physician's or physical therapist's services and the rental of the stimulator from a supplier should not exceed the amount which would be payable for the total service, including the stimulator, furnished by the physician or physical therapist alone.

Rating: 8a

Medical Board of California. Guidelines for Prescribing Controlled Substances for Pain. Adopted Unanimously by the Board in 1994 and Recently Revised. Available at http://www.mbc.ca.gov/Painmgmt_Guidelines.htm

"No physician and surgeon shall be subject to disciplinary action by the Board for prescribing or administering controlled substances in the course of treatment of a person for intractable pain."

Business and Professions Code section 2241.5(c)

Patients with pain who are managed with controlled substances should be seen monthly, quarterly, or semiannually as required by the standard of care.

Rating: 8b

Medtronic, MDT Webpage, Indications for stimulator (medtronic) implantation, 2008

Indications: Implantable neurostimulation systems - A Medtronic implantable neurostimulation system is indicated for spinal cord stimulation (SCS) system as an aid in the management of chronic, intractable pain of the trunk and/or limbs-including unilateral or bilateral pain associated with the following conditions:
• Failed Back Syndrome (FBS) or low back syndrome or failed back
• Radicular pain syndrome or radiculopathies resulting in pain secondary to FBS or herniated disk
• Postlaminectomy pain
• Multiple back operations
• Unsuccessful disk surgery
• Degenerative Disk Disease (DDD)/herniated disk pain refractory to conservative and surgical interventions
• Peripheral causalgia
• Epidural fibrosis
• Arachnoiditis or lumbar adhesive arachnoiditis

• Complex Regional Pain Syndrome (CRPS), Reflex Sympathetic Dystrophy (RSD), or causalgia

Medtronic Inc
710 Medtronic Parkway
Minneapolis, MN 55432
Phone: (763) 514-4000
Fax: (763) 514-6272
Web Site: http://www.medtronic.com/

Medtronic, Inc. is a medical technology company that provides lifelong solutions for people with chronic disease. The Company offers products and therapies for use by medical professionals to meet the healthcare needs of their patients. Primary products include those for bradycardia pacing, tachy-arrhythmia management, heart failure, atrial fibrillation, coronary vascular disease, endovascular disease, peripheral vascular disease, heart valve replacement, extra-corporeal cardiac support, minimally invasive cardiac surgery, malignant and non-malignant pain, diabetes, urological disorders, gastroenterological ailments, movement disorders, spinal surgery, neurosurgery, neurodegenerative disorders and ear, nose and throat surgery.

Rating: 5c

Melchart D, Streng A, Hoppe A, Brinkhaus B, Witt C, Wagenpfeil S, Pfaffenrath V, Hammes M, Hummelsberger J, Irnich D, Weidenhammer W, Willich SN, Linde K. Acupuncture in patients with tension-type headache: randomised controlled trial. BMJ. 2005 Aug 13;331(7513):376-82. Epub 2005 Jul 29.

Centre for Complementary Medicine Research, Department of Internal Medicine II, Technische Universitat Munchen, Kaiserstr 9, 80801 Munich, Germany.

OBJECTIVE: To investigate the effectiveness of acupuncture compared with minimal acupuncture and with no acupuncture in patients with tension-type headache. DESIGN: Three armed randomised controlled multicentre trial. SETTING: 28 outpatient centres in Germany. PARTICIPANTS: 270 patients (74% women, mean age 43 (SD 13) years) with episodic or chronic tension-type headache. INTERVENTIONS: Acupuncture, minimal acupuncture (superficial needling at non-acupuncture points), or waiting list control. Acupuncture and minimal acupuncture were administered by specialised physicians and consisted of 12 sessions per patient over eight weeks. MAIN OUTCOME MEASURE: Difference in numbers of days with headache between the four weeks before randomisation and weeks 9-12 after randomisation, as recorded by participants in headache diaries. RESULTS: The number of days with headache decreased by 7.2 (SD 6.5) days in the acupuncture group compared with 6.6 (SD 6.0) days in the minimal acupuncture group and 1.5 (SD 3.7) days in the waiting list group (difference: acupuncture v minimal acupuncture, 0.6 days, 95% confidence interval -1.5 to 2.6 days, P = 0.58;

acupuncture v waiting list, 5.7 days, 3.9 to 7.5 days, P < 0.001). The proportion of responders (at least 50% reduction in days with headache) was 46% in the acupuncture group, 35% in the minimal acupuncture group, and 4% in the waiting list group. CONCLUSIONS: The acupuncture intervention investigated in this trial was more effective than no treatment but not significantly more effective than minimal acupuncture for the treatment of tension-type headache. TRIAL REGISTRATION NUMBER: ISRCTN9737659.

Publication Types:
Clinical Trial
Multicenter Study
Randomized Controlled Trial

PMID: 16055451

Rating: 2a

Melhorn JM. Workers' compensation: avoiding work-related disability. J Bone Joint Surg Am. 2000 Oct;82-A(10):1490-3.

The Hand Center, Wichita, Kansas 67208-4510, USA.

PMID: 11057476

Menigaux C, Adam F, Guignard B, Sessler DI, Chauvin M. Preoperative gabapentin decreases anxiety and improves early functional recovery from knee surgery. Anesth Analg. 2005 May;100(5):1394-9, table of contents.

Departmernt of Anesthesia, Hopital Ambroise Pare, Publique-Hopitaux de Paris, 92100 Boulogne, France.

Gabapentin has antihyperalgesic and anxiolytic properties. We thus tested the hypothesis that premedication with gabapentin would decrease preoperative anxiety and improve postoperative analgesia and early postoperative knee mobilization in patients undergoing arthroscopic anterior cruciate ligament repair under general anesthesia. Forty patients were randomly assigned to receive 1200 mg oral gabapentin or placebo 1-2 h before surgery; anesthesia was standardized. Patients received morphine, 0.1 mg/kg, 30 min before the end of surgery and postoperatively via a patient-controlled pump. Pain scores and morphine consumption were recorded over 48 h. Degrees of active and passive knee flexion and extension were recorded during physiotherapy on days 1 and 2. Preoperative anxiety scores were less in the gabapentin than control group (visual analog scale scores of 28 +/- 16 mm versus 66 +/- 15

mm, respectively; P < 0.001). The gabapentin group required less morphine than the control group (29 +/- 22 mg versus 69 +/- 40 mg, respectively; P < 0.001). Visual analog scale pain scores at rest and after mobilization were significantly reduced in the gabapentin group. First and maximal passive and active knee flexions at 24 and 48 h were significantly more extensive in the gabapentin than in the control group. In conclusion, premedication with 1200 mg gabapentin improved preoperative anxiolysis, postoperative analgesia, and early knee mobilization after arthroscopic anterior cruciate ligament repair.

PMID: 15845693

Rating: 2b

Mens JM. The use of medication in low back pain. Best Pract Res Clin Rheumatol. 2005 Aug;19(4):609-21.

Department of Rehabilitation Medicine, Erasmus Medical Centre, University Medical Center, P.O. Box 1738, 3000 DR Rotterdam, The Netherlands. j.mens@erasmusmc.nl

The choice of medication for low back pain should be evidence based and tailored as much as possible to suit the individual patient. Acetaminophen (paracetamol), mild opioids and NSAIDs are the first-line drugs for low back pain but there is no evidence that one is more effective than the others. Non-benzodiazepine muscle relaxants (with or without pain medication) could be considered as second-line drugs in acute low back pain, and cyclic antidepressants in chronic low back pain. The risk of adverse side effects can be reduced by taking account of the patient's medical history and by using a test dose. The realization that symptoms other than pain are sometimes more important and/or easier to overcome can increase the benefits of medication. The long-term effects of medication can be improved when it is combined with non-drug interventions.

Publication Types:
Review

PMID: 15949779

Rating: 5b

Michna E, Ross EL, Hynes WL, Nedeljkovic SS, Soumekh S, Janfaza D, Palombi D, Jamison RN. Predicting aberrant drug behavior in patients treated for chronic pain: importance of abuse history. J Pain Symptom Manage. 2004 Sep;28(3):250-8.

Pain Management Center, Brigham and Women's Hospital, Boston, Massachusetts 02115, USA.

Physicians can encounter problems in prescribing opioids for some patients with chronic pain such as multiple unsanctioned dose escalations, episodes of lost or stolen prescriptions, and positive urine drug screenings for illicit substances. This study explored the usefulness of questions on abuse history in predicting problems with prescribing opioids for patients at a hospital-based pain management program. One hundred forty-five (145) patients who were taking long- and short-acting opioids for their pain were classified as high or low risk on the basis of their responses to interview questions about 1) substance abuse history in their family, 2) past problems with drug or alcohol abuse, and 3) history of legal problems. The treating physicians completed a questionnaire about problems that they had encountered with their patients. Problem behaviors were verified through chart review. No differences in demographic characteristics were found between those classified as high and low risk. Patients who admitted to a family history of substance abuse, a history of legal problems, and drug or alcohol abuse were prone to more aberrant drug-related behaviors, including a higher incidence of lost or stolen prescriptions and the presence of illicit substances in their urine ($P < 0.05$). Patients classified as high risk also had a significantly higher frequency of reported mental health problems and motor vehicle accidents. More of these patients smoked cigarettes, tended to need a cigarette within the first hour of the day, took higher doses of opioids, and reported fewer adverse effects from the medications than did those without such a history ($P < 0.05$). This study demonstrates that questions about abuse history and legal problems can be useful in predicting aberrant drug-related behavior with opioid use in persons with chronic noncancer pain.

PMID: 15336337

Rating: 4b

Micromedex® Healthcare Series. Drugdex. Greenwood Village, CO: Thomson Micromedex®. 2008.

Ratying: 9a

Miller L, Mattison P, Paul L, Wood L. The effects of transcutaneous electrical nerve stimulation (TENS) on spasticity in multiple sclerosis. Mult Scler. 2007 May;13(4):527-33. Epub 2007 Jan 29.

Ayrshire Central Hospital, Irvine, UK. linda.miller@aaaht.scot.nhs.uk.

Spasticity is a common and often disabling symptom associated with multiple sclerosis (MS). Transcutaneous electrical nerve stimulation (TENS) has been found effective in reducing spasticity in conditions such as stroke, but there is little evidence to support its use in MS. The aim of this study was to evaluate the effectiveness of TENS on spasticity in MS and, furthermore, to compare two different application times. Thirty-two subjects were randomized into two groups, and a single, blind, crossover design was used to compare two weeks of 60 minutes and 8 hours daily of TENS applications (100 Hz and 0.125 ms pulse width). Outcomes were examined using the Global Spasticity Score (GSS), the Penn Spasm Score (PSS), and a visual analogue scale (VAS) for pain. The results of the study demonstrated

that there were no statistically significant differences in the GSS following either 60 minutes or 8 hours daily of TENS (P=0.433 and 0.217, respectively). The 8-hour application time led to a significant reduction in muscle spasm (P=0.038) and pain (P = 0.008). Thus, this study suggests that, whilst TENS does not appear to be effective in reducing spasticity, longer applications may be useful in treating MS patients with pain and muscle spasm.

PMID: 17463075

Rating: 2b

Mitchinson AR, Kim HM, Rosenberg JM, Geisser M, Kirsh M, Cikrit D, Hinshaw DB. Acute postoperative pain management using massage as an adjuvant therapy: a randomized trial. Arch Surg. 2007 Dec;142(12):1158-67.

Section of General Surgery, Geriatrics and Palliative Care Program, VA Ann Arbor Healthcare System, 2215 Fuller Rd, Ann Arbor, MI 48105, USA.

HYPOTHESIS: Adjuvant massage therapy improves pain management and postoperative anxiety among many patients who experience unrelieved postoperative pain. Pharmacologic interventions alone may not address all of the factors involved in the experience of pain. DESIGN: Randomized controlled trial. SETTING: Department of Veterans Affairs hospitals in Ann Arbor, Michigan, and Indianapolis, Indiana. PATIENTS: Six hundred five veterans (mean age, 64 years) undergoing major surgery from February 1, 2003, through January 31, 2005. INTERVENTIONS: Patients were assigned to the following 3 groups: (1) control (routine care), (2) individualized attention from a massage therapist (20 minutes), or (3) back massage by a massage therapist each evening for up to 5 postoperative days. Main Outcome Measure Short- and long-term (> 4 days) pain intensity, pain unpleasantness, and anxiety measured by visual analog scales. RESULTS: Compared with the control group, patients in the massage group experienced short-term (preintervention vs postintervention) decreases in pain intensity (P = .001), pain unpleasantness (P < .001), and anxiety (P = .007). In addition, patients in the massage group experienced a faster rate of decrease in pain intensity (P = .02) and unpleasantness (P = .01) during the first 4 postoperative days compared with the control group. There were no differences in the rates of decrease in long-term anxiety, length of stay, opiate use, or complications across the 3 groups. CONCLUSION: Massage is an effective and safe adjuvant therapy for the relief of acute postoperative pain in patients undergoing major operations.

PMID: 18086982

Rating: 2b

December 17, 2007 — Massage is an effective adjunct treatment to relieve acute postoperative pain in patients who had major surgery, according to the results of a randomized controlled trial published in the

December issue of the Archives of Surgery. "Massage is an effective and safe adjuvant therapy for the relief of acute postoperative pain in patients undergoing major operations," the authors write. "With proper training, health care providers at the bedside (especially nurses) may now have a powerful nonpharmacologic tool to directly address their patients' pain and anxiety." Study limitations include virtually all participants being elderly men; potential self-selection bias because patients who did not want to be touched refused to participate; and inability to perform dose-response interventions. "As health care systems have become more complex and administrative demands on nursing time have increased, the tradition of nurse-administered massage has been largely lost," the authors conclude. "With the recent emphasis on assessing pain as the fifth vital sign tempered by renewed concerns for patient safety, it is time to reintegrate the use of effective and less dangerous approaches to relieve patient distress."
Pearls for Practice: Massage therapy in postoperative patients results in short-term decrease in pain intensity, pain unpleasantness, and anxiety. Massage therapy in postoperative patients results in faster rate of decrease in pain intensity and pain unpleasantness, but not anxiety, in the first 4 postoperative days.

Mitte K. A meta-analysis of the efficacy of psycho- and pharmacotherapy in panic disorder with and without agoraphobia. J Affect Disord. 2005; 88:27-45.

University of Jena, Germany. mail@kristin-mitte.de

The efficacy of (cognitive) behavioural ((C)BT) and pharmacological therapy was investigated using meta-analytic techniques. After a comprehensive review of the literature, the results of 124 studies were included. (C)BT was more effective than a no-treatment control and a placebo control. No difference of efficacy was found when using cognitive elements compared to not using them for anxiety; for associated depressive symptoms, additional cognitive elements seems superior. Pharmacotherapy was more effective than a placebo control; there was no superiority of any drug class. Sample size was related to effect size in pharmacotherapy and publication bias was found. (C)BT was at least as effective as pharmacotherapy and depending on type of analysis even significantly more effective. There were no significant differences between (C)BT alone and a combination approach but characteristics of studies have to be considered.
PMID: 16005982

Rating: 1b

Montgomery B. Does paracetamol cause hypertension? BMJ. 2008;336:1190-1.

Discipline of General Practice, School of Primary, Aboriginal and Rural Health Care, University of Western Australia, 328 Stirling Highway, Claremont, WA 6010, Australia. brett@multiline.com.au

A review of articles that discuss hypertension and acetaminophen.

Rating: 5c

Moore, S and Shurman J. Combined Neuromuscular Electrical Stimulation and Transcutaneous Electrical Nerve Stimulation for Treatment of Chronic Back Pain: A Double-Blind, Repeated Measures Comparison. Archive of Physical Medicine and Rehabilitation. 1997; Volume 78, January: 55-60.

Rating: 2c

Quality: Low. Total Rating: 3.5. Comment: Does not meet inclusion criteria for evidence-based review. [CA DWC]

Morin AK, Jarvis CI, Lynch AM. Therapeutic options for sleep-maintenance and sleep-onset insomnia. Pharmacotherapy. 2007 Jan;27(1):89-110.

Department of Pharmacy Practice, Massachusetts College of Pharmacy and Health Sciences, Worcester, Massachusetts 01608-1715, USA. anna.morin@mcphs.edu

Insomnia, defined as difficulty falling asleep, staying asleep, and/or experiencing restorative sleep with associated impairment or significant distress, is a common condition resulting in significant clinical and economic consequences. Many options are available to treat insomnia, to assist with either falling asleep (sleep onset) or maintaining sleep. We searched MEDLINE for articles published between January 1996 and January 2006, evaluated abstracts from recent professional meetings, and contacted the manufacturer of the most recent addition to the pharmacologic armamentarium for insomnia treatment (ramelteon) to gather information. Nonpharmacologic options include stimulus control, sleep hygiene education, sleep restriction, paradoxical intention, relaxation therapy, biofeedback, and cognitive behavioral therapy. Prescription and over-the-counter drug therapies include benzodiazepine and nonbenzodiazepine sedative-hypnotic agents; ramelteon, a melatonin receptor agonist; trazodone; and sedating antihistamines. Herbal and alternative preparations include melatonin and valerian. Before recommending any treatment, clinicians should consider patient-specific criteria such as age, medical history, and other drug use, as well as the underlying cause of the sleep disturbance. All pharmacotherapy should be used with appropriate caution, at minimum effective doses, and for minimum duration of time.

Rating: 1b

Morley S, Eccleston C, Williams A. Systematic review and meta-analysis of randomized controlled trials of cognitive behaviour therapy and behaviour therapy for chronic pain in adults, excluding headache. Pain. 1999 Mar;80(1-2):1-13.

Division of Psychiatry and Behavioural Sciences, School of Medicine, University of Leeds, UK. s.j.morley@leeds.ac.uk

A computer and a hand search of the literature recovered 33 papers from which 25 trials suitable for meta-analysis were identified. We compared the effectiveness of cognitive-behavioural treatments with the waiting list control and alternative treatment control conditions. There was a great diversity of measurements which we grouped into domains representing major facets of pain. Effect sizes, corrected for measurement unreliability, were estimated for each domain. When compared with the waiting list control conditions cognitive-behavioural treatments were associated with significant effect sizes on all domains of measurement (median effect size across domains = 0.5). Comparison with alternative active treatments revealed that cognitive-behavioural treatments produced significantly greater changes for the domains of pain experience, cognitive coping and appraisal (positive coping measures), and reduced behavioural expression of pain. Differences on the following domains were not significant; mood/affect (depression and other, non-depression, measures), cognitive coping and appraisal (negative, e.g. catastrophization), and social role functioning. We conclude that active psychological treatments based on the principle of cognitive behavioural therapy are effective. We discuss the results with reference to the complexity and quality of the trials.

PMID: 10204712

Rating: 1a

Moskowitz M, Mackie K, Huestis MA, Ratcliffe S, Mead AP, Fishman SM. Cannabinoids - a new class of analgesics. Program and abstracts of the American Academy of Pain Medicine 23rd Annual Meeting; February 7-10, 2007; New Orleans, Louisiana.

In total, 11 states have approved the use of medical marijuana for the treatment of chronic pain or for nausea associated with chemotherapy. The medical community has lagged behind a bit and partly because there are really very little, quality, controlled clinical data with cannabinoids. Restricted legal access to Schedule I drugs, such as marijuana, tends to hamper research in this area. It is also very hard to do controlled studies with a drug that is psychoactive because it is hard to blind these effects. It is similarly difficult to do studies with opioid analgesics; as it is difficult to come up with a control population in which you can fool patients into not knowing which drug they are getting. The two major issues with medical marijuana were discussed. One is that there are just not a lot of good solid clinical data. Some animal data definitely provide clear evidence for cannabinoid receptors producing a modulating effect on pain and nausea. However, human studies are more anecdotal, and most reports are uncontrolled and simply descriptive. It is hard to come forward as a medical professional and say that we should use this treatment without good evidence. This is the problem that the American Academy of Pain Medicine and many other medical specialty societies have faced in approaching the medical marijuana issue. In this age of "evidence-based medicine," organized medicine finds it difficult to promote untested treatments. It is difficult to justify advising our patients to smoke street-grade

marijuana, presuming that they will experience benefit, when they may also be harmed. One of the conclusions that came out of our discussions is that we would like to see greater emphasis and support from the government to evaluate medical marijuana further and allow legitimate testing. At the present time, you can only get research-grade marijuana or THC [delta-9-tetrahydrocannabinol] from one location, which leads to the belief that this restricts the development of a greater understanding of medical marijuana.

Rating: 10a

Moulin DE, Iezze A, Amireh R, Sharpe WK, Boyd D, Merskey H. Randomised trial of oral morphine for chronic non-cancer pain. Lancet 1996;347:143-7.

Department of Clinical Neurological Sciences, University of Western Ontario, London, Canada.
This study concluded, "Oral morphine for musculoskeletal conditions has analgesic benefit, but unlikely to confer functional benefit compared to placebo."
Publication Type: RCT, 46 cases
PMID: 8544547

Moulin DE, Systemic drug treatment for chronic musculoskeletal pain, Clin J Pain. 2001 Dec;17(4 Suppl):S86-93.

Department of Clinical Neurological Sciences/Oncology, University of Western Ontario, London, Canada. dwight.moulin@lhsc.on.ca

OBJECTIVE: The purpose of this review was to determine how effective different classes of analgesic agents are in the management of chronic pain. METHODOLOGY: The literature search identified five systematic reviews and 18 randomized controlled trials to provide evidence about systemic drug treatment for chronic pain. RESULTS: Studies in the systematic reviews were mainly of low back pain, and studies in the randomized controlled trials were mainly of fibromyalgia. Other studies investigated of rheumatic pain, musculoskeletal pain, chronic low back pain, and temporomandibular pain. Classes of analgesic agents reviewed were antidepressants, nonsteroidal anti-inflammatory drugs, muscle relaxants, opioid analgesics, and a number of miscellaneous agents. CONCLUSIONS: For chronic pain, opioid analgesics provide benefit for up to 9 weeks (level 2). For chronic low back pain, the evidence shows that various types of nonsteroidal antiinflammatory drugs are equally effective or ineffective, and that antidepressants provide no benefit in the short to intermediate term (level 2). Muscle relaxants showed limited effectiveness (level 3) for chronic neck pain and for chronic low back pain for up to 4 weeks. For fibromyalgia, there is limited evidence (level 3) of the effectiveness of amitryptiline, ondansetron, zoldipem, or growth hormone, and evidence of no effectiveness for nonsteroidal anti-inflammatory drugs, malic acid with magnesium, calcitonin injections, or s-adenyl-L-methionine. For temporomandibular pain, oral sumatriptan is not effective (level 2). The remaining evidence was inadequate (level 4a) or contradictory (level 4b).

Publication Types:
- Review
- Review, Tutorial

PMID: 11783837

Rating: 5b

Muehlbacher M, Nickel MK, Kettler C, Tritt K, Lahmann C, Leiberich PK, Nickel C, Krawczyk J, Mitterlehner FO, Rother WK, Loew TH, Kaplan P. Topiramate in treatment of patients with chronic low back pain: a randomized, double-blind, placebo-controlled study. Clin J Pain. 2006;22:526-31.

University Clinic for Psychiatry 1, PMU, Salzburg, Austria.

OBJECTIVE: Chronic low back pain (CLBP) is a widespread ailment. The aim of this study was to assess the efficacy of topiramate in the treatment of CLBP and the changes in anger status and processing, body weight, subjective pain-related disability and health-related quality of life during the course of treatment. METHODS: We conducted a 10-week, randomized, double-blind, placebo-controlled study of topiramate in 96 (36 women) patients with CLBP. The subjects were randomly assigned to topiramate (n=48) or placebo (n=48). Primary outcome measures were changes on the McGill Pain Questionnaire, State-Trait Anger Expression Inventory, Oswestry Low Back Pain Disability Questionnaire and SF-36 Health Survey scales, and in body weight. RESULTS: In comparison with the placebo group (according to the intent-to-treat principle), significant changes on the pain rating index of McGill Pain Questionnaire (Ps<0.001), State-Trait Anger Expression Inventory Scales (all Ps<0.001), Oswestry Low Back Pain Disability Questionnaire (P<0.001), and SF-36 Health Survey scales (all P<0.001, except on the role-emotional scale) were observed after 10 weeks in the patients treated with topiramate. Weight loss was also observed and was significantly more pronounced in the group treated with topiramate than in those treated with placebo (P<0.001). Most patients tolerated topiramate relatively well but 2 patients dropped out because of side effects. DISCUSSION: Topiramate seems to be a relatively safe and effective agent in the treatment of CLBP. Significantly positive changes in pain sensitivity, anger status and processing, subjective disability, health-related quality of life, and loss of weight were observed.

PMID: 16788338

Rating: 2b

Nader A, Benzon HT. Peripheral Sympathetic Blocks. In. Essentials of Pain Medicine and Regional Anesthesia. 2nd ed. Eds. Benzon HT, Raja SN, Molloy RE, Liu SP, Fishman SM. Elsevier Churchill Livingstone. Philadelphia. 2005.

Rating: 9a

Nakazawa, R., et al. Hormone Profiles after Intramuscular Injection of Testosterone Enanthate in Patients with Hypogonadism. Endocrine Journal, 2006; Volume 53, Number 3, 305-103.

Rating: 2c

Quality: Low. Total Rating: .5. Comment: Does not meet inclusion criteria for evidence-based review.

Naliboff BD, Wu SM, Pham Q. Clinical considerations in the treatment of chronic pain with opiates. J Clin Psychol. 2006 Aug 25; [Epub ahead of print]

Greater Los Angeles Veterans Affairs Healthcare System, UCLA Center for Neurovisceral Sciences and Women's Health, and David Geffen School of Medicine at UCLA.

This article considers assessment and treatment issues for mental health practitioners working with patients using opiate medications to treat chronic pain with a particular emphasis on their potential relationship to substance abuse. We review general opiate medications, including a discussion of medications with increased addiction potential. Practice guidance is offered regarding long-term opiate treatment, including definitions of addiction, initial assessments, ongoing substance misuse monitoring, use of psychological assessment instruments, and managing medication misuse problems. Additionally, we examine the role of the mental health professional within this area and examine the incorporation of psychological interventions for patients using opiates. A case illustration includes several of these complicated issues of managing chronic pain with opiate medications. (c) 2006 Wiley Periodicals, Inc. J Clin Psychol: In Session.

PMID: 16937352

Rating: 5a

Namaka M, Gramlich CR, Ruhlen D, Melanson M, Sutton I, Major J. A treatment algorithm for neuropathic pain. Clin Ther. 2004 Jul;26(7):951-79.

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BACKGROUND: Neuropathic pain is a chronic pain syndrome caused by drug-, disease-, or injury-induced damage or destruction of sensory neurons within the dorsal root ganglia of the peripheral nervous system. Characteristic clinical symptoms include the feeling of pins and needles; burning, shooting, and/or stabbing pain with or without throbbing; and numbness. Neuronal hyperexcitability

represents the hallmark cellular mechanism involved in the underlying pathophysiology of neuropathic pain. Although the primary goal is to alleviate pain, clinicians recognize that even the most appropriate treatment strategy may be, at best, only able to reduce pain to a more tolerable level. OBJECTIVE: The purpose of this review is to propose a treatment algorithm for neuropathic pain that health care professionals can logically follow and adapt to the specific needs of each patient. The algorithm is intended to serve as a general guide to assist clinicians in optimizing available therapeutic options. METHODS: A comprehensive review of the literature using the PubMed, MEDLINE, Cochrane, and Toxnet databases was conducted to design and develop a novel treatment algorithm for neuropathic pain that encompasses agents from several drug classes, including antidepressants, antiepileptic drugs, topical antineuralgic agents, narcotics, and analgesics, as well as various treatment options for refractory cases. RESULTS: Any of the agents in the first-line drug classes (tricyclic antidepressants, antiepileptic drugs, topical antineuralgics, analgesics) may be used as a starting point in the treatment of neuropathic pain. If a patient does not respond to treatment with at least 3 different agents within a drug class, agents from a second drug class may be tried. When all first-line options have been exhausted, narcotic analgesics or refractory treatment options may provide some benefit. Patients who do not respond to monotherapy with any of the first- or second-line agents may respond to combination therapy or may be candidates for referral to a pain clinic. Because the techniques used at pain clinics tend to be invasive, referrals to these clinics should be reserved for patients who are truly refractory to all forms of pharmacotherapy. CONCLUSIONS: Neuropathic pain continues to be one of the most difficult pain conditions to treat. With the proposed algorithm, clinicians will have a framework from which to design a pain treatment protocol appropriate for each patient. The algorithm will also help streamline referrals to specialized pain clinics, thereby reducing waiting list times for patients who are truly refractory to traditional pharmacotherapy.

Publication Types:
Review

PMID: 15336464

Rating: 8a

Naumann M, So Y, Argoff CE, Childers MK, Dykstra DD, Gronseth GS, Jabbari B, Kaufmann HC, Schurch B, Silberstein SD, Simpson DM; Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Assessment: Botulinum neurotoxin in the treatment of autonomic disorders and pain (an evidence-based review): report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology. 2008 May 6;70(19):1707-14.

Department of Neurology, Klinikum Augsburg, Germany.

RESULTS: The highest quality literature available for the respective indications was as follows: axillary hyperhidrosis (two Class I studies); palmar hyperhidrosis (two Class II studies); drooling (four Class II

studies); gustatory sweating (five Class III studies); neurogenic detrusor overactivity (two Class I studies); sphincter detrusor dyssynergia in spinal cord injury (two Class II studies); chronic low back pain (one Class II study); episodic migraine (two Class I and two Class II studies); chronic daily headache (four Class II studies); and chronic tension-type headache (two Class I studies). RECOMMENDATIONS: Botulinum neurotoxin (BoNT) should be offered as a treatment option for the treatment of axillary hyperhidrosis and detrusor overactivity (Level A), should be considered for palmar hyperhidrosis, drooling, and detrusor sphincter dyssynergia after spinal cord injury (Level B), and may be considered for gustatory sweating and low back pain (Level C). BoNT is probably ineffective in episodic migraine and chronic tension-type headache (Level B). There is presently no consistent or strong evidence to permit drawing conclusions on the efficacy of BoNT in chronic daily headache (mainly transformed migraine) (Level U).

PMID: 18458231

Rating: 1c

Nelemans PJ, Bie RA de, Vet HCW de, Sturmans F. Injection therapy for subacute and chronic benign low back pain (Cochrane Review). In: The Cochrane Library, Issue 2, 2002. Oxford: Update Software.
Abstract:
Background: Injection with anaesthetics and/or steroids is one of the treatment modalities used in patients with chronic low back pain which needs evaluation with respect to the effectiveness on short and long term pain relief.
Objectives: To evaluate the effectiveness of injection therapy in patients with low back pain lasting longer than one month. We distinguished between three injection sites: facet joint, epidural or local injections.
Search strategy: We searched the Medline and Embase databases up to 1996 and other search methods as advocated by the Back Review Group search strategy. Abstracts and unpublished studies were not included.
Selection criteria: Randomized controlled trials of injection therapy for pain relief (although additional treatments were allowed) in patients with benign low back pain lasting longer than one month and not originating from cancer.
Data collection and analysis: Two reviewers independently assessed the trials for methodological quality. Subgroup analyses were made between trials with different control groups (placebo and active injections), with different injection site (facet joint, epidural and local injection), and timing of outcome measurement (short and long term). Within the resulting 12 subcategories of studies (2*3*2), the overall relative risks and corresponding 95% confidence intervals were estimated, using a random effects model (DerSimonian and Laird). In the case of trials in which control groups were active injections, we refrained from pooling the results.
Main results: Twenty-one randomized trials were included in this review. All studies involved patients with low back pain lasting longer than one month.

Only 11 studies compared injection therapy with placebo injections (explanatory trials). The methodologic quality of many studies was low: only 8 studies had a methodologic score of 50 or more points. There were only three well designed explanatory clinical trials: one on injections into the facet joints with a short-term RR of 0.89 (95% CI: 0.65-1.21) and a long-term RR of 0.90 (95% CI: 0.69-1.17); one on epidural injections with a short-term RR of 0.94 (95% CI: 0.76-1.15) and a long-term RR of 1.00 (95% CI: 0.71-1.41); and one on local injections with a long-term RR of 0.79 (95% CI: 0.65-0.96).
Within the 6 subcategories of explanatory studies the pooled RRs with 95% confidence intervals were: facet joint, short-term: RR=0.89 (0.65-1.21); facet joint, long-term: RR=0.90 (0.69-1.17); epidural, short-term: RR=0.93 (0.79-1.09); epidural, long-term: RR=0.92 (0.76-1.11); local, short-term: RR=0.80 (0.40-1.59); local, long-term: RR=0.79 (0.65-0.96).
Reviewers' conclusions: Convincing evidence is lacking on the effects of injection therapies for low back pain. There is a need for more, well designed explanatory trials in this field.
Publication Type: Meta-Analysis

Nelson DV. Pieces of the puzzle: management of complex regional pain syndrome. Clin J Pain. 2006; 22:413-4.

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PMID: 16772793

No abstract is available. The authors for this special series have generally been in the forefront of their respective disciplines in refining the focus on important issues about CRPS or neuropathic pain more broadly. Functional restoration was stressed.

Rating: 5b

Nemeth et al. Journal of Workers Compensation. Summer 2005.

This article describes the etiology and prevention of the "Wounded Worker Syndrome", an important condition in workers compensation that is preventable, but under-diagnosed and over-treated while accounting for the majority of prolonged disability and cost in the system.

Rating: 5b

Newton-John TR, Spence SH, Schotte D. Cognitive-behavioural therapy versus EMG biofeedback in the treatment of chronic low back pain. Behav Res Ther. 1995 Jul;33(6):691-7.

Department of Clinical Health Psychology, St Mary's Hospital, London, England.

Forty-four chronic, but relatively well functioning, low back pain patients were assigned to either Cognitive Behaviour Therapy (CBT). Electromyographic Biofeedback (EMGBF) or Wait List Control (WLC). Both treatments were conducted over eight sessions in groups of four subjects. Results at post-treatment indicated significant improvements in functioning on measures of pain intensity, perceived level of disability, adaptive beliefs about pain and the level of depression in both the CBT and EMGBF conditions. These improvements were not evident for the WLC condition. At 6 months follow-up, treatment gains were maintained in the areas of pain intensity, pain beliefs, and depression, for both treatment groups, with further improvements occurring in anxiety and use of active coping skills. No significant differences were found between CBT and EMGBF on any of the outcome measures at either post-treatment or at 6 months follow-up. Further research is required to determine the degree to which these results reflect the mild level of psychological impairment and disability status of patients in the present study.

PMID: 7654161

Rating: 2c

Ney JP, Difazio M, Sichani A, Monacci W, Foster L, Jabbari B. Treatment of chronic low back pain with successive injections of botulinum toxin a over 6 months: a prospective trial of 60 patients. Clin J Pain. 2006 May;22(4):363-9.

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OBJECTIVES: The aim of this study was to evaluate the effects of two successive neurotoxin treatments for chronic low back pain using multiple pain rating scales in an open-label, prospective study. METHODS: Adult patients with chronic low back pain received multiple paraspinal muscle injections with a maximum dosing of 500 units of botulinum A toxin per session. Those with a beneficial clinical response received a second treatment at 4 months. Pain was assessed by visual analog scale (VAS), modified low back pain questionnaire (OLBPQ), and a clinical low back pain questionnaire (CLBPQ) at baseline, 3 weeks, 2 months, 4 months, and 6 months after the first treatment. RESULTS: Eighteen women and 42 men, ages 21 to 79 years (mean 46.6 years), with low back pain of a mean duration of 9.1 years were included. Significant improvement in back and radicular pain occurred at 3 weeks in 60% and at 2 months in 58% of the cohort. Beneficial clinical response to the first injection predicted response to reinjection in 94%. A significant minority of patients had a sustained beneficial effect from the first injection at 4 (16.6%) and 6 months (8.3%). Two patients had a transient flu-like reaction after the initial treatment. CONCLUSIONS: Botulinum toxin A improves refractory chronic low back pain with a low incidence of side effects. The beneficial clinical response is sustained with a second treatment.

PMID: 16691090

Rating: 4c

NICE (National Institute for Health and Clinical Excellence). Pain (chronic neuropathic or ischaemic) - spinal cord stimulation: final appraisal determination. 01 September 2008.

1 Guidance: 1.1 Spinal cord stimulation is recommended as a treatment option for adults with chronic pain of neuropathic origin who: • continue to experience chronic pain (measuring at least 50 mm on a 0–100 mm visual analogue scale) for at least 6 months despite appropriate conventional medical management, and • who have had a successful trial of stimulation as part of the assessment specified in recommendation 1.3. 1.2 Spinal cord stimulation is not recommended as a treatment option for adults with chronic pain of ischaemic origin except in the context of research as part of a clinical trial. Such research should be designed to generate robust evidence about the benefits of spinal cord stimulation (including pain relief, functional outcomes and quality of life) compared with standard care. 1.3 Spinal cord stimulation should be provided only after an assessment by a multidisciplinary team experienced in chronic pain assessment and management of people with spinal cord stimulation devices, including experience in the provision of ongoing monitoring and support of the person assessed. 1.4 When assessing the severity of pain and the trial of stimulation, the multidisciplinary team should be aware of the need to ensure equality of access to treatment with spinal cord stimulation. Tests to assess pain and response to spinal cord stimulation should take into account a person's disabilities (such as physical or sensory disabilities), or linguistic or other communication difficulties, and may need to be adapted. 1.5 If different spinal cord stimulation systems are considered to be equally suitable for a person, the least costly should be used. Assessment of cost should take into account acquisition costs, the anticipated longevity of the system, the stimulation requirements of the person with chronic pain and the support package offered. 1.6 People who are currently using spinal cord stimulation for the treatment of chronic pain of ischaemic origin should have the option to continue treatment until they and their clinicians consider it appropriate to stop.
2 Clinical need and practice: 2.1 Pain that persists for more than several months, or beyond the normal course of a disease or expected time of healing, is often defined as chronic. This pain becomes a significant medical condition in itself rather than being a symptom. Chronic pain can affect people of all ages, although in general, its prevalence increases with age. Estimates of the prevalence of this condition in the UK vary from less than 10% to greater than 30% depending on the specific definition of chronic pain used. Chronic pain is accompanied by physiological and psychological changes such as sleep disturbances, irritability, medication dependence and frequent absence from work. Emotional withdrawal and depression are also common, which can strain family and social interactions. 2.2 Neuropathic pain is initiated or caused by nervous system damage or dysfunction. Neuropathic pain is difficult to manage because affected people often have a complex history with unclear or diverse causes and comorbidities. Neuropathic conditions include failed back surgery syndrome (FBSS) and complex regional pain syndrome (CRPS). People with FBSS continue to have back and/or leg pain despite anatomically successful lumbar spine surgery. It is not easy to identify a specific cause of neuropathic pain and people with FBSS may experience mixed back and leg pain. CRPS may happen after a harmful

event or period of immobilisation (type I) or nerve injury (type II). Pain and increased sensitivity to pain are the most significant symptoms and are present in almost all people with CRPS. Other symptoms can include perceived temperature changes, weakness of movement and changes in skin appearance and condition.

Rating: 8a

Nicholas MK, Molloy AR, Brooker C. Using opioids with persisting noncancer pain: a biopsychosocial perspective. Clin J Pain. 2006 Feb;22(2):137-46.

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OBJECTIVE: Despite the growing use of opioids for persisting noncancer pain, evidence for their effectiveness is limited, especially in relation to functional outcomes. Guidelines have been developed for prescribers, but their utility is untested. This review examines the use of opioids in this population from a biopsychosocial perspective and makes a number of recommendations. DATA SOURCES: Published comparison studies and reviews of oral opioids in chronic noncancer pain, as well as 5 published guidelines for the prescription of opioids and systematic reviews of cognitive-behavioral pain management programs. METHODS: Outcomes of the opioid comparison studies were reviewed and compared to those achieved by pain management programs. CONCLUSIONS: The available evidence indicates that by themselves, oral opioids generally achieve only modest reductions in pain levels in patients with chronic noncancer pain. Functional outcomes are inconsistent across studies. There are questions about the timing of their use and patient selection. There are risks in trials of opioids only after other conservative interventions have been tried unsuccessfully. Also, in some patients, ongoing use of opioids risks repeated over-doing of pain-generating activities and reinforcing escape/avoidance responses that promote disability. These risks may be lessened by assessment of current use of pain self-management strategies among potential candidates for opioids. This offers advantages in promoting collaborative management of persisting pain as well as better pain and functional outcomes. In this view, opioids may be considered as one possible element of a management plan rather than the primary treatment.

Publication Types:
Review

PMID: 16428947

Rating: 5a

Nielsen OH, Ainsworth M, Csillag C, Rask-Madsen J. Systematic review: coxibs, non-steroidal anti-inflammatory drugs or no cyclooxygenase inhibitors in gastroenterological high-risk patients? Aliment Pharmacol Ther. 2006 Jan 1;23(1):27-33.

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Selective cyclooxygenase-2 inhibitors have been marketed as alternatives of conventional, non-steroidal anti-inflammatory drugs with the purpose of reducing/eliminating the risk of ulcer complications. Unexpectedly, randomized-controlled trials revealed that long-term use of coxibs, such as rofecoxib, significantly increased the risk of myocardial infarction and stroke, while the use of valdecoxib was associated with potentially life-threatening skin reactions. Subsequently, rofecoxib and valdecoxib were withdrawn from the market. Although more strict precautions for other coxibs, such as celecoxib, etoricoxib, lumiracoxib and parecoxib, may be accepted/recommended by regulatory agencies, a critical review of published data suggests that their use may not be justified - even in high-risk patients - taking benefits, costs and risks into consideration. Clinicians should, therefore, never prescribe coxibs to patients with cardiovascular risk factors, and should only reluctantly prescribe coxibs to patients with a history of ulcer disease or dyspepsia to overcome persistent pain due to, e.g. rheumatoid arthritis or osteoarthritis. Instead, they should consider using conventional non-steroidal anti-inflammatory drugs in combination with a proton pump inhibitor or a prostaglandin analogue, especially for patients with increased cardiovascular risks, i.e. established ischaemic heart disease, cerebrovascular disease and/or peripheral arterial disease, or alternatively acetaminophen. An evidence-based algorithm for treatment of a chronic arthritis patient with one or more gastrointestinal risk factors is presented.

Publication Types:
Review

PMID: 16393277

Rating: 5a

Niv D, Maltsman-Tseikhin A. Postherpetic neuralgia: the never-ending challenge. Pain Pract. 2005 Dec;5(4):327-40.

Center for Pain Medicine, Tel-Aviv Sourasky Medical Center, Sackler Faculty of Medicine, Tel-Aviv University, Tel-Aviv, Israel.

Postherpetic neuralgia (PHN) is defined as pain that persists 1 to 3 months following the rash of herpes zoster (HZ). PHN affects about 50% of patients over 60 years of age and 15% of all HZ patients. Patients with PHN may experience two types of pain: a steady, aching, boring pain and a paroxysmal lancinating pain, usually exacerbated by contact with the involved skin. Herpes zoster is initially a

clinical diagnosis, based on the observation of a typical dermatomal distribution of rash and radicular pain. HZ is pathologically characterized by inflammatory necrosis of dorsal root ganglia, occasionally associated with evidence of neuritis, leptomeningitis, and segmental unilateral degeneration of related motor and sensory roots. Although acyclovir has been used successfully as standard therapy for varicella zoster virus (VZV) infection in the past decade, resistant strains of VZV are often recognized in immunocompromised patients. Therapy with acyclovir and the use of corticosteroids have been reported to prevent PHN in up to 60% of HZ patients. Management of chronic pain in PHN is more problematic. The only therapy proven effective for PHN in controlled study is the use of tricyclic antidepressants, including amitriptyline and desipramine. There is good evidence of efficacy from randomized trials that gabapentin and pregabalin (new anticonvulsant drugs) are of benefit in the reduction of pain from PHN. As alternative therapies, topical agents such as capsaicin, lidocaine or opioid analgesic treatment may give satisfactory results. Interventions with low risk, such as transcutaneous electrical nerve stimulation (TENS), are appropriate. Evidence is scant for the value of surgical and procedural interventions in general, although there are numerous, small studies supporting the use of specific interventions such as nerve blocks, neurosurgical procedures, and neuroaugmentation. Although antiviral agents are appropriate for acute HZ, and the use of neural blockade and sympathetic blockade may be helpful in reducing pain in selected patients with HZ, there is little evidence that these interventions will reduce the likelihood of developing PHN. Postherpetic neuralgia remains a difficult pain problem. This review describes the epidemiology and pathophysiology of PHN and discusses proposed mechanisms of pain generation with emphasis on the various pharmacological treatments and invasive modalities currently available.

PMID: 17177766

Rating: 5b

North RB, Calkins SK, Campbell DS, Sieracki JM, Piantadosi S, Daly MJ, Dey PB, Barolat G, Automated, patient-interactive, spinal cord stimulator adjustment: a randomized controlled trial, Neurosurgery. 2003 Mar;52(3):572-80; discussion 579-80.

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OBJECTIVE: Programmable, multicontact, implanted stimulation devices represent an important advance in spinal cord stimulation for the management of pain. They facilitate the technical goal of covering areas of pain by stimulation-evoked paresthesiae. Adjustment after implantation requires major investments of time and effort, however, if the capabilities of these devices are to be used to full advantage. The objective of maximizing coverage should be met while using practitioners' time efficiently. METHODS: We have developed a patient-interactive, computerized system designed for greater ease and safety of operation, compared with the standard external devices used to control and adjust implanted pulse generators. The system automatically and rapidly presents to the patient the

contact combinations and pulse parameters specified by the practitioner. The patient adjusts the amplitude of stimulation and then records drawings of stimulation paresthesiae (for comparison with pain drawings), followed by visual analog scale ratings for each setting. Test results are analyzed and sorted to determine the optimal settings. We compared the automated, patient-interactive system with traditional, practitioner-operated, manual programming methods in a randomized controlled trial at two study centers, with 44 patients. RESULTS: The automated, patient-interactive system yielded significantly ($P < 0.0001$) better technical results than did traditional manual methods, in achieving coverage of pain by stimulation paresthesiae (mean 100-point visual analog scale ratings of 70 and 46, respectively). The visual analog scale ratings were higher for automated testing for 38 patients, higher for manual testing for 0 patients, and equal (tied) for 6 patients. Multivariate analysis demonstrated that the advantage of automated testing occurred independently of practitioner experience; the advantage was significantly greater, however, for experienced patients. The rate of testing (number of settings tested per unit time) was significantly ($P < 0.0001$) greater for the automated system, in comparison with the rate with a human operator using traditional, manual, programming methods (mean of 0.73 settings/min versus 0.49 settings/min). The automated system also identified settings with improved estimated battery life (and corresponding anticipated cost savings). No complications were observed with automated testing; one complication (transient discomfort attributable to excessive stimulation) occurred with manual testing. CONCLUSION: Automated, patient-interactive adjustment of implanted spinal cord stimulators is significantly more effective and more efficient than traditional manual methods of adjustment. It offers not only improved clinical efficacy but also potential cost savings in extending implanted battery life. It has the additional potential advantages of standardization, quality control, and record keeping, to facilitate clinical research and patient care. It should enhance the clinical application of spinal cord stimulation for the treatment of chronic intractable pain.

Publication Types:
- Clinical Trial
- Multicenter Study
- Randomized Controlled Trial

PMID: 12590681

Rating: 2c

North RB, Wetzel FT, Spinal cord stimulation for chronic pain of spinal origin: a valuable long-term solution, Spine. 2002 Nov 15;27(22):2584-91; discussion 2592

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STUDY DESIGN: A literature review was conducted. OBJECTIVE: To review the indications and efficacy of spinal cord stimulation, particularly in reference to chronic pain of spinal origin.

SUMMARY OF BACKGROUND DATA: The first spinal cord stimulation was implanted by Shealy in 1967 via a subarachnoid route. Early systems were plagued with a high rate of complications and technical problems. With the evolving technology, especially the advent of multichannel programmable systems and more precise epidural placement, the ability of spinal cord stimulation to treat various pain syndromes improved. This article reviews the literature on spinal cord stimulation from 1967 to the present. METHODS: The literature is reviewed, with a particular focus on recent studies investigating the efficacy of spinal cord stimulation for low back pain. RESULTS: Most studies are limited by the same flaws, namely, retrospective study design. At this writing, the few published randomized prospective studies have suggested that spinal cord stimulation may be superior to repeat surgery. Complication rates have declined to approximately 8%, and reoperation is necessary in approximately 4% of patients. When current percutaneous techniques are used, a lead migration rate lower than 3% may be achieved. For certain topographies, laminotomy leads may be superior, particularly with regard to low back pain. CONCLUSIONS: The ultimate efficacy of spinal cord stimulation remains to be determined, primarily because of limitations associated with the published literature. However, on the basis of the current evidence, it may represent a valuable treatment option, particularly for patients with chronic pain of predominantly neuropathic origin and topographical distribution involving the extremities. The potential treatment of other pain topographies and etiologies by spinal cord stimulation continues to be studied.

Publication Types:
- Review
- Review, Tutorial

PMID: 12435997

Rating: 5b

North RB, Kidd DH, Olin JC, Sieracki JM, Spinal cord stimulation electrode design: prospective, randomized, controlled trial comparing percutaneous and laminectomy electrodes-part I: technical outcomes, Neurosurgery. 2002 Aug;51(2):381-9; discussion 389-90

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OBJECTIVE: The clinical use of spinal cord stimulation for treatment of chronic intractable pain has been increasingly successful because of recent technical improvements, particularly the development of multiple-contact electrodes supported by programmable implanted pulse generators. Contemporary electrodes can be placed percutaneously in some cases and require a limited laminectomy in other cases. METHODS: We performed a prospective, randomized, controlled trial comparing two prototypical electrode designs, using a computerized system that allows direct patient interaction and quantitative measurements. A series of 24 patients with chronic lumbosacral pain syndromes first underwent testing

with percutaneous four-contact electrodes and then underwent implantation, at the same spinal level, of one of two different electrode configurations; 12 patients received a new percutaneous four-contact electrode of the same design and 12 received an insulated four-contact array, which was implanted via laminectomy. RESULTS: The insulated array performed significantly (P = 0.0005-0.0047) better than the temporary percutaneous electrode for the same patients, according to all three measures tested (ratings of paresthesia coverage of pain, coverage calculated from patient drawings, and amplitudes), at the "usage" amplitude for the three standard bipoles examined. The insulated array also performed significantly (P = 0.0000-0.026) better than the permanent percutaneous electrode in terms of coverage ratings and amplitude requirements. Low back coverage ratings were significantly better for the insulated array than for the temporary percutaneous electrode, and scaled amplitudes necessary for low back coverage were significantly better for the permanent percutaneous electrode than for the temporary electrode. In comparison with the percutaneous temporary electrode, at subjectively identical stimulation intensities, the permanent insulated array required significantly lower amplitude. CONCLUSION: We can immediately infer from these technical data that the use of an insulated array, in comparison with a percutaneous electrode, would double battery life. Extended follow-up monitoring will be required to assess the extent to which the technical advantages we observed for the insulated array might be associated with improved clinical outcomes.

Publication Types:
- Clinical Trial
- Evaluation Studies
- Randomized Controlled Trial

PMID: 12182776

Rating: 2c

North RB et al, Spinal Cord Stimulator Adjustment to Maximize Implanted Battery Longevity: A Randomized, Controlled Trial Using a Computerized, Patient-Interactive Programmer, Neuromodulation, Volume: 7, 2004, Issue: 1, January 2004

Richard B. North, David D. Brigham, Alexander Khalessi, Sherri-Kae Calkins, Steven Piantadosi, David S. Campbell, Michael John Daly, P. Bobby Dey, Giancarlo Barolat, Rod Taylor

Internally powered, implanted pulse generators (IPGs) have been an important advance in spinal cord stimulation for the management of pain, but they require surgical replacement, with attendant cost and risk, when the implanted battery is depleted. Battery life is determined by the programmed settings of the implant, but until now the technical means to optimize settings for maximal battery life, delaying surgical replacement as long as possible,

Materials and Methods.

We have developed a patient-interactive, computerized programmer for use with IPGs. It has been designed for easy operation and comprehensive data management, which have not been features of the standard programmers available until now. It automatically and rapidly presents to the patient a sequence of settings (contact combinations and pulse parameters) specified by the practitioner. Test results are analyzed and sorted to determine the optimal settings by multiple criteria, including battery life. In the present study we used new, improved algorithms to estimate battery life.

We have compared the computerized, patient-interactive system with standard practitioner-operated, manual programming methods in a randomized, controlled trial in 44 patients at two study centers. In 95% of patients (41/43), the computerized, patient-interactive system identified new settings with improved estimated battery life (and corresponding anticipated cost savings) which had not been recognized as such using manual methods. The estimated battery life for the setting chosen by each patient using manual methods averaged 25.4 ± 49.5 (mean ± standard deviation) months; the longest battery life identified by computerized methods averaged 55.0 ± 71.7, a 2.2-fold or 29.6 month improvement. Seventy-two percent of patients (31/43) achieved better battery life at settings with technical results (visual analog scale rating of overlap or coverage of pain by stimulation paresthesias) equal or superior to those achieved by manual methods. The overall improvement over the setting chosen by manual methods was 1.41-fold or 10.5 months; averaged by patient, the improvement was 1.63-fold. Estimated cost savings averaged just over one-third. As reported previously, the new system also yields significantly ($p < 0.0001$) better technical results than traditional, manual methods in achieving coverage of pain by stimulation paresthesias; the very best technical results were achieved at some expense in estimated battery life (assuming the same frequency of use). We conclude that significant potential savings in longevity of the implanted battery are possible in the majority of patients with implanted spinal cord stimulators, but have not been realized until now for lack of appropriate methods. Computerized, patient-interactive programming addresses this problem and allows optimization of estimated battery life along with other treatment goals. Long-term clinical follow up will be required to establish the full magnitude of the resulting savings.

Rating: 2c

North RB, Kidd DH, Farrokhi F, Piantadosi SA. Spinal cord stimulation versus repeated lumbosacral spine surgery for chronic pain: a randomized, controlled trial. Neurosurgery. 2005; 56(1):98-106; discussion 106-7.

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OBJECTIVE: Persistent or recurrent radicular pain after lumbosacral spine surgery is often associated with nerve root compression and is treated by repeated operation or, as a last resort, by spinal cord stimulation (SCS). We conducted a prospective, randomized, controlled trial to test our hypothesis that SCS is more likely than reoperation to result in a successful outcome by standard measures of pain relief

and treatment outcome, including subsequent use of health care resources. METHODS: For an average of 3 years postoperatively, disinterested third-party interviewers followed 50 patients selected for reoperation by standard criteria and randomized to SCS or reoperation. If the results of the randomized treatment were unsatisfactory, patients could cross over to the alternative. Success was based on self-reported pain relief and patient satisfaction. Crossover to the alternative procedure was an outcome measure. Use of analgesics, activities of daily living, and work status were self-reported. RESULTS: Among 45 patients (90%) available for follow-up, SCS was more successful than reoperation (9 of 19 patients versus 3 of 26 patients, P <0.01). Patients initially randomized to SCS were significantly less likely to cross over than were those randomized to reoperation (5 of 24 patients versus 14 of 26 patients, P=0.02). Patients randomized to reoperation required increased opiate analgesics significantly more often than those randomized to SCS (P <0.025). Other measures of activities of daily living and work status did not differ significantly. CONCLUSION: SCS is more effective than reoperation as a treatment for persistent radicular pain after lumbosacral spine surgery, and in the great majority of patients, it obviates the need for reoperation.

Publication Type:
Clinical Trial

PMID: 15617591

Rating: 2c

North RB. Spinal Cord Stimulation Provides Long-Term Relief in Failed-Back-Surgery Syndrome. American Academy of Pain Medicine 24th Annual Meeting: Abstract 198. 2008.

February 15, 2008 (Kissimmee, FL) — Results of a randomized trial suggest that implanting a device that delivers electric impulses to the spine may offer long-term relief to patients with failed–back-surgery syndrome (FBSS). Patients with FBSS continue to experience persistent or recurrent pain, disability, and reduced quality of life despite anatomically successful lumbosacral spine surgery, the authors, led by Richard B. North, MD, from LifeBridge Brain & Spine Institute, in Baltimore, Maryland, note. In this trial, compared with conventional treatment alone, the addition of spinal cord stimulation improved pain relief, health-related quality of life, and functionality in predominantly neuropathic back-surgery patients at 6 months. In a subset of patients treated longer term, study results suggest that spinal cord stimulation can maintain significant pain relief over 24 months. The findings, from the multicenter PROCESS trial, were presented here at the American Academy of Pain Medicine 24th Annual Meeting. "This is the most gratifying procedure I perform," Dr. North told Medscape Neurology & Neurosurgery. He feels the future of spinal cord stimulation will be even more promising as the implantable devices continue to improve, becoming, for example, more compact. The study included 100 patients with persistent neuropathic pain predominantly in the legs — some in the lower back — despite successful lumbosacral spine surgery, and randomized them to receive conventional medical management or conventional medical management plus spinal cord stimulation. The primary outcome variable in this

study was greater than 50% leg pain relief at 6 months. Secondary outcomes assessed were functional capacity, health-related quality of life (HRQoL), patient satisfaction, and adverse effects. At 6 months, in an intention-to-treat (ITT) analysis, patients randomized to spinal cord stimulation had 9 times the odds of achieving the primary end point, the authors write. Compared with conventional treatment alone, spinal cord stimulation patients experienced improved functionality, improved HRQoL in 7 of 8 domains, and greater satisfaction in pain relief provided by their treatment. At 6 months, 32 patients (73%) in the conventional-treatment group requested to switch to spinal cord stimulation — compared with 5 patients (10%) in the spinal cord group who crossed over to conventional management. Current results focused on the subset of 42 patients who were randomized to spinal cord stimulation and continued with that treatment for 2 years. For these patients, the researchers report statistically significant improvements (P < .001) at 24 months in all pain, quality-of-life, and function outcomes. Over the 24 months, 25% of 87 patients receiving an electrode experienced a device-related complication requiring additional surgery, they note. Funding was provided by Medtronic. Dr. North reports no relevant financial relationships.

Rating: 10b

North RB, Kidd D, Shipley J, Taylor RS. Spinal cord stimulation versus reoperation for failed back surgery syndrome: a cost effectiveness and cost utility analysis based on a randomized, controlled trial. Neurosurgery. 2007 Aug;61(2):361-8; discussion 368-9.

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OBJECTIVE: We analyzed the cost-effectiveness and cost-utility of treating failed back-surgery syndrome using spinal cord stimulation (SCS) versus reoperation. MATERIALS AND METHODS: A disinterested third party collected charge data for the first 42 patients in a randomized controlled crossover trial. We computed the difference in cost with regard to success (cost-effectiveness) and mean quality-adjusted life years (cost-utility). We analyzed the patient-charge data with respect to intention to treat (costs and outcomes as a randomized group), treated as intended (costs as randomized; crossover failure assigned to a randomized group), and final treatment costs and outcomes. RESULTS: By our mean 3.1-year follow-up, 13 of 21 patients (62%) crossed to reoperation versus 5 of 19 patients (26%) who crossed to SCS (P < 0.025). The mean cost per success was US $117,901 for crossovers to SCS. No crossovers to reoperation achieved success despite a mean per-patient expenditure of US $260,584. The mean per-patient costs were US $31,530 for SCS versus US $38,160 for reoperation (intention to treat), US $48,357 for SCS versus US $105,928 for reoperation (treated as intended), and US $34,371 for SCS versus US $36,341 for reoperation (final treatment). SCS was dominant (more effective and less expensive) in the incremental cost-effectiveness ratios and incremental cost-utility ratios. A bootstrapped simulation for incremental costs and quality-adjusted life years confirmed SCS's dominance, with approximately 72% of the cost results occurring below US policymakers' "maximum willingness to pay" threshold. CONCLUSION: SCS was less expensive and more effective than

reoperation in selected failed back-surgery syndrome patients, and should be the initial therapy of choice. SCS is most cost-effective when patients forego repeat operation. Should SCS fail, reoperation is unlikely to succeed.

PMID: 17762749

Rating: 4b

Nouwen A. EMG biofeedback used to reduce standing levels of paraspinal muscle tension in chronic low back pain. Pain. 1983 Dec;17(4):353-60.

Twenty chronic low back pain (LBP) patients with relatively high standing paraspinal EMG levels (greater than 5 microV) were randomly assigned to 2 groups. One group (N = 10) received EMG biofeedback training to reduce standing paraspinal EMG levels, the other group (N = 10) served as a waiting list control group. Changes in perceived pain (duration X intensity) and paraspinal EMG in standing position were measured at a 3 week pretreatment baseline, during the 3 week treatment period, and at a 3 week post-treatment baseline. Compared to patients in the waiting list control group, those who received EMG biofeedback showed a significant decrease in standing paraspinal EMG from pretreatment to post-treatment baseline. However, no significant differences in reported pain were found during these periods. It is concluded that reduction of standing paraspinal EMG does not lead to reduction in pain.

PMID: 6229707

Rating: 2c

Novak S, Nemeth WC, Lawson KA. Trends in medical use and abuse of sustained-release opioid analgesics: a revisit. Pain Med. 2004 Mar;5(1):59-65.

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OBJECTIVE: Previous literature suggests that increases in the medical use of opioids over the early 1990s did not contribute to increased morbidity secondary to opioid abuse. Our objective was to evaluate the period 1997-2001 to analyze trends in medical use and medical abuse of three classes of opioid analgesics that are commonly used in sustained-release formulations: fentanyl, morphine, and oxycodone. DESIGN AND SETTING: A retrospective analysis of the Drug Abuse Warning Network (DAWN) database and the Automation of Reports and Consolidated Orders System (ARCOS) database for the years 1997-2001 was used for this study. RESULTS: The analysis of the DAWN database showed that there was an 83.5% increase in all opioid analgesic mentions from 1997 to 2001. Mentions involving any fentanyl compound increased 249.8%, any morphine compound increased 161.8%, and

any oxycodone-containing compound increased 267.3%. Mentions of each of these three classes of opioids remained less than 2% of all total drug mentions per year for each year studied. Medical use of the selected opioid classes, as reported in the ARCOS database and measured by grams distributed, all increased substantially (fentanyl 151.2%, morphine 48.8%, oxycodone 347.9%). CONCLUSION: Using this method of analysis, the rates of drug abuse, and resultant morbidity secondary to the use of opioid analgesics, remain low in spite of the increase in medical use of these substances. Copyright American Academy of Pain Medicine

PMID: 14996238

Rating: 4a

Novak S, Nemeth WC. How clinically relevant is a meta-analysis of electrical nerve stimulation when based on heterogeneous disease states? Pain. 2007 Sep;131(1-2):228-9; author reply 229-30. Epub 2007 Jul 26.

Comment on: Johnson M, Martinson M. Efficacy of electrical nerve stimulation for chronic musculoskeletal pain: A meta-analysis of randomized controlled trials. Pain. 2007 Jul;130(1-2):157-65.

PMID: 17662532

Rating: 11b

A recent meta-analysis by Johnson and Martinson came to the conclusion that electrical nerve stimulation (ENS) for the treatment of chronic musculoskeletal pain provided effective treatment for this condition (Johnson and Martinson, 2007). Multiple studies were included that utilized ENS for pain due to musculoskeletal origin. Any modality of ENS could be utilized. The proposed mechanisms of action for ENS given were the gate control theory and/or the release of endogenous endorphins. Any anatomic location could be represented based on the rationale that "mechanism, rather than anatomical location of pain, is likely to be a critical factor for therapy." This statement was made based on an editorial published by Woolf et al. (Woolf et al., 1998). Multiple underlying disease states were combined for this meta-analysis, including rheumatoid arthritis, osteoarthritis, chronic low back pain, ankylosing spondylitis, and myofascial trigger points. Apparent in such a wide range of disease conditions is the diversity and interdependence of multiple possible pain mechanisms.
The authors of a recent systematic review for the use of transcutaneous electrical nerve stimulation for chronic low-back pain (a specific anatomic study using a specific modality) were unwilling to perform a meta-analysis due to heterogeneity of published research in terms of study design, methodological quality, sample size, study population, stimulation mode, method of application, treatment duration and concurrent interventions. (Khadikar et al., 2005) These authors noted pain was a multidimensional experience that had both "peripheral and central substrates." They also noted that particular subgroups

with chronic low back pain might better respond to TENS than others, and that clarifying the underlying pathophysiological mechanisms of pain would help to promote more uniform study populations. There are certainly different philosophies of how the use of ENS should be evaluated. However, based on this analysis, it is unclear as to how helpful this study is for recommendations for clinical treatment. Musculoskeletal pain does have multiple pathophysiological mechanisms (nociceptive, neuropathic, central, etc.) which would appear to prohibit a generalization that is useful for a meta-analysis of this type. The grouping of inflammatory disease states into the study population mix is particularly troublesome due to the acute nociceptive pain features concomitant in this chronic disease state. It would therefore appear that due to the tremendous heterogeneity of the analyzed studies that a statement as strong as "ENS is an effective treatment modality for chronic musculoskeletal pain" overextends the final interpretation of this statistical analysis.

Oakley JC, Prager JP, Spinal cord stimulation: mechanisms of action, Spine. 2002 Nov 15;27(22):2574-83.

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STUDY DESIGN: A literature review and synthesis were performed. OBJECTIVE: To present the current understanding of the mechanisms of spinal cord stimulation in relation to the physiology of pain. SUMMARY OF BACKGROUND DATA: Spinal cord stimulation has been used for more than 30 years in the armamentarium of the interventional pain specialist to treat a variety of pain syndromes. Traditionally used for persisting leg pain after lumbar spinal surgery, it has been applied successfully in the treatment of angina pectoris, ischemic pain in the extremity, complex regional pain syndrome Types 1 and 2, and a variety of other pain states. This review presents the current status of what is known concerning how electrical stimulation of the spinal cord may achieve pain relief. METHODS: A literature review was conducted. RESULTS: The literature supports the theory that the mechanism of spinal cord stimulation cannot be completely explained by one model. It is likely that multiple mechanisms operate sequentially or simultaneously. CONCLUSION: Some clinical or experimental support can be found in the literature for 10 specific mechanisms or proposed mechanisms of spinal cord stimulation.

Publication Types:
- Review
- Review, Tutorial

PMID: 12435996

Rating: 5c

Ohnmeiss DD, Rashbaum RF, Patient satisfaction with spinal cord stimulation for predominant complaints of chronic, intractable low back pain, Spine J. 2001 Sep-Oct;1(5):358-63.

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BACKGROUND CONTEXT: Results of subsequent surgical intervention in patients with intractable pain after lumbar spine surgery are typically worse than for initial surgery, particularly in those with predominant complaints of back pain rather than lower extremity pain. Spinal cord stimulation (SCS) has been found to yield good results in patients with primary complaints of intractable lower extremity pain. Technological advances have broadened the indications for this treatment. PURPOSE: The purpose of this study was to evaluate patient satisfaction after SCS in the treatment of patients with predominant complaints of chronic, intractable, low back pain. STUDY DESIGN/SETTING: Data were collected from retrospective chart review and patient follow-up questionnaire. Patients were treated at a spine specialty center. PATIENT SAMPLE: The study group consisted of the consecutive series of our first 41 patients who underwent SCS for predominant complaints of low back pain. The mean symptom duration was 82.9 months, and the mean age was 47.9 years (range, 28-83 years). All but three patients had previously undergone lumbar spine surgery (mean, 2.3 prior surgeries). OUTCOME MEASURES: At the time of follow-up (5.5-19 months after SCS implantation), patients completed questionnaires assessing their satisfaction with their outcome, if they would have the procedure again knowing what their outcome would be and if they would recommend SCS to someone with similar problems. In determining outcome, a negative response was assigned for patients who had the device removed. A worst-case analysis was also conducted in which a negative response was assigned for patients lost to follow-up or who failed to respond to a particular question. Data were also collected on complications and re-operations. METHODS: All trial stimulation procedures were performed under local anesthetic with the patient providing feedback concerning pain relief achieved with various lead placements and settings. If one lead did not provide acceptable relief in all the areas needed, placement of a second lead was pursued. If the patient failed to maintain acceptable pain relief (> or =50% pain relief) during a multiday trial period, the leads were removed. If adequate relief was maintained during the trial period, the receiver was implanted. RESULTS: Responses to the follow-up questionnaire indicated that 60% of patients considered themselves improved from their preoperative condition and the remaining 40% did not; 78.1% of patients would recommend SCS to someone with similar problems, 69.0% were satisfied, 75.0% would have the procedure performed again if they had known their outcome before implantation. Among the 36 patients in whom the system was implanted, it was later removed in 4 because of lack of sufficient pain relief. Other re-operations included repositioning of the leads to regain pain relief in the areas needed, replacement of a malfunctioning unit and revision of lead extension wires. CONCLUSIONS: In this retrospective study, the majority of patients were satisfied with the results of SCS and would have the procedure again knowing what their outcome would be. These results suggest that further investigation of SCS is warranted in this difficult to treat patient population presenting with predominant complaints of chronic, intractable, axial low back pain.

PMID: 14588316

Rating: 4b

Olesen J, Bousser MG, Diener HC, Dodick D, First M, Goadsby PJ, Göbel H, Lainez MJ, Lance JW, Lipton RB, Nappi G, Sakai F, Schoenen J, Silberstein SD, Steiner TJ, Headache Classification Committee. New appendix criteria open for a broader concept of chronic migraine. Cephalalgia. 2006; 26:742-6.

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After the introduction of chronic migraine and medication overuse headache as diagnostic entities in The International Classification of Headache Disorders, Second Edition, ICHD-2, it has been shown that very few patients fit into the diagnostic criteria for chronic migraine (CM). The system of being able to use CM and the medication overuse headache (MOH) diagnosis only after discontinuation of overuse has proven highly unpractical and new data have suggested a much more liberal use of these diagnoses. The International Headache Classification Committee has, therefore, worked out the more inclusive criteria for CM and MOH presented in this paper. These criteria are included in the appendix of ICHD-2 and are meant primarily for further scientific evaluation but may be used already now for inclusion into drug trials, etc. It is now recommended that the MOH diagnosis should no longer request improvement after discontinuation of medication overuse but should be given to patients if they have a primary headache plus ongoing medication overuse. The latter is defined as previously, i.e. 10 days or more of intake of triptans, ergot alkaloids mixed analgesics or opioids and 15 days or more of analgesics/NSAIDs or the combined use of more than one substance. If these new criteria for CM and MOH prove useful in future testing, the plan is to include them in a future revised version of ICHD-2.

PMID: 16686915

Rating: 5b

Ontario Workplace Safety and Insurance Board. Report of the Chronic Pain Expert Advisory Panel. Ontario: Ontario Workplace Safety and Insurance Board 2000.

Chronic Pain Study. One of the most comprehensive studies ever done on work-related chronic pain has resulted in guidelines that will help workers and employers reach healthier outcomes in the workplace. The two-year, independent study was commissioned by the WSIB, and was carried out by scientific experts and representatives from Ontario's employer and worker communities. The report contains four recommendations that will be implemented by the WSIB:
1. The Workplace Safety and Insurance Act and the WSIB will treat chronic pain the same way they treat any other injury.

2. The WSIB will investigate and report on the panels' recommendations for more effective treatment, management, and return to work strategies, and a revised approach to rating permanent impairment.
3. The WSIB will conduct a review in five years to assess the effectiveness of any prevention and management strategies that were implemented as a result of the Initiative,
any new scientific evidence about the work-relatedness of chronic pain, and
any developments in the courts concerning compensation law.
4. The WSIB will support continued research into the treatment and management of chronic pain.

To obtain copies of the Report of the Chronic Pain Policy Advisory Panel and the Report of the Chronic Pain Expert Advisory Panel, both published February 2000, call 416-344-4365 or e-mail modpb@wsib.on.ca.

Rating: 8a

Osenbach RK, Harvey S. Neuraxial infusion in patients with chronic intractable cancer and noncancer pain. Curr Pain Headache Rep. 2001 Jun;5(3):241-9.

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Ever since the application in 1980 of morphine for spinal analgesia in patients with refractory cancer pain, spinal infusion therapy has become one of the cornerstones for the management of chronic, medically intractable pain. Initially, spinal infusion therapy was indicated only for patients with cancer pain that could not be adequately controlled with systemic narcotics. However, over the past decade, there has been a significant increase in the number of pumps implanted for the treatment of nonmalignant pain. Indeed, "benign" pain syndromes, particularly failed back surgery syndrome, are the most common indication for intrathecal opiates. As we have gained more experience with this therapy, it has become apparent that even intrathecal opiates, when administered in the long term, can be associated with problems such as tolerance, hyperalgesia, and other side effects. Consequently, long-term efficacy has not been as significant as had been hoped. Because of the difficulties associated with long-term intrathecal opiate therapy, much of the research, both basic and clinical, has focused on developing alternative nonopioid agents to be used either alone or in combination with opiates. Clinical trials have been and continue to be conducted to evaluate drugs such as clonidine, SNX-111, local anesthetics, baclofen, and many other less common agents to determine their efficacy and potential toxicity for intrathecal therapy. This article reviews the agents developed as alternatives to intrathecal opiates.

Publication Types:
- Review
- Review, Tutorial

PMID: 11309212

Rating: 5b

Ostelo RW, van Tulder MW, Vlaeyen JW, Linton SJ, Morley SJ, Assendelft WJ. Behavioural treatment for chronic low-back pain. Cochrane Database Syst Rev. 2005 Jan 25;(1):CD002014.

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BACKGROUND: Behavioural treatment, commonly used in the treatment of chronic low-back pain (CLBP), is primarily focused at reducing disability through the modification of environmental contingencies and cognitive processes. In general, three behavioural treatment approaches are distinguished: operant, cognitive and respondent. OBJECTIVES: To determine if behavioural therapy is more effective than reference treatments for CLBP, and which type of behavioural treatment is most effective. SELECTION CRITERIA: Only randomised trials on behavioural treatment for non-specific CLBP were included. MAIN RESULTS: Seven studies (33%) were considered high quality. Comparing behavioural treatment to waiting list control (WLC) revealed strong evidence (4 trials, 134 people) in favour of a combined respondent-cognitive therapy for a medium positive effect on pain, and moderate evidence (2 trials, 39 people) in favour of progressive relaxation for a large positive effect on pain and behavioural outcomes (short-term only). When comparing operant treatment to WLC no significant differences could be detected on general functional status (strong evidence: 2 trials, 87 people) or on behavioural outcomes (moderate evidence; 3 trials, 153 people) (short-term only). There is limited evidence (1 trial, 98 people) that a graded activity program in an industrial setting is more effective than usual care for early return to work and reduced long-term sick leave. There is limited evidence (1 trail, 39 people) that there are no differences between behavioural treatment and exercises. Finally, there is moderate evidence (6 trials, 210 people) that there are no significant differences in short-term and long-term effectiveness when behavioural components are added to usual treatment programs for CLBP (i.e. physiotherapy, back education) on pain, generic functional status and behavioural outcomes. AUTHORS' CONCLUSIONS: Combined respondent-cognitive therapy and progressive relaxation therapy are more effective than WLC on short-term pain relief. However, it is unknown whether these results sustain in the long term. No significant differences could be detected between behavioural treatment and exercise therapy. Whether clinicians should refer patients with CLBP to behavioural treatment programs or to active conservative treatment cannot be concluded from this review.

PMID: 15674889

Rating: 1a

Otis JD, Macdonald A, Dobscha SK. Integration and coordination of pain management in primary care. J Clin Psychol. 2006 Aug 25; [Epub ahead of print]

VA Boston Healthcare System and Boston University.

Pain is one of the most common symptoms reported to primary care providers and has significant implications for health care costs. The primary aim of this article is to describe and illustrate how to integrate the treatment of chronic pain in the primary care setting. First, we address the integration and coordination of care between mental health and primary care. We then present a typical case and discuss the patient's treatment, outcome, and prognosis. The article concludes with a discussion of issues that frequently arise when integrating psychological treatment for pain in primary care settings. (c) 2006 Wiley Periodicals, Inc. J Clin Psychol: In Session.

PMID: 16937344

Rating: 5b

Otto MW, Tuby KS, Gould RA, McLean RY, Pollack MH. An effect-size analysis of the relative efficacy and tolerability of serotonin selective reuptake inhibitors for panic disorder. Am J Psychiatry. 2001;158:1989-92.

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OBJECTIVE: Serotonin selective reuptake inhibitors (SSRIs) are now considered the first-line pharmacotherapy for panic disorder. The preferential use and the presumption of greater tolerability of SSRIs relative to older agents, such as tricyclic antidepressants, occurred without direct comparisons between the two classes of medication. In this study the authors used an effect-size analysis to provide an initial comparison. METHOD: The authors conducted an effect-size analysis of 12 placebo-controlled, efficacy trials of SSRIs for panic disorder and compared these results to findings obtained in a recent meta-analysis of non-SSRI treatments for panic disorder. RESULTS: The mean effect size for acute treatment outcome for SSRIs relative to placebo was 0.55, not significantly different from that for antidepressants in general (0.55) and for imipramine in particular (0.48). More recent studies of SSRIs, and studies using larger samples, were associated with lower effect sizes. No significant differences were found in dropout rates between those taking SSRIs and those taking older agents during acute treatment. CONCLUSIONS: An effect-size analysis of controlled studies of treatments for panic disorder revealed no significant differences between SSRIs and older antidepressants in terms of efficacy or tolerability in short-term trials. An inverse relationship was evident between sample size and effect size for SSRIs. Early studies of small samples may have led to initial overestimations of the efficacy of SSRIs for panic disorder.

PMID: 11729014

Rating: 1b

Page, S., et al. Exogenous Testosterone (T) alone or with Finasteride Increases Physical Performance, Grip Strength, and Lean Body Mass in Older Men with Low Serum T. Journal of Clinical Endocrinology & Metabolism, Volume 90, Number 3, 1502-1510. 2005.

Rating: 2b

Quality: Intermediate. Total Rating: 7.0. Comment: Study looks at an older population of men than typically represented in the Work Comp setting 70+. Has a high dropout rate. However, it does score high in areas of randomization and blinding. In the end it finds that Exogenous Testosterone therapy and Exogenous Testosterone therapy with Finasteride Increases Physical Performance and can increase physical function in older men with low levels of serum Testosterone. [CA DWC]

Paice JA, Winkelmuller W, Burchiel K, Racz GB, Prager JP. Clinical realities and economic considerations: efficacy of intrathecal pain therapy. J Pain Symptom Manage. 1997 Sep;14(3 Suppl):S14-26.

Rush Neuroscience Institute, Rush Medical Center, Chicago, Illinois 60612, USA.

Studies of analgesia in cancer patients have revealed that intrathecal administration of opioids can deliver potent analgesia with fewer systemic side effects than equivalent doses of systemic opioids. In addition, several trials have examined the safety and efficacy of this modality in patients with pain of nonmalignant origin. In one survey of 35 physicians involving 429 patients treated with intrathecal therapy, physician reports of global pain relief scores were excellent in 52.4% of patients, good in 42.9%, and poor in 4.8%. In another study of 120 patients, the mean pain intensity score had fallen from 93.6 to 30.5 six months after initiation of therapy. In both studies, patients reported significant improvement in activities of daily living, quality of life measures, and satisfaction with the therapy. Constipation, urinary retention, nausea, vomiting, and pruritus are typical early adverse effects of intrathecal morphine and are readily managed symptomatically. Other potential adverse effects include amenorrhea, loss of libido, edema, respiratory depression, and technical issues with the intrathecal system.

Publication Types:
Systematic review

PMID: 9291707

Rating: 1b

Pandey CK, Navkar DV, Giri PJ, Raza M, Behari S, Singh RB, Singh U, Singh PK. Evaluation of the optimal preemptive dose of gabapentin for postoperative pain relief after lumbar diskectomy: a randomized, double-blind, placebo-controlled study. J Neurosurg Anesthesiol. 2005 Apr;17(2):65-8.

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We evaluated the optimal preemptive dose of gabapentin for postoperative pain relief after single-level lumbar diskectomy and its effect on fentanyl consumption during the initial 24 hours in a randomized, double-blinded, placebo-controlled study in 100 patients with American Society of Anesthesiologists physical status I and II. Patients were divided into five groups to receive placebo or gabapentin 300, 600, 900, or 1200 mg 2 hours before surgery. After surgery, patients were transferred to the postanesthesia care unit (PACU). A blinded anesthesiologist recorded the pain scores at time points of 6, 12, 18, and 24 hours in the PACU on a Visual Analog Scale (VAS; 0-10 cm) at rest. Patients received patient-controlled analgesia (fentanyl 1.0 mug/kg on each demand with lockout interval of 10 minutes); total fentanyl consumption during initial 24 hours was recorded. Data were entered into the statistical software package SPSS 9.0 for analysis (one-way analysis of variance and Student-Newman-Keuls test). Patients who received gabapentin 300 mg had significantly lower VAS score at all time points. They consumed less fentanyl (patients who received placebo processed 1217.5 +/- 182.0 versus 987.5 +/- 129.6 mug; $P < 0.05$). Patients who received gabapentin 600, 900, and 1200 mg had lower VAS scores at all time points than patients who received gabapentin 300 mg ($P < 0.05$). Increasing the dose of gabapentin from 600 to 1200 mg did not decrease the VAS score, nor did the increasing dose of gabapentin significantly decrease fentanyl consumption (702.5, 635, and 626.5 microg). Thus, gabapentin 600 mg is the optimal dose for postoperative pain relief following lumbar diskectomy.

PMID: 15840990

Rating: 2b

Paraskevas KI, Michaloglou AA, Briana DD, Samara M. Treatment of complex regional pain syndrome type I of the hand with a series of intravenous regional sympathetic blocks with guanethidine and lidocaine. Clin Rheumatol. 2005 Dec 7;:1-7.

Department of Vascular Surgery, Athens University Medical School, Athens, Greece.

The aim of this study was to evaluate the efficacy of guanethidine and lidocaine in the treatment of complex regional pain syndrome (CRPS) type I of the hand. Seventeen patients, aged between 33 and 72 years, suffering from CRPS type I of the hand received two series of intravenous regional sympathetic block (Bier's block) sessions with guanethidine and lidocaine according to the following therapeutic protocol: (1) 5 sessions (once every second day) composed of intravenous regional administration of 15 mg guanethidine and 1 mg lidocaine/kg body weight each and (2) 20 sessions (twice a week) composed

of intravenous regional administration of 10 mg guanethidine and 1 mg lidocaine/kg body weight each. Complete disappearance of pain and return of the normal function and movement of the extremity were achieved. No side effects were observed. The above-described therapeutic protocol method resulted in excellent pain relief and full restoration of both function and range of movement of the affected extremity in 17 patients suffering from CRPS type I of the hand.

PMID: 16333562

Rating: 4c

Passik SD, Weinreb HJ. Managing chronic nonmalignant pain: overcoming obstacles to the use of opioids. Adv Ther. 2000 Mar-Apr;17(2):70-83.

Oncology Symptom Control Research, Community Cancer Care, Inc., Indianapolis, IN 46202, USA.

Physicians involved in cancer pain management treat thousands of patients with opioids, whose effective analgesia improves overall functioning. Side effects generally are tolerable, and treatment can be maintained with stable doses for long periods. Problems with addiction are infrequent. Many physicians, however, assume that opioids should be used only for chronic malignant pain. Research and clinical experience have demonstrated that opioids can safely and effectively relieve most chronic moderate to severe nonmalignant pain. Fears of addiction, disciplinary action, and adverse effects result in ineffective pain management. With current information on the use of opioids in chronic nonmalignant pain, primary care physicians can overcome these obstacles. Guidelines must clearly define the role of the primary care physician in the proper management of pain and the integration of opioid therapy. Used appropriately, opioids may represent the only source of relief for many patients.

PMID: 11010058

Rating: 5c

The 4 A's for Ongoing Monitoring
Four domains have been proposed as most relevant for ongoing monitoring of chronic pain patients on opioids: pain relief, side effects, physical and psychosocial functioning, and the occurrence of any potentially aberrant (or nonadherent) drug-related behaviors. These domains have been summarized as the "4 A's" (analgesia, activities of daily living, adverse side effects, and aberrant drug-taking behaviors). The monitoring of these outcomes over time should affect therapeutic decisions and provide a framework for documentation of the clinical use of these controlled drugs. To test this notion, Passik and colleagues conducted a study to examine the relationship between aberrant drug-taking behaviors and pain outcomes during long-term treatment with opioids for nonmalignant pain. In particular, the focus of the study was on providing the nature, frequency, and predictive value of drug-taking behaviors in pain management. This effort could ultimately assist physicians in the assessment and management of

these behaviors, whether they resulted from the undertreatment of pain or a substance use disorder. The main objective of the study was to develop a user-friendly checklist that physicians could employ to examine the 4 A's. In addition, it was hoped that this checklist could also be used to monitor pain and treatment outcomes for patients receiving long-term opioid therapy for chronic pain. The checklist was developed by a group of experts in pain and addiction medicine and distributed to participating physicians throughout the United States who treat pain patients. These physicians evaluated patients who had been receiving opioid therapy for at least a period of 3 months with a structured interview approach and clinical observations. Cross-sectional results suggested that the majority of patients with chronic pain achieve relatively positive outcomes in the eyes of their prescribing physicians in all 4 relevant domains with opioid therapy. Analgesia was modest but meaningful, functionality generally stabilized or improved, and side effects were tolerable. Potentially aberrant behaviors were common (44.6% of the sample engaged in at least 1 aberrant behavior), but only viewed as an indicator of a problem (ie, addiction or diversion) in approximately 10% of cases. Thus, there is a clear need to document and assess the intricacies of aberrant drug-taking behavior in chronic pain patients.

Patrick LE, Altmaier EM, Found EM. Long-term outcomes in multidisciplinary treatment of chronic low back pain: results of a 13-year follow-up. Spine. 2004 Apr 15;29(8):850-5.

Northwest Occupational Medicine Center, Portland, OR 97223, USA. lpatrick@nwomc.com

STUDY DESIGN: Patients completing a multidisciplinary pain treatment were contacted to obtain 13-year follow-up information on pain, mood, employment, and general health. OBJECTIVES: Study objectives were to determine if post-treatment improvements were maintained over a lengthy follow-up period and to compare patients' general health to norms of comparably aged persons. SUMMARY OF BACKGROUND DATA: Although many studies have demonstrated the short-term effectiveness of multidisciplinary pain treatment programs for chronic low back pain, few studies have documented that these treatment gains are maintained over time. Only two studies have reported patient outcomes on a long-term basis (10+ years). Those studies have documented that patient gains during treatment are generally maintained during follow-up. METHODS: An attempt was made to contact all patients completing an inpatient chronic back pain rehabilitation program at the University of Iowa's Spine Diagnostic and Treatment Center. Of the 45 participants, 28 were located and 26 agreed to participate in a telephone interview. Analyses of pretreatment and posttreatment data revealed these follow-up participants did not differ from the larger study sample. RESULTS: Patients maintained their treatment gains in all areas (pain intensity and interference, negative mood). Additionally, patients showed levels of general health comparable to similarly aged peers with the exceptions of pain (more pain) and physical functioning (lower functioning, more pain interference). More than half the sample was employed; of those not employed, few reported this was due to pain. CONCLUSIONS: The data lend support to the long-term effectiveness of multidisciplinary treatment programs for chronic low back pain.

PMID: 15082983

Rating: 4c

Pavelka K, Gatterova J, Olejarova M, Machacek S, Giacovelli G, Rovati LC, Glucosamine sulfate use and delay of progression of knee osteoarthritis: a 3-year, randomized, placebo-controlled, double-blind study, Arch Intern Med. 2002 Oct 14;162(18):2113-23.

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BACKGROUND: Conventional symptomatic treatments for osteoarthritis do not favorably affect disease progression. The aim of this randomized, placebo-controlled trial was to determine whether long-term (3-year) treatment with glucosamine sulfate can modify the progression of joint structure and symptom changes in knee osteoarthritis, as previously suggested. METHODS: Two hundred two patients with knee osteoarthritis (using American College of Rheumatology criteria) were randomized to receive oral glucosamine sulfate, 1500 mg once a day, or placebo. Changes in radiographic minimum joint space width were measured in the medial compartment of the tibiofemoral joint, and symptoms were assessed using the algo-functional indexes of Lequesne and WOMAC (Western Ontario and McMaster Universities). RESULTS: Osteoarthritis was of mild to moderate severity at enrollment, with average joint space widths of slightly less than 4 mm and a Lequesne index score of less than 9 points. Progressive joint space narrowing with placebo use was -0.19 mm (95% confidence interval, -0.29 to -0.09 mm) after 3 years. Conversely, there was no average change with glucosamine sulfate use (0.04 mm; 95% confidence interval, -0.06 to 0.14 mm), with a significant difference between groups (P =.001). Fewer patients treated with glucosamine sulfate experienced predefined severe narrowings (>0.5 mm): 5% vs 14% (P =.05). Symptoms improved modestly with placebo use but as much as 20% to 25% with glucosamine sulfate use, with significant final differences on the Lequesne index and the WOMAC total index and pain, function, and stiffness subscales. Safety was good and without differences between groups. CONCLUSION: Long-term treatment with glucosamine sulfate retarded the progression of knee osteoarthritis, possibly determining disease modification.

Publication Types:
- Clinical Trial
- Randomized Controlled Trial

PMID: 12374520

Rating: 2b

P-Codrea Tigaran S, Sidenius P, Dam M. Lamotrigine-induced rash--worth a rechallenge. Acta Neurol Scand. 2005 Mar;111(3):191-4.

Department of Neurology, Aahus University Hospital, Aahus, Denmark. simonacodrea@yahoo.com

METHODS: A total of 688 patients (350 as monotherapy, and 338 as add-on therapy) with either idiopathic generalized epilepsy or focal epilepsy were treated with LTG. The patients with LTG-induced rash were rechallenged to LTG. The dosage schedule was: 5 mg every day or every second day for 14 days, increased by 5 mg every 14th day to 25 mg a day. After achieving the daily dosage of 25 mg/day, the up-titration was completed following the current guidelines. RESULTS: Nineteen (38%) of the initial cohort were rechallenged with LTG, with a success rate of 84%. CONCLUSION: This study is the first one to provide a successful recipe verified in time for the rechallenge with LTG after the initial drug-induced rash.

PMID: 15736314

Rating: 4b

Peloso PM, Gross AR, Haines TA, Trinh K, Goldsmith CH, Aker P. Medicinal and injection therapies for mechanical neck disorders: a cochrane systematic review. J Rheumatol. 2006 May;33(5):957-67.

From Amgen Inc., Thousand Oaks, California, USA; and the Departments of Epidemiology and Biostatistics and Occupational Health and Safety, Schools of Rehabilitation Sciences and Medicine, McMaster University, Hamilton, Ontario, Canada.

OBJECTIVE: To systematically review randomized trials on medicines and injections used to improve pain, function/disability, and patient satisfaction in adults with mechanical neck disorders (MND) with or without associated headache or radicular findings. METHODS: We searched CENTRAL (Issue 4, 2002), and MEDLINE, EMBASE, MANTIS, CINHAL from their start to March 2003. Two authors independently selected articles, abstracted data, and assessed methodological quality using the Jadad criteria. When clinical heterogeneity was absent, we combined studies using random-effects metaanalysis models. RESULTS: Thirty-two selected trials had an overall methodological quality of mean 3.2/5. For acute whiplash, administering intravenous methylprednisolone within 8 hours reduced pain at one week [SMD -0.90 (95% CI -1.57 to -0.24)], and sick leave but not pain at 6 months compared to placebo. For chronic MND at short-term followup, intramuscular injection of lidocaine was superior to placebo [SMD 1.36 (95% CI -1.93 to -0.80)]. In chronic MND with radicular findings, epidural methylprednisolone and lidocaine reduced neck pain [SMD -1.46 (95% CI -2.16 to -0.76)] and improved function at one-year followup compared to the intramuscular route. In subacute/chronic MND, we found conflicting evidence for oral psychotropic agents. In chronic MND with or without radicular findings or headache, there was moderate evidence from 5 high quality trials showing that botulinum toxin (Botox A) intramuscular injections were not better than saline in improving pain [SMD pooled -0.39 (95% CI -1.25 to 0.47)], disability, or global perceived effect. CONCLUSION: Intramuscular injection of lidocaine for chronic MND and intravenous injection of methylprednisolone for acute whiplash were effective treatments. There was limited evidence of effectiveness of epidural injection of

methylprednisolone and lidocaine for chronic MND with radicular findings. Muscle relaxants and nonsteroidal antiinflammatory drugs have unclear benefits. There was moderate evidence that Botox-A intramuscular injections for chronic MND were not better than saline.

PMID: 16652427

Rating: 1b

Peng PW, Wijeysundera DN, Li CC. Use of gabapentin for perioperative pain control -- a meta-analysis. Pain Res Manag. 2007 Summer;12(2):85-92.

Department of Anesthesiology and Pain Management, Toronto Western, University Health Network, University of Toronto, Toronto, Canada. philip.peng@uhn.on.ca

BACKGROUND: Gabapentin, an anticonvulsant, has recently been suggested as an effective postoperative 'analgesic' agent. The objective of the present study was to examine the analgesic effectiveness, opioid-sparing effects and side effects associated with the use of gabapentin in a perioperative setting. METHODS: Following the Quality of Reporting of Meta-analyses recommendations, nine electronic databases until February 2006 were searched, without language restriction, for randomized controlled trials comparing gabapentin with control for postoperative pain control. Outcome measures, namely, 24 h cumulative opioid consumption, visual analogue scale pain scores and adverse effects, were expressed as odds ratios, ratio of means or weighted mean differences (as appropriate), which were aggregated under the fixed or random effects models. RESULTS: Gabapentin caused a 35% reduction in total opioid consumption over the first 24 h following surgery (ratio of means 0.65, 95% CI 0.59 to 0.72), a significant reduction in postoperative pain at rest (in the first 24 h) and with movement (at 2 h, 4 h and 12 h), regardless of whether treatment effects were expressed as ratios of means or weighted mean differences, and a reduction of vomiting (relative risk [RR] 0.73, 95% CI 0.56 to 0.95) and pruritus (RR 0.30, 95% CI 0.13 to 0.70). It was associated with a significant increase in dizziness (RR 1.40, 95% CI 1.06 to 1.84) and an increase in sedation of borderline significance (RR 1.65, 95% CI 1.00 to 2.74). CONCLUSION: Gabapentin improves the analgesic efficacy of opioids both at rest and with movement, reduces analgesic consumption and opioid-related adverse effects, but is associated with an increased incidence of sedation and dizziness.

PMID: 17505569

Rating: 1c

Perez R, Kwakkel G, Zuurmond W, et al. Treatment of Reflex Sympathetic Dystrophy (CRPS Type 1): A Research Synthesis of 21 Randomized Clinical Trials. J Pain Symptom Manage 2001:21:511-526. Department of Anesthesiology, Research Institute for Clinical and Fundamental Human Movement Sciences, University Hospital Vrije Universiteit Amsterdam, Amsterdam, The Netherlands.

Abstract:
A blinded meta analysis was performed on randomized clinical trials (RCT) on the medicinal treatment of reflex sympathetic dystrophy (complex regional pain syndrome type I) to assess the methodological quality and quantify the analgesic effect of treatments by calculating individual and summary effect sizes. The internal validity of 21 RCTs was investigated and the quality weighted summary effect size was calculated using a fixed effect model (Glass Delta). The methodological quality ranged from moderate to good (average 46%). Differences were found between the trials in inclusion/exclusion criteria, treatment methods, duration of treatments and trials, and measurement instruments. Statistical analysis was possible for four subgroups; one evaluating the analgesic effects of sympathetic suppressors in general (n = 12), one subgroup concerning the analgesic effects of guanethidine (n = 6), one investigating the analgesic effect of intravenous regional sympathetic blocks (n = 9), and one subgroup (n = 5) evaluating the analgesic effect of calcitonin. Except for the calcitonin subgroup (P = 0.002), the quality-weighted summary effect size of these subgroups were not significant. No significant analgesic effect by sympathetic suppressing agents could be established. Calcitonin seems to provide effective pain relief in reflex sympathetic dystrophy patients. The results of the present study show that weighting methodological quality influences the magnitude of the effect sizes of specific treatment methods. Future studies should control for methodological quality.
Publication Type: Meta-Analysis
PMID: 11397610

Perez RS, Keijzer C, Bezemer PD, Zuurmond WW, de Lange JJ. Predictive value of symptom level measurements for complex regional pain syndrome type I. Eur J Pain. 2005 Feb;9(1):49-56.

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The validity with respect to presence or absence of CRPS I according to Veldman's criteria was assessed for measured pain, temperature, volume differences and limitations in range of motion. Evaluated were 155 assessments of 66 outpatients, initially diagnosed with CRPS I, but many of them not so on follow up visits. Pain was measured with VAS and McGill, temperature by infrared thermometry, volume differences by water displacement volumeters and limitations in range of motion by universal goniometers. Sensitivity, specificity, positive and negative predictive value of the measurement instruments at different cut-off points was calculated. Combined symptom scores were evaluated in a similar fashion. High sensitivity was found for the VAS, McGill, and range of motion. The specificity was overall lower, but highest values were obtained for volume differences. The positive predictive value was good for all measurement instruments. Negative predictive value was lower, especially for measurement of temperature and volume asymmetries. If sensitivity and specificity are equally important, VAS>3 cm, McGill>6 words, temperature difference>or=0.4 degrees C, volume difference>6.5% and ROM limitation>15% provide the best results. Using these cut off values, the highest value of sensitivity and of sensitivity and specificity combined, was found for a combination of VAS, McGill and ROM. The highest value of specificity was found for different combinations of 3, 4

and 5 instruments, all containing the VAS. We conclude that the measured pain, temperature, volume and range of motion can be used as diagnostic indicators for establishing presence or absence of CRPS I.

Rating: 4b

Perez RS, Collins S, Marinus J, Zuurmond WW, de Lange JJ. Diagnostic criteria for CRPS I: differences between patient profiles using three different diagnostic sets. Eur J Pain. 2007 Nov;11(8):895-902. Epub 2007 Apr 2.

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Complex Regional Pain Syndrome type I (CRPS I) is an illness which usually occurs due to major or minor tissue injury to the extremities. Because a unique pathophysiological mechanism for CRPS I has not yet been established, the diagnosis is based on observation and measurement of clinical symptoms and signs. In this study, a comparison was made between three sets of diagnostic criteria (the IASP, Bruehl et al. and Veldman et al.) based on patient reports and physicians' assessments of signs and symptoms associated with CRPS I, in 372 outpatients suspected of having CRPS I. Agreement between CRPS I diagnosis among the three sets was poor (kappa-range: 0.29-0.42), leading to positive CRPS I diagnoses according to Veldman et al.'s criteria in 218 cases (59%), according to the IASP in 268 cases (72%), and according to Bruehl et al. in 129 cases (35%). Significant differences in patient profiles were found between the diagnostic sets for the number of patients reporting continuing disproportionate pain, larger area affected than the initial trauma (both $p<0.001$), increase of symptoms due to exercise ($p=0.009$), edema ($p=0.015$), temperature asymmetry ($p=0.015$), hyperesthesia, allodynia (both $p<0.001$) and hyperalgesia ($p=0.036$). Similarly, significant differences emerged for physicians' observations of hyperesthesia and allodynia (both $p<0.001$). Highest combined values of sensitivity (SE) and specificity (SP) for the strongest cases of presence (n=108) or absence (n=62) of CRPS I were found for reported hyperesthesia (SE+SP:165%), allodynia (160%), observed color asymmetry (162%), hyperesthesia (157%), temperature asymmetry (154%) and edema (152%). The lack of agreement between the different diagnostic sets for CRPS I and the different clinical profiles that result from it may lead to different therapeutic and study populations, hampering adequate treatment and scientific development for this illness. We propose explicit reference to diagnostic criteria used in studies, and registration in trials of a broad variety of CRPS I features, as used in this study, to make subgroup phenotyping and post hoc analyses based on different diagnostic criteria possible.

PMID: 17400490

Rating: 5b

Pergolizzi J, Böger RH, Budd K, Dahan A, Erdine S, Hans G, Kress HG, Langford R, Likar R, Raffa RB, Sacerdote P. Opioids and the management of chronic severe pain in the elderly: consensus

statement of an International Expert Panel with focus on the six clinically most often used World Health Organization step III opioids (buprenorphine, fentanyl, hydromorphone, methadone, morphine, oxycodone). Pain Pract. 2008;8:287-313.

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SUMMARY OF CONSENSUS: The transdermal formulation of buprenorphine is available in most European countries, particularly those with high opioid usage, with the exception of France; however, the availability of the sublingual formulation of buprenorphine in Europe is limited, as it is marketed in only a few countries, including Germany and Belgium. Buprenorphine shows a distinct benefit in improving neuropathic pain symptoms, which is considered a result of its specific pharmacological profile. For all opioids except buprenorphine, half-life of the active drug and metabolites is increased in the elderly and in patients with renal dysfunction. It is, therefore, recommended that--except for buprenorphine--doses be reduced, a longer time interval be used between doses, and creatinine clearance be monitored. Thus, buprenorphine appears to be the top-line choice for opioid treatment in the elderly. Taking into consideration all the very limited available evidence from preclinical and clinical work, buprenorphine can be recommended, while morphine and fentanyl cannot.

PMID: 18503626

Rating: 5b

Perrot S, Maheu E, Javier RM, Eschalier A, Coutaux A, LeBars M, Bertin P, Bannwarth B, Treves R. Guidelines for the use of antidepressants in painful rheumatic conditions. Eur J Pain. 2006 Apr;10(3):185-92. Epub 2005 Apr 18.

Cercle d'etude de la douleur en rhumatologie, CEDR, Limoges, France. serge.perrot@cch.ap-hop-paris.fr

OBJECTIVES: Antidepressants are widely used to treat painful chronic rheumatic conditions but, contrary to neuropathic conditions, little is known about their true analgesic properties and value in these situations. Our group, which focuses on pain in rheumatology, aimed to develop recommendations for the use of antidepressants in rheumatology, based on evidence-based review of published data and expert opinion. METHOD: We identified relevant drugs and conditions and searched Medline, Embase and Pascal (1966-2003) for relevant publications in a number of European languages. We scored each study for quality, and used an expert consensus approach to formulate recommendations. RESULTS: We identified 77 studies and 12 meta-analyses and literature review on the use of antidepressant to treat painful rheumatological conditions. Forty-nine of these clinical studies were considered valid and were used to develop the recommendations. When evidence was lacking we based recommendations on our clinical experience. CONCLUSIONS: These recommendations for the treatment of painful rheumatological conditions with antidepressants were developed using evidence-based and expert

consensus approaches and are the first of their kind in this field. Our review of the literature highlights the need for further, well-designed clinical studies of the use of antidepressants to treat painful rheumatological conditions.

PMID: 16490727

Rating: 8a

Perrot S, Javier RM, Marty M, Le Jeunne C, Laroche F. Antidepressant use in painful rheumatic conditions. Rheum Dis Clin North Am. 2008;34:433-53.

Service de Médecine Interne et Thérapeutique, Consultation de la Douleur, Hôtel Dieu, Université Paris Descartes, 1 Place du Parvis Notre Dame, 75004 Paris, France.

This article reviews the pharmacologic and clinical evidence supporting the use of antidepressant drugs for treating painful rheumatologic conditions. Clinical studies have shown that tricyclic antidepressants, even at low doses, have analgesic effects in rheumatologic conditions equivalent to those of serotonin and noradrenalin reuptake inhibitors, but are less well tolerated. Selective serotonin reuptake inhibitors may also have analgesic effects, but higher doses are required to achieve analgesia in conditions such as fibromyalgia and low back pain. Antidepressant drugs may be useful in painful rheumatologic conditions, but in some studies the analgesic effects of antidepressants may be associated with functional impairment, sleep disorders, and fatigue. Further studies are required to determine antidepressants' analgesic mechanism of action and the specific role they should play in the management of chronic painful rheumatologic conditions.

PMID: 18638685

Rating: 5a

Peyron R, Laurent B, Garcia-Larrea L. Functional imaging of brain responses to pain. A review and meta-analysis (2000). Neurophysiol Clin. 2000 Oct;30(5):263-88.

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Brain responses to pain, assessed through positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) are reviewed. Functional activation of brain regions are thought to be reflected by increases in the regional cerebral blood flow (rCBF) in PET studies, and in the blood oxygen level dependent (BOLD) signal in fMRI. rCBF increases to noxious stimuli are almost constantly observed in second somatic (SII) and insular regions, and in the anterior cingulate cortex (ACC), and with slightly less consistency in the contralateral thalamus and the primary somatic area (SI). Activation of the lateral thalamus, SI, SII and insula are thought to be related to the sensory-

discriminative aspects of pain processing. SI is activated in roughly half of the studies, and the probability of obtaining SI activation appears related to the total amount of body surface stimulated (spatial summation) and probably also by temporal summation and attention to the stimulus. In a number of studies, the thalamic response was bilateral, probably reflecting generalised arousal in reaction to pain. ACC does not seem to be involved in coding stimulus intensity or location but appears to participate in both the affective and attentional concomitants of pain sensation, as well as in response selection. ACC subdivisions activated by painful stimuli partially overlap those activated in orienting and target detection tasks, but are distinct from those activated in tests involving sustained attention (Stroop, etc.). In addition to ACC, increased blood flow in the posterior parietal and prefrontal cortices is thought to reflect attentional and memory networks activated by noxious stimulation. Less noted but frequent activation concerns motor-related areas such as the striatum, cerebellum and supplementary motor area, as well as regions involved in pain control such as the periaqueductal grey. In patients, chronic spontaneous pain is associated with decreased resting rCBF in contralateral thalamus, which may be reverted by analgesic procedures. Abnormal pain evoked by innocuous stimuli (allodynia) has been associated with amplification of the thalamic, insular and SII responses, concomitant to a paradoxical CBF decrease in ACC. It is argued that imaging studies of allodynia should be encouraged in order to understand central reorganisations leading to abnormal cortical pain processing. A number of brain areas activated by acute pain, particularly the thalamus and anterior cingulate, also show increases in rCBF during analgesic procedures. Taken together, these data suggest that hemodynamic responses to pain reflect simultaneously the sensory, cognitive and affective dimensions of pain, and that the same structure may both respond to pain and participate in pain control. The precise biochemical nature of these mechanisms remains to be investigated.

PMID: 11126640

Rating: 5b

Pincus T, Vlaeyen JW, Kendall NA, Von Korff MR, Kalauokalani DA, Reis S. Cognitive-behavioral therapy and psychosocial factors in low back pain: directions for the future. Spine. 2002 Mar 1;27(5):E133-8.
Royal Holloway, University of London, London, United Kingdom, Maastricht University, Maastricht, The Netherlands. t.pincus@rhbnc.ac.uk
Abstract:
STUDY DESIGN: An amalgamated review of the current state of knowledge about psychosocial factors in low back pain (LBP), as presented at the plenary session at the Fourth International Forum on LBP Research in Primary Care (March 16-18, 2000, Israel). OBJECTIVES: To outline evidence-based theories that have lead to the identification of yellow flags (psychosocial risk factors for developing long-term disability) for nonspecific LBP. To discuss the role of clinicians in primary care in detecting and addressing these psychosocial factors and to outline future directions for research to clarify this role. SUMMARY OF BACKGROUND DATA: It is widely accepted that psychological and social factors play an important role in LBP; however, it is currently unclear which specific factors merit intervention

to reduce the burden of disease. METHOD: The review is an integration based on the plenary session presented at the Fourth International Forum on LBP Research in Primary Care. The presentations included original research studies, a systematic review, and theoretical descriptions of models of risk and treatment. RESULTS: There is good evidence to support the role of psychological risk factors at early stages of LBP in the development of long-term disability. There are evidence-based theories and models that provide directions for future interventions. CONCLUSION: In the treatment of psychological factors, the role of clinicians in primary care remains unclear. Further evidence is needed to identify specific psychological risk factors, primary care tools for their identification need developing, and interventions at different stages of LBP by different professionals need to be tested.
Publication Type: Review
PMID: 11880850

Pittman DM, Belgrade MJ, Complex regional pain syndrome, Am Fam Physician 1997 Dec;56(9):2265-70, 2275-6
(click hyperlink above to go to full text of article.)

Sister Kenny Institute, Minneapolis, Minnesota, USA.

The term "complex regional pain syndrome" encompasses causalgia and reflex sympathetic dystrophy. Symptoms of burning pain with autonomic and tissue changes begin shortly after an injury, usually to a distal extremity. The diagnosis is based on the history and the clinical findings. No confirmatory tests are available, although plain radiographs or a three-phase bone scan may be helpful in diagnosing some cases. Aggressive treatment, which may include sympathetic blockade, medications, physical therapy and psychotherapy, is essential for a favorable outcome. Despite treatment, many patients are left with varying degrees of chronic pain and disability.

Publication Types:
- Review
- Review, Tutorial

PMID: 9402812
Rating: 5b

Pollack MH, Allgulander C, Bandelow B, Cassano GB, Greist JH, Hollander E, Nutt DJ, Okasha A, Swinson RP; World Council of Anxiety. WCA recommendations for the long-term treatment of panic disorder. CNS Spectr. 2003 Aug;8(8 Suppl 1):17-30

Division of Psychiatry, Huddinge University Hospital, Stockholm, Sweden. mpollack@partners.org

What are the symptoms of panic disorder and how is the disorder most effectively treated? One of the most commonly encountered anxiety disorders in the primary care setting, panic disorder is a chronic

and debilitating illness. The core symptoms are recurrent panic attacks coupled with anticipatory anxiety and phobic avoidance, which together impair the patient's professional, social, and familial functioning. Patients with panic disorder have medically unexplained symptoms that lead to overutilization of healthcare services. Panic disorder is often comorbid with agoraphobia and major depression, and patients may be at increased risk of cardiovascular disease and, possibly, suicide. Research into the optimal treatment of this disorder has been undertaken in the past 2 decades, and numerous randomized, controlled trials have been published. Selective serotonin reuptake inhibitors have emerged as the most favorable treatment, as they have a beneficial side-effect profile, are relatively safe (even if taken in overdose), and do not produce physical dependency. High-potency benzodiazepines, reversible monoamine oxidase inhibitors, and tricyclic antidepressants have also shown antipanic efficacy. In addition, cognitive-behavioral therapy has demonstrated efficacy in the acute and long-term treatment of panic disorder. An integrated treatment approach that combines pharmacotherapy with cognitive-behavioral therapy may provide the best treatment. Long-term efficacy and ease of use are important considerations in treatment selection, as maintenance treatment is recommended for at least 12-24 months, and in some cases, indefinitely.

Publication Types:
- Guideline
- Practice Guideline
- Review
- Review, Academic

PMID: 14767395
Rating: 5a

Portenoy RK and Lesage P. Management of Cancer Pain: Lancet 1999;353:1695-1700.
Department of Pain Medicine and Palliative Care, Beth Israel Medical Center, New York, NY 10003, USA. Rportenoy@bethisraelny.org
Publication Type: Review
PMID: 10335806

Portenoy RK, Payne R. Acute and chronic pain. In: Lowinson J, Ruiz P, Millman R, Langrod J. eds. Substance abuse: a comprehensive textbook, Williams & Wilkins, Baltimore; 1997:563-90.

The premier text on substance abuse and addictive behaviors is now in its updated and expanded Fourth Edition, with up-to-the-minute insights from more than 150 experts at the front lines of patient management and research. This edition features expanded coverage of the neurobiology of abused substances, new pharmacologic therapies for addictions, and complete information on "club drugs" such as Ecstasy. New sections focus on addiction in children, adolescents, adults, and the elderly and women's health issues, including pregnancy. The expanded behavioral addictions section now includes hoarding, shopping, and computer/Internet abuse

Rating: 9

Portenoy RK. Opioid therapy for chronic nonmalignant pain: a review of the critical issues. J Pain Symptom Manage. 1996 Apr;11(4):203-17.

Department of Neurology, Memorial Sloan-Kettering Cancer Center, New York, NY 10021, USA.

The controversy surrounding the long-term use of opioid drugs in patients with nonmalignant pain has intensified in recent years. This debate is driven by a new willingness to consider the potential benefits of an approach that has been traditionally rejected as invariably ineffective and unsafe. The published literature continues to be very limited, but a growing clinical experience, combined with a critical reevaluation of issues related to efficacy, safety, and addiction or abuse, suggests that there is a subpopulation of patients with chronic pain that can achieve sustained partial analgesia from opioid therapy without the occurrence of intolerable side effects or the development of aberrant drug-related behaviors. Future research must confirm this impression through controlled clinical trials and clarify those factors that may predict therapeutic success or failure. For the present, the clinician who contemplates this approach must have a clear grasp of the relevant issues and an understanding of the guidelines for treatment and monitoring that have proved useful in practice.

PMID: 8869456

Rating: 5b

Prager JP, Mackey S, Alexander G, Schwartzman R. Breaking concepts in diagnosis and treatment of complex regional pain syndromes. Program and abstracts of the American Academy of Pain Medicine 23rd Annual Meeting; February 7-10, 2007; New Orleans, Louisiana.

This topic focused on the use of functional brain imaging to look for areas of the brain that are active in response to pain stimuli. This new technology is still in a very early stage, but holds great promise for enhancing our understanding of how the brain processes pain. Functional brain imaging may represent an excellent opportunity to provide an objective measurement of pain and provide a means to monitor treatment efficacy. Preliminary data suggest that we can see distinct alterations in neurologic patterns associated with various stimuli in patients suffering with complex regional pain syndromes.

Rating: 10b

Prager J. Four decades of neuromodulation. Program and abstracts of the American Academy of Pain Medicine 23rd Annual Meeting; February 7-10, 2007; New Orleans, Louisiana.

This was a review of the field concerning what we have been evolving from and to with neuromodulation. Rather dramatic results have been seen with neuromodulation techniques in the treatment of Parkinson's disease with deep brain stimulation, radicular and low back pain, and for the management of refractory major depression. One of the areas that is of considerable interest to many pain specialists is the evolving role of neuromodulation in the management of visceral pain syndromes. Although there are still not a lot of hard, randomized controlled trial data on the use of neuromodulation for visceral pain, such as for problems involving the intestines, stomach, and pelvic organs, mounting case study evidence suggests a valuable role for neuromodulation in this area. Various case reports have been presented showing that neuromodulation may be successfully applied in the treatment of abdominal pain and for pain associated with the genitourinary tract where more traditional analgesic treatments have been unsuccessful.

Rating: 10a

Pransky G, et al."Outcome in Work-Related Upper Extremity and Low Back Injuries: Results of a Retrospective Study," American Journal of Industrial Medicine 2000, 37: 400-409.
Center for Disability Research, Liberty Mutual Insurance Company, Hopkinton, MA 01701, USA. glenn.pransky@libertymutual.com
Abstract:
BACKGROUND: The outcomes of treatment for work-related injuries and illnesses are multidimensional and complex, but have rarely been explored in detail. This study was intended to provide information on a sample of workers representing a range of jobs and employers typical of the workers compensation system. METHODS: A mailed, self-report survey measuring multiple dimensions was conducted. Identified through the New Hampshire Division of Workers' Compensation First Report of Injury database, a sample of workers with injuries to their lower back (60%) or upper extremities (40%) a year prior to the study were surveyed. Response rate was 80% (N=169; upper extremity cases=70; low back cases=99). RESULTS: Most (82.8%) were working one year post-injury. Over half reported residual effects of the injury on work or activities of daily living. Many working subjects reported persistent injury-related anxiety and pain at the end of the work day, worse in those with low back pain compared to those with upper extremity injuries. Almost 40% of those who returned to work suffered a reinjury. Forty-four percent of respondents suffered significant injury-related financial problems, which were worse in those who had been out of work for longer periods. CONCLUSIONS: Occupational musculoskeletal injuries do result in significant, long-term adverse physical, economic, and psychological consequences, as demonstrated in self-reported surveys. Copyright 2000 Wiley-Liss, Inc.
Publication Type: Case Control Study, 169 cases
PMID: 10706752

Price DD, Long S, Wilsey B, Rafii A, Analysis of peak magnitude and duration of analgesia produced by local anesthetics injected into sympathetic ganglia of complex regional pain syndrome patients, Clin J Pain. 1998 Sep;14(3):216-26.

Department of Oral and Maxillofacial Surgery, University of Florida, Gainesville 32610, USA.

CONCLUSION: "The combination of these results provides evidence that duration of pain relief is affected by injection of local anesthetics into sympathetic ganglia. These results indicate that both magnitude and duration of pain reduction should be closely monitored to provide optimal efficacy in procedures that use local anesthetics to treat CRPS."

PMID: 9758071

Rating: 2c

Prommer E. Levorphanol: the forgotten opioid. Support Care Cancer. 2007;15:259-64.

VIP Palliative Care Program, Greater Los Angeles Healthcare, Division of Hematology/Oncology, UCLA School of Medicine, 11301 Wilshire 111-H, Los Angeles, CA, USA. eric.prommer@med.va.gov

BACKGROUND: Levorphanol (levo-3-hydroxy-N-methylmorphinan) is a strong opioid that is the only available opioid agonist of the morphinan series. Levorphanol was originally synthesized as a pharmacological alternative to morphine more than 40 years ago. It is considered a step-3 opioid by the World Health Organization (WHO) and has a greater potency than morphine. Analgesia produced by levorphanol is mediated via its interactions with mu, delta, and kappa opioid receptors. Levorphanol is also an N-methyl-D-aspartate (NMDA) receptor antagonist. There is evidence that levorphanol may inhibit uptake of norepinephrine and serotonin. Similar to morphine, levorphanol undergoes glucuronidation in the liver, and the glucuronidated products are excreted in the kidney. Levorphanol can be given orally, intravenously, and subcutaneously. OBJECTIVE: This article reviews the pharmacodynamics, pharmacology, and clinical efficacy for this often overlooked step-3 opioid. CONCLUSION: The long half-life of the drug increases the potential for drug accumulation. Levorphanol has clinical efficacy in neuropathic pain.

Rating; 5c

Pulliam CB, Gatchel RJ, Gardea MA. Psychosocial differences in high risk versus low risk acute low-back pain patients. Journal of Occupational Rehabilitation. 2001 Mar;11(1):43-52.
University of Texas Southwestern Medical Center at Dallas, Texas, USA.
Abstract:
The current study built upon previous research that predicted with 90.7% accuracy which patients presenting with acute low-back pain go on to develop chronic disability problems. Fifty-seven patients were classified as high risk (HR) or low risk (LR) according to a predictive algorithm, and were

evaluated with a variety of psychosocial measures. Overall, HR patients had more Axis I pathology than LR patients, and used poorer coping styles. Logistic regression analyses identified variables that differentiated, with 80% accuracy, between the HR and LR patients. The results highlight the importance of identifying patients who are at risk for developing chronic pain following acute injury so that prophylactic intervention can be offered before chronic pain disability status becomes entrenched. Publication Type: Case Control Study, 57 cases

PMID: 11706776

Quigley C. Hydromorphone for acute and chronic pain. The Cochrane Database of Systematic Reviews 2006 Issue 3. Copyright © 2006 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Plain language summary
While hydromorphone appears to be a potent analgesic, evidence to date does not support its superiority over morphine for the management of moderate to severe pain.

Morphine is the gold standard for the management of moderate to severe cancer-related pain. Alternatives to morphine are now available, including hydromorphone. This review found that hydromorphone is a potent analgesic for the management of acute and chronic pain. In terms of analgesic efficacy and tolerability, hydromorphone behaves like other strong opioids. The limited evidence available does not demonstrate any clinically significant difference between hydromorphone and other strong opioids, such as morphine.

Rating : 1a

Quisel A, Gill JM, Witherell P. Complex regional pain syndrome: which treatments show promise? J Fam Pract. 2005 Jul;54(7):599-603.

Family Medicine Center, 1401 Foulk Road, Wilmington, DE 19803, USA. DrQuisel@comcast.net

Treatments for CRPS type 1 supported by evidence of efficacy and little likelihood for harm are: topical DMSO cream (B), IV bisphosphonates (A) and limited courses of oral corticosteroids (B). Despite some contradictory evidence, physical therapy and calcitonin (intranasal or intramuscular) are likely to benefit patients with CRPS type 1 (B). Due to modest benefits and the invasiveness of the therapies, epidural clonidine injection, intravenous regional sympathetic block with bretylium and spinal cord stimulation should be offered only after careful counseling (B). Therapies to avoid due to lack of efficacy, lack of evidence, or a high likelihood of adverse outcomes are IV regional sympathetic blocks with anything but bretylium, sympathetic ganglion blocks with local anesthetics, systemic IV sympathetic inhibition, acupuncture, and sympathectomy (B).

Publication Types:

Review

PMID: 16009087

Rating: 5a

Quisel A, Gill JM, Witherell P. Complex regional pain syndrome underdiagnosed. J Fam Pract. 2005 Jun;54(6):524-32.

Family Medicine Center, 1401 Foulk Road, Wilmington, DE 19803, USA. bretandanna@comcast.net

Complex regional pain syndrome (CRPS) type 1 may be diagnosed by history and physical exam with no further testing. Several different diagnostic criteria have undergone validity testing: the 1993 IASP criteria, Bruehl's criteria, and Veldman's criteria; there is no compelling reason to recommend 1 set of criteria over the others. Some cases of CRPS type 1 may be preventable. Some cases of CRPS type 1 in post-stroke upper extremity hemiplegia (also known as shoulder-hand syndrome) may be prevented by early inpatient rehabilitation and avoidance of shoulder trauma to the affected arm. Some cases of post-fracture CRPS type 1 may be prevented with 500 mg vitamin C daily started upon diagnosis of fracture and continued through healing.

PMID: 15939004

Rating: 5b

Rabben, T. Prolonged Analgesic Effect of Ketamine, a N-Methyl-D-Asparate Receptor Inhibitor, in Patients with Chronic Pain. The Journal of Pharmacology and Experimental Therapeutics. 1999; Volume 289:1060-66.

Rating: 2c

Quality: Low Total Rating: 3.0 Comment: Does not meet inclusion criteria for evidence-based review. [CA DWC]

Rajagopal, A., et al. Symptomatic Hypogonadism in Male Survivors of Cancer with Chronic Exposure to Opioids. Cancer. 2004; Volume 100, Number 4, 851-858.

Rating: 2c

Quality: Low. Total Rating: 1.5. Comment: Does not meet inclusion criteria for evidence-based review. [CA DWC]

Ramakrishnan K, Scheid DC. Treatment options for insomnia. Am Fam Physician. 2007 Aug 15;76(4)517-26.

Department of Family and Preventive Medicine, University of Oklahoma Health Sciences Center, Oklahoma City 73104, USA. kramakrishnan@ouhsc.edu

The frequency of sleep disruption and the degree to which insomnia significantly affects daytime function determine the need for evaluation and treatment. Physicians may initiate treatment of insomnia at an initial visit; for patients with a clear acute stressor such as grief, no further evaluation may be indicated. However, if insomnia is severe or long-lasting, a thorough evaluation to uncover coexisting medical, neurologic, or psychiatric illness is warranted. Treatment should begin with nonpharmacologic therapy, addressing sleep hygiene issues and exercise. There is good evidence supporting the effectiveness of cognitive behavior therapy. Exercise improves sleep as effectively as benzodiazepines in some studies and, given its other health benefits, is recommended for patients with insomnia. Hypnotics generally should be prescribed for short periods only, with the frequency and duration of use customized to each patient's circumstances. Routine use of over-the-counter drugs containing antihistamines should be discouraged. Alcohol has the potential for abuse and should not be used as a sleep aid. Opiates are valuable in pain-associated insomnia. Benzodiazepines are most useful for short-term treatment; however, long-term use may lead to adverse effects and withdrawal phenomena. The better safety profile of the newer-generation nonbenzodiazepines (i.e., zolpidem, zaleplon, eszopidone, and ramelteon) makes them better first-line choices for long-term treatment of chronic insomnia.

Rating: 5b

Ramamurthy S, Hoffman J, Guanethidine Study Group. Intravenous Regional Guanethidine in the Treatment of Reflex Sympathetic Dystrophy/Causalgia: A Randomized, Double-Blind Study. Anesth Analg 1995;81:718-23.

Department of Anesthesiology, University of Texas Health Science Center at San Antonio 78284-7838, USA.

Conclusion: "Placebo is as effective as guanethidine in improving pain scores in RSD, perhaps because of tourniquet, interactions with physicians, and repeated measurements, or co-administration of lidocaine to all groups"

Publication Type: RCT, 60 cases

PMID: 7574000

Rating: 2b

Ramamurthy S, et al. Intravenous Regional Guanethidine in the Treatment of Reflex Sympathetic Dystrophy/Causalgia: A Randomized, Double-Blind Study. Anesth Analg. 1995; Volume 81:718-23.

Rating: 2b

Quality: Intermediate. Total Rating: 8. Comment: Found that guanethidine was no better than the placebo in improving pain scores for patients with RSD. [CA DWC]

Ranavaya M, Talmage J. AMA Guides to the Evaluation of Permanent Impairment: What's New in the 5th edition? Disability Medicine. American Board of Independent Medical Examiners. Vol. 1, No. 1. January-March 2001.

Abstract:

The AMA Guidelines now allow for impairment percentage to be increased by up to 3 percent for pain by using the pain chapter. MEDICINE
Publication Type: Review

Raphael, J., et al. Long-term experience with implanted intrathecal drug administration systems for failed back syndrome and chronic mechanical low back pain. BMC Musculoskeletal Disorders. 2002; Volume 3, Number 17.

Rating: 2c

Quality: Low. Total Rating: 2.0. Comment: Does not meet inclusion criteria for evidence-based review. [CA DWC]

Rauck RL, Wallace MS, Leong MS, Minehart M, Webster LR, Charapata SG, Abraham JE, Buffington DE, Ellis D, Kartzinel R; Ziconotide 301 Study Group. A randomized, double-blind, placebo-controlled study of intrathecal ziconotide in adults with severe chronic pain. J Pain Symptom Manage. 2006;31:393-406.

Wake Forest University School of Medicine, The Center for Clinical Research, Carolinas Pain Institute, Winston-Salem, North Carolina 27103, USA. RRauck@ccrpain.com

Safety and efficacy data from a study of slow intrathecal (IT) ziconotide titration for the management of severe chronic pain are presented. Patients randomized to ziconotide (n = 112) or placebo (n = 108) started IT infusion at 0.1 microg/hour (2.4 microg/day), increasing gradually (0.05-0.1 microg/hour increments) over 3 weeks. The ziconotide mean dose at termination was 0.29 microg/hour (6.96 microg/day). Patients' baseline Visual Analogue Scale of Pain Intensity (VASPI) score was 80.7 (SD 15). Statistical significance was noted for VASPI mean percentage improvement, baseline to Week 3

(ziconotide [14.7%] vs. placebo [7.2%; P = 0.036]) and many of the secondary efficacy outcomes measures. Significant adverse events (AEs) reported in the ziconotide group were dizziness, confusion, ataxia, abnormal gait, and memory impairment. Discontinuation rates for AEs and serious AEs were comparable for both groups. Slow titration of ziconotide, a nonopioid analgesic, to a low maximum dose resulted in significant improvement in pain and was better tolerated than in two previous controlled trials that used a faster titration to a higher mean dose.

PMID: 16716870

Rating: 2c

This study showed a fairly small effect size but was helpful in determining appropriate dosing.

Reeder CE, Franklin M, Bramley TJ. Current landscape of insomnia in managed care. Am J Manag Care. 2007;13:S112-6.

Xcenda, 1528 Preston St, Salt Lake City, UT 84108, USA.

Insomnia affects a large percentage of the population, particularly the elderly. Literature reports varying estimates of prevalence, a variation that relates to the lack of definition and consistency in diagnostic criteria. Primary insomnia (not caused by known physical/mental conditions) responds to pharmacologic therapy, while secondary insomnia(resulting from other illnesses, medications, or sleep disorders) responds to pharmacologic and psychologic treatments (cognitive therapy, relaxation techniques, stimulus control). Use of certain agents in the elderly and patients with abuse/addiction potential is a concern. Medicare Part D does not cover benzodiazepines (classified as controlled substances). Nonprescription agents are affordable but have sedation and anticholinergic side effects. Medication use should be considered a possible contributing factor. Insomnia patients experience significantly more limited activity and higher total health services than those without insomnia. Annual costs are between $92.5 billion and $107.5 billion. A standard definition and better pathways to recognize and treat insomnia are needed.

PMID: 1804187

Rating: 5b

Reeves RR, Parker JD. Somatic dysfunction during carisoprodol cessation: evidence for a carisoprodol withdrawal syndrome. J Am Osteopath Assoc. 2003 Feb;103(2):75-80.

G.V. (Sonny) Montgomery VA Medical Center and University of Mississippi, Jackson 39216, USA. roy.reeves@med.va.gov

Carisoprodol is a commonly used skeletal muscle relaxant with potential for abuse because of its active metabolite, meprobamate, and several reports have suggested that patients abruptly stopping intake of carisoprodol may have a withdrawal syndrome. The authors studied changes in the occurrence of somatic dysfunctions in five patients during an 8-day period following discontinuation from large doses of carisoprodol. Results showed that the number of somatic dysfunctions changed significantly during the withdrawal period. Each patient had an increase in the number of somatic dysfunctions during the first 3 days after cessation of carisoprodol with return to at or near baseline by the eighth day. This was reflected statistically in a significant-within-subjects effect for time. Results of supplemental analyses revealed a significant component of the effect and a trend for the quadratic component to be significant. Increases in the number of somatic dysfunctions during carisoprodol discontinuation support the existence of a carisoprodol withdrawal syndrome.

PMID: 12622352

Rating: 4c

Reeves RR, Burke RS. Is it time for carisoprodol to become a controlled substance at the federal level? South Med J. 2008;101:127-8.

An article discussing the current status of carisoprodol including abuse potential and withdrawal.

Rating: 5b

Reeves RR, Hammer JS, Pendarvis RO. Is the frequency of carisoprodol withdrawal syndrome increasing? Pharmacotherapy. 2007;27:1462-6.

Mental Health Service, G.V. (Sonny) Montgomery Veterans Affairs Medical Center, Jackson, Mississippi 39216, USA. roy.reeves@med.va.gov

Symptoms of carisoprodol withdrawal include anxiety, tremulousness, insomnia, jitteriness, muscle twitching, and hallucinations. These symptoms are most likely caused by withdrawal from the meprobamate that accumulates after large amounts of carisoprodol are ingested.

PMID: 17896902

Rating: 4c

Reeves RR, Beddingfield JJ, Mack JE. Carisoprodol withdrawal syndrome. Pharmacotherapy. 2004;24:1804-6.

G.V. (Sonny) Montgomery VA Medical Center, School of Medicine, University of Mississippi, Jackson, Mississippi, USA. roy.reeves@med.va.gov

Within 48 hours he developed anxiety, tremors, muscle twitching, insomnia, auditory and visual hallucinations, and bizarre behavior. The patient required brief treatment with olanzapine and tapering dosages of lorazepam while the symptoms gradually resolved. The symptoms most likely resulted because of accumulation of meprobamate, the active metabolite of carisoprodol in humans.

PMID: 15585447

Rating: 4c

Reeves RR, Liberto V. Abuse of combinations of carisoprodol and tramadol. South Med J. 2001;94:512-4.

Department of Psychiatry, G.V. (Sonny) Montgomery VA Medical Center and the University of Mississippi School of Medicine, Jackson 39216, USA.

Carisoprodol or tramadol should be prescribed with caution for patients at risk for substance abuse, and extreme caution should be used when prescribing both drugs simultaneously for any patient.

PMID: 11372804

Rating: 4c

Reeves RR, Carter OS, Pinkofsky HB, Struve FA, Bennett DM. Carisoprodol (soma): abuse potential and physician unawareness. J Addict Dis. 1999;18:51-6.

G.V. (Sonny) Montgomery VA Medical Center, University of Mississippi School of Medicine, Jackson 39216, USA.

Findings showed that some patients using carisoprodol for over three months may abuse the medication, especially those individuals with a history of substance abuse. A significant percentage of the physician population is unaware of the potential of carisoprodol for abuse and of its metabolism to meprobamate, a controlled substance. Physicians should exercise caution when prescribing carisoprodol, especially if the patient has a history of substance abuse.

PMID: 10334375

Rating: 4b

Reginster JY, Deroisy R, Rovati LC, Lee RL, Lejeune E, Bruyere O, Giacovelli G, Henrotin Y, Dacre JE, Gossett C. Long-term effects of glucosamine sulphate on osteoarthritis progression: a randomised, placebo-controlled clinical trial. Lancet. 2001 Jan 27;357(9252):251-6.

Bone and Cartilage Metabolism Research Unit (WHO Collaborating Center for Public Aspects of Osteoarticular Disorders), University of Liege, Belgium. jyreginster@ulg.ac.be

BACKGROUND: Treatment of osteoarthritis is usually limited to short-term symptom control. We assessed the effects of the specific drug glucosamine sulphate on the long-term progression of osteoarthritis joint structure changes and symptoms. METHODS: We did a randomised, double-blind placebo controlled trial, in which 212 patients with knee osteoarthritis were randomly assigned 1500 mg sulphate oral glucosamine or placebo once daily for 3 years. Weightbearing, anteroposterior radiographs of each knee in full extension were taken at enrolment and after 1 and 3 years. Mean joint-space width of the medial compartment of the tibiofemoral joint was assessed by digital image analysis, whereas minimum joint-space width--ie, at the narrowest point--was measured by visual inspection with a magnifying lens. Symptoms were scored by the Western Ontario and McMaster Universities (WOMAC) osteoarthritis index. FINDINGS: The 106 patients on placebo had a progressive joint-space narrowing, with a mean joint-space loss after 3 years of -0.31 mm (95% CI -0.48 to -0.13). There was no significant joint-space loss in the 106 patients on glucosamine sulphate: -0.06 mm (-0.22 to 0.09). Similar results were reported with minimum joint-space narrowing. As assessed by WOMAC scores, symptoms worsened slightly in patients on placebo compared with the improvement observed after treatment with glucosamine sulphate. There were no differences in safety or reasons for early withdrawal between the treatment and placebo groups. INTERPRETATION: The long-term combined structure-modifying and symptom-modifying effects of gluosamine sulphate suggest that it could be a disease modifying agent in osteoarthritis.

PMID: 11214126

Rating: 2b

Reichenbach S, Sterchi R, Scherer M, Trelle S, Burgi E, Burgi U, Dieppe PA, Juni P. Meta-analysis: chondroitin for osteoarthritis of the knee or hip. Ann Intern Med. 2007 Apr 17;146(8):580-90.

University of Bern, Bern, Switzerland.

BACKGROUND: Previous meta-analyses described moderate to large benefits of chondroitin in patients with osteoarthritis. However, recent large-scale trials did not find evidence of an effect. PURPOSE: To determine the effects of chondroitin on pain in patients with osteoarthritis. DATA SOURCES: The authors searched the Cochrane Central Register of Controlled Trials (1970 to 2006), MEDLINE (1966 to 2006), EMBASE (1980 to 2006), CINAHL (1970 to 2006), and conference proceedings; checked reference lists; and contacted authors. The last update of searches was performed

on 30 November 2006. STUDY SELECTION: Studies were included if they were randomized or quasi-randomized, controlled trials that compared chondroitin with placebo or with no treatment in patients with osteoarthritis of the knee or hip. There were no language restrictions. DATA EXTRACTION: The authors extracted data in duplicate. Effect sizes were calculated from the differences in means of pain-related outcomes between treatment and control groups at the end of the trial, divided by the pooled SD. Trials were combined by using random-effects meta-analysis. DATA SYNTHESIS: 20 trials (3846 patients) contributed to the meta-analysis, which revealed a high degree of heterogeneity among the trials (I2 = 92%). Small trials, trials with unclear concealment of allocation, and trials that were not analyzed according to the intention-to-treat principle showed larger effects in favor of chondroitin than did the remaining trials. When the authors restricted the analysis to the 3 trials with large sample sizes and an intention-to-treat analysis, 40% of patients were included. This resulted in an effect size of -0.03 (95% CI, -0.13 to 0.07; I2 = 0%) and corresponded to a difference of 0.6 mm on a 10-cm visual analogue scale. A meta-analysis of 12 trials showed a pooled relative risk of 0.99 (CI, 0.76 to 1.31) for any adverse event. LIMITATIONS: For 9 trials, the authors had to use approximations to calculate effect sizes. Trial quality was generally low, heterogeneity among the trials made initial interpretation of results difficult, and exploring sources of heterogeneity in meta-regression and stratified analyses may be unreliable. CONCLUSIONS: Large-scale, methodologically sound trials indicate that the symptomatic benefit of chondroitin is minimal or nonexistent. Use of chondroitin in routine clinical practice should therefore be discouraged.

PMID: 17438317

Rating: 1b

In a related editorial, Dr. David T. Felson, from Boston University, comments that despite the current findings, many patients are convinced that chondroitin works for them, possibly as a result of a placebo effect. He adds that because its use seems to be safe, "if patients say that they benefit from chondroitin, I see no harm in encouraging them to continue taking it as long as they perceive a benefit."

Reynoldson JN, Elliott ES, Nelson LA. Ramelteon: A Novel Approach in the Treatment of Insomnia (CE). Ann Pharmacother. 2008 Jul 23.

Psychiatric Pharmacy Practice Resident, Kansas City, MO.

OBJECTIVE: To review the pharmacology, pharmacokinetics, efficacy, and safety of ramelteon in the treatment of primary insomnia in adults, including elderly adults. DATA SOURCES: MEDLINE (1966-July 2008) and PsycINFO (1985-July 2008) literature searches were conducted to identify clinical data involving ramelteon. The manufacturer provided a summary of clinical data and abstracts of unpublished studies. STUDY SELECTION AND DATA EXTRACTION: All primary literature, including abstracts, focusing on the pharmacology and pharmacokinetics of ramelteon and clinical trials evaluating its use was reviewed. Information deemed most relevant was incorporated. Our search

revealed 5 controlled trials evaluating the shortterm efficacy and safety of ramelteon in the treatment of primary insomnia: 3 in adults and 2 in geriatric patients. Additionally, 2 studies in abstract form that evaluated the long-term effects of ramelteon were included. DATA SYNTHESIS: Ramelteon is the first selective melatonin receptor agonist approved by the Food and Drug Administration. It has no affinity for the gamma-aminobutyric acid receptor complex or for receptors that bind acetylcholine, cytokines, dopamine, norepinephrine, neuropeptides, opiates, and serotonin. In the only published Phase 3 trial in adults, investigators found that latency to persistent sleep decreased with ramelteon to 31.5 +/- 2.91 minutes with 8 mg and 29.5 +/- 2.96 minutes with 16 mg compared with 42.5 +/- 2.97 minutes with placebo (p = 0.007 and p = 0.002, respectively). Total sleep time was not significantly different from that with placebo. Safety data from short-term studies showed advantages of ramelteon over other sleep agents including no potential for abuse, no rebound insomnia, and lack of effect on motor and cognitive function. The adverse effects seen most frequently in ramelteon clinical trials were headache, somnolence, fatigue, nausea, dizziness, and insomnia. The overall incidence was similar to that of placebo. CONCLUSIONS: Ramelteon offers a novel mechanism of action for the treatment of insomnia. Studies support its short- and long-term use in adults and elderly adults for the treatment of primary insomnia characterized by difficulty with sleep initiation. Efficacy studies comparing ramelteon with other sleep agents are needed to further solidify the role of ramelteon in the treatment of insomnia.

Rating: 1c

Rho RH, Brewer RP, Lamer TJ, Wilson PR. Complex regional pain syndrome. Mayo Clin Proc. 2002 Feb;77(2):174-80.

Division of Pain Medicine, Mayo Clinic, Rochester, MN 55905, USA.

Complex regional pain syndrome (CRPS), formerly known as reflex sympathetic dystrophy, is a regional, posttraumatic, neuropathic pain problem that most often affects 1 or more limbs. Like most medical conditions, early diagnosis and treatment increase the likelihood of a successful outcome. Accordingly, patients with clinical signs and symptoms of CRPS after an injury should be referred immediately to a physician with expertise in evaluating and treating this condition. Physical therapy is the cornerstone and first-line treatment for CRPS. Mild cases respond to physical therapy and physical modalities. Mild to moderate cases may require adjuvant analgesics, such as anticonvulsants and/or antidepressants. An opioid should be added to the treatment regimen if these medications do not provide sufficient analgesia to allow the patient to participate in physical therapy. Patients with moderate to severe pain and/or sympathetic dysfunction require regional anesthetic blockade to participate in physical therapy. A small percentage of patients develop refractory, chronic pain and require long-term multidisciplinary treatment, including physical therapy, psychological support, and pain-relieving measures. Pain-relieving measures include medications, sympathetic/somatic blockade, spinal cord stimulation, and spinal analgesia.

PMID: 11838651

Rating: 5b

Ribbers GM, Geurts AC, Stam HJ, Mulder T. Pharmacologic treatment of complex regional pain syndrome I: a conceptual framework. Arch Phys Med Rehabil. 2003 Jan;84(1):141-6.

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Pain may be a leading symptom in complex regional pain syndrome type I (CRPS I) and may hinder functional recovery. In this case, a pharmacotherapeutic approach to pain should be part of the individually tailored interdisciplinary treatment regimen. However, operational criteria for determining which patient may profit from what therapeutic intervention are lacking. This article discusses a conceptual framework in which the rapid progress made in basic pain research may contribute to the clinical management of pain in CRPS I. First, recent insights in the pathophysiologic mechanisms underlying CRPS I are reviewed. CRPS I is considered a neuropathic pain syndrome with a mixed and time-dependent profile of a regional inflammation, sensitization of primary somatosensory afferents (peripheral sensitization), and sensitization of spinal neurons (central sensitization). The dominant mechanisms may vary across individual patients with different time profiles. Second, a model was constructed in which signs and symptoms in an individual patient are related to these mechanisms. Finally, relating the clinical picture to the underlying pathophysiology may help determine the pharmacotherapeutic approach for an individual patient. Pharmacologic options are discussed in this context. The presented framework does not aim to provide an evidence-based treatment algorithm, ready to be used in daily clinical practice; rather it offers a crude, first step toward a mechanism-based pharmacotherapy in CRPS I, in an effort to shift from a mainly empirical treatment paradigm toward theory-driven treatment procedures. Copyright 2003 by the American Congress of Rehabilitation Medicine and the American Academy of Physical Medicine and Rehabilitation

Publication Types:
Review

PMID: 12589636

Rating: 5b

Richy F, Bruyere O, Ethgen O, Cucherat M, Henrotin Y, Reginster JY, Structural and symptomatic efficacy of glucosamine and chondroitin in knee osteoarthritis: a comprehensive meta-analysis, Arch Intern Med. 2003 Jul 14;163(13):1514-22.

Faculty of Medicine, Department of Public Health, Public Health and Epidemiology, University of Liege, Liege, Belgium.

OBJECTIVE: To assess the structural and symptomatic efficacy of oral glucosamine sulfate and chondroitin sulfate in knee osteoarthritis through independent meta-analyses of their effects on joint space narrowing, Lequesne Index, Western Ontario MacMaster University Osteoarthritis Index (WOMAC), visual analog scale for pain, mobility, safety, and response to treatment. METHODS: An exhaustive systematic research of randomized, placebo-controlled clinical trials published or performed between January 1980 and March 2002 that assessed the efficacy of oral glucosamine or chondroitin on gonarthrosis was performed using MEDLINE, PREMEDLINE, EMBASE, Cochrane Database of Systematic Reviews, Current Contents, BIOSIS Previews, HealthSTAR, EBM Reviews, manual review of the literature and congressional abstracts, and direct contact with the authors and manufacturers of glucosamine and chondroitin. Inclusion, quality scoring, and data abstraction were performed systematically by 2 independent reviewers who were blinded to sources and authors. Conservative approaches were used for clear assessment of potential efficacy. RESULTS: Our results demonstrated a highly significant efficacy of glucosamine on all outcomes, including joint space narrowing and WOMAC. Chondroitin was found to be effective on Lequesne Index, visual analog scale pain, mobility, and responding status. Safety was excellent for both compounds. CONCLUSIONS: Our study demonstrates the structural efficacy of glucosamine and indistinguishable symptomatic efficacies for both compounds. Regarding the relatively sparse data on glucosamine and joint space narrowing and the absence of data on structural effects of chondroitin, further studies are needed to investigate the relationship among time, dose, patient baseline characteristics, and structural efficacy for an accurate, disease-modifying characterization of these 2 compounds.

Publication Types:
- Meta-Analysis

PMID: 12860572

Rating: 1b
Robbins W, Clinical applications of capsaicinoids, Clin J Pain. 2000 Jun;16(2 Suppl):S86-9.

University of California, San Francisco, USA. wendye_robbins@quickmail.ucsf.edu

PMID: 10870746

Rating: 5c

A UC San Francisco study has found that capsaicin, a derivative of hot chili peppers, may significantly reduce chronic, debilitating nerve pain associated with a range of diseases when used in high doses. The study found that seven out of ten patients who suffered from

debilitating improved by at least 50 percent after being treated by creams with capsaicin concentrates of five percent to ten percent. The patients, who found no relief from other systemic or topical pain-killers, reported that capsaicin alleviated their pain for up to six
to eight months, and allowed them to reduce their intake of medications and increase their daily activities. The study marks the first time capsaicin has been administered in such high concentrations to humans. It could become the foundation for more widespread use of capsaicin in treating pain related to nerve injuries, a growing focus of the medical and bioscience fields.
Capsaicin has long been used in low dosages, and is widely available in creams containing capsaicin concentrations of less than one percent. Capsaicin in concentrations higher than one percent had not previously been used as a treatment because it causes intense burning when
applied, a result of capsaicin activating nerves before anaesthetizing them. In the UCSF study, however, patients were able to tolerate the burning because they were given regional anesthesia before the capsaicin was administered. The role of the anesthesia in promoting the effects of
the capsaicin has not been determined. Patients also took morphine to curb burning in the days following treatment, as the burning could last up to five days. Though the morphine
was not effective in treating the initial pain that caused the patients' suffering, it did successfully treat the pain from burning, Robbins said. The initial burning was the only side effect of capsaicin treatment identified in the study. Researchers were concerned that high dosages of capsaicin could affect the patients' abilities to sense extreme temperatures and pain,
therefore increasing their chances for further injuries.

Roberts LJ, Finch PM, Pullan PT, Bhagat CI, Price LM. Sex hormone suppression by intrathecal opioids: a prospective study. Clin J Pain. 2002 ;18:144-8.

Western Australian Pain Management Centre, Department of Anesthesia, Sir Charles Gairdner Hospital, Western Australia, Australia. lindyr@cyllene.uwa.edu.au

OBJECTIVE: Sexual dysfunction and low testosterone levels have been observed previously in males with chronic noncancer pain treated with intrathecal opioids. To investigate the hypothesis that intrathecal opioids suppress the hypothalamic-pituitary-gonadal axis, a prospective nonrandomized investigation of the function of this axis was undertaken. DESIGN: Ten males with chronic noncancer pain were evaluated for clinical and biochemical evidence of hypogonadism at baseline and during the first twelve weeks of intrathecal opioid therapy. RESULTS: Intrathecal opioid administration resulted in a significant ($p < 0.0001$) reduction in serum testosterone, from 7.7 +/- 1.1 (mean +/- SEM) nmol/L at baseline to 2.0 +/- 0.7, 2.8 +/- 0.5, and 4.0 +/- 0.9 nmol/L at 1, 4, and 12 weeks, respectively. This was associated with a reduction in libido and potency. Luteinizing hormone and follicle-stimulating hormone levels remained within reference ranges, indicating central rather than peripheral suppression. CONCLUSIONS: Administration of intrathecal opioids may result in hypogonadotrophic hypogonadism. As part of the consent for therapy process, patients should be informed about this effect and its management. With long-term intrathecal opioid administration, the hypothalamic-pituitary-

gonadal axis should be monitored. Where indicated, testosterone replacement should be undertaken to improve sexual function and prevent the potential metabolic effects of hypogonadism, in particular, osteoporosis.

PMID: 12048415

Rating: 4c

Roberts LJ, Price L, Hadlow NC, Pullan PT. Hypogonadism in patients treated with intrathecal morphine. Clin J Pain. 2000;16:251-4.

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OBJECTIVE: The objective of this study was to investigate the hypothalamic-pituitary-gonadal response to intrathecal opioids. PATIENTS: Thirty patients receiving intrathecal morphine for chronic nonmalignant pain were studied for clinical and biochemical evidence of hypogonadism. Ten men and 10 postmenopausal women with chronic pain of similar duration but who were not receiving any form of opioid therapy acted as control subjects. RESULTS: Men and both premenopausal and postmenopausal women had evidence of hypogonadism with low levels of serum testosterone or estrogen coupled with low levels of pituitary gonadotrophins. Control subjects had hormone levels in the expected range for their sex and age. Two men demonstrated recovery after ceasing intrathecal opioid therapy. CONCLUSIONS: Hypogonadotrophic hypogonadism is a common complication of intrathecal opioid therapy in both men and women.

PMID: 11014399

Rating: 3c

Roberts, L. J., et al. Outcome of intrathecal opioids in chronic non-cancer pain European Journal of Pain. 2001; Number 5: 353-361.

Rating: 5c

Quality: N/A. Total Rating: N/A. Comment: Does not meet inclusion criteria for evidence-based review. [CA DWC]

Robertson VJ, Baker KG. A review of therapeutic ultrasound: effectiveness studies. Phys Ther. 2001 Jul;81(7):1339-50.

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BACKGROUND AND PURPOSE: Therapeutic ultrasound is one of the most widely and frequently used electrophysical agents. Despite over 60 years of clinical use, the effectiveness of ultrasound for treating people with pain, musculoskeletal injuries, and soft tissue lesions remains questionable. This article presents a systematic review of randomized controlled trials (RCTs) in which ultrasound was used to treat people with those conditions. Each trial was designed to investigate the contributions of active and placebo ultrasound to the patient outcomes measured. Depending on the condition, ultrasound (active and placebo) was used alone or in conjunction with other interventions in a manner designed to identify its contribution and distinguish it from those of other interventions. METHODS: Thirty-five English-language RCTs were published between 1975 and 1999. Each RCT identified was scrutinized for patient outcomes and methodological adequacy. RESULTS: Ten of the 35 RCTs were judged to have acceptable methods using criteria based on those developed by Sackett et al. Of these RCTs, the results of 2 trials suggest that therapeutic ultrasound is more effective in treating some clinical problems (carpal tunnel syndrome and calcific tendinitis of the shoulder) than placebo ultrasound, and the results of 8 trials suggest that it is not. DISCUSSION AND CONCLUSION: There was little evidence that active therapeutic ultrasound is more effective than placebo ultrasound for treating people with pain or a range of musculoskeletal injuries or for promoting soft tissue healing. The few studies deemed to have adequate methods examined a wide range of patient problems. The dosages used in these studies varied considerably, often for no discernable reason.

Publication Types:
Review

PMID: 11444997

Rating: 1b

Robinson JP, Fulton-Keohe D, Martin C, Franklin GM. Outcomes of Pain Center Treatment in Washington State Workers' Compensation. Am J Ind Med 2001;227-236.

Abstract:

BACKGROUND: Injured workers with chronic pain who have failed conventional therapies often receive treatment at pain centers. This study evaluated the effect of pain center treatment on time loss status of Washington State injured workers. The primary hypothesis was that treatment at a pain center would lead to a reduction in the probability of a worker's receiving time loss benefits at a 2-year follow-up. METHODS: A population-based retrospective cohort study was performed on 2,032 Washington State workers' compensation patients who underwent pain center evaluations. Subjects who received

pain center treatment were compared to those who were evaluated but not treated with respect to time loss status at 2-year follow-up. RESULTS: Univariate analysis revealed that at 2-year follow-up, 35% of treated subjects were receiving time loss payments vs. 40% of evaluated only subjects ($P < 0.05$). Subjects who were younger, female, and less chronic were more likely to undergo pain center treatment and were less likely to be on time loss at 2-year follow-up. In multivariate analyses, which statistically controlled baseline differences between the two groups, there was no difference between treated subjects and evaluated only subjects. CONCLUSIONS: There was no evidence that pain center treatment alters 2-year time loss status of already disabled workers.

Conclusion:

Crude comparison showed that odds of receiving time loss payments was lower in treated than in untreated group (OR=0.83, 95% C.I.=0.68-1.00)
Apparent advantage of treated group was due to confounders, since pain centers enroll patients with more favorable prognoses (younger, female, less chronic)
Publication Type: Case Control Study, 2032 cases
Rating: 4b

Robinson JP, Fulton-Kehoe D, Franklin GM, Wu R, Multidisciplinary pain center outcomes in Washington State Workers' Compensation, J Occup Environ Med. 2004 May;46(5):473-8.

University of Washington Pain Center, Seattle, Washington, USA. jimrob@u.washington.edu

We conducted this study to evaluate the clinical and disability status of injured workers 4.6 years after undergoing multidisciplinary pain center evaluation, comparing subjects who received treatment to subjects who were evaluated only. Three hundred injured workers were selected for a telephone survey; 150 had received pain center treatment and 150 had been evaluated but not treated. The survey included the SF-12, and questions about subjects' pain intensity and current work status. A workers' compensation database indicated the disability status of subjects. The response rate was 50%. In multivariate analyses, treated and evaluated-only subjects did not differ significantly in disability status, pain intensity, SF-12 scores, or current work status. At 4.6 years follow up, there was no evidence that pain center treatment affects either disability status or clinical status of injured workers.

PMID: 15167396
Rating: 4b

Rome JD, Townsend CO, Bruce BK, Sletten CD, Luedtke CA, Hodgson JE. Chronic noncancer pain rehabilitation with opioid withdrawal: comparison of treatment outcomes based on opioid use status at admission. Mayo Clin Proc. 2004 Jun;79(6):759-68.

Pain Rehabilitation Center, Mayo Clinic College of Medicine, Rochester, MN 55905, USA.
rome.jeffrey@mayo.edu

OBJECTIVE: To study differences in treatment outcomes between patients with chronic noncancer pain taking vs those not taking maintenance opioids at admission to a pain rehabilitation program. PATIENTS AND METHODS: A nonrandomized 2-group prepost design was used to compare 356 patients admitted to the Mayo Comprehensive Pain Rehabilitation Center from January 2002 to December 2002 at admission and discharge by opioid status at admission. Measures of pain severity, interference due to pain, perceived life control, affective distress, activity level, depression, and catastrophyzing (an exaggerated negative mental set associated with actual or anticipated pain experiences) were used to compare opioid and nonopioid groups. The patients entered a 3-week intensive outpatient multidisciplinary pain rehabilitation program designed to improve adaptation to chronic noncancer pain. The program uses a cognitive-behavioral model and incorporates opioid withdrawal. RESULTS: More than one third of patients (135/356) were taking opioids daily at admission. At completion of the program, all but 3 of the 135 patients had successfully discontinued opioid treatment. No significant pretreatment differences were found between the opioid and nonopioid group regarding demographics, pain duration, treatment completion, or all outcome variables, including pain severity. Significant improvement was noted at discharge for all outcome variables assessed regardless of opioid status at admission. CONCLUSION: Patients with symptomatically severe and disabling pain while taking maintenance opioid therapy can experience significant improvement in physical and emotional functioning while participating in a pain rehabilitation program that incorporates opioid withdrawal.

PMID: 15182090

Rating: 4b

Note: This was primarily a female, non-workers' compensation population.

Rooks DS. Fibromyalgia treatment update. Curr Opin Rheumatol. 2007 Mar;19(2):111-7.

Division of Rheumatology and the Center for the Study of Nutrition Medicine, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, Massachusetts 02215, USA.
drooks@bidmc.harvard.edu

PURPOSE OF REVIEW: Fibromyalgia is a common chronic pain disorder characterized by complex symptomatology and few consistently effective treatments. The purpose of this review is to highlight the recent literature from April 2005 through September 2006 involving treatment options. RECENT FINDINGS: Prior evidence suggests that medication and self-management approaches to care can improve symptoms, function and well-being in this patient population. Recent studies examining the efficacy of two serotonin and norepinephrine-reuptake inhibitors--duloxetine and milnacipran--and the

anticonvulsant pregabalin are encouraging. Studies evaluating different forms of exercise continue to support the belief that increased physical activity is an essential component of any treatment plan for the patient with fibromyalgia. Three studies added to the understanding of treatment adherence. Finally, three studies evaluating the efficacy of acupuncture in the treatment of fibromyalgia showed conflicting results, but added to the knowledge needed for clinicians to have substantive conversations with patients. SUMMARY: Recent studies support the recommendation of a multimodal approach to treatment involving individualized, evidence-based pharmacotherapy and self-management. Treatment goals should include the improvement of symptoms, primarily pain and sleep, and the promotion of positive health behaviors with the aim of improving physical function and emotional well-being.

PMID: 17278924

Rating: 1b

Rooks DS, Gautam S, Romeling M, Cross ML, Stratigakis D, Evans B, Goldenberg DL, Iversen MD, Katz JN. Group Exercise, Education, and Combination Self-management in Women With Fibromyalgia: A Randomized Trial. Arch Intern Med. 2007 Nov 12;167(20):2192-200.
Novartis Institutes for Biomedical Research, Inc, Translational Medicine, 400 Technology Sq, Eighth Floor, Room 836, Cambridge, MA 02139. daniel.rooks@novartis.com.

BACKGROUND: Self-management has increasingly been recommended as part of standard care for fibromyalgia, a common, poorly understood condition with limited treatment options. Data that assess popular self-management recommendations are scarce. We evaluated and compared the effectiveness of 4 common self-management treatments on function, symptoms, and self-efficacy in women with fibromyalgia. METHODS: A total of 207 women with confirmed fibromyalgia were recruited from September 16, 2002, through November 30, 2004, and randomly assigned to 16 weeks of (1) aerobic and flexibility exercise (AE); (2) strength training, aerobic, and flexibility exercise (ST); (3) the Fibromyalgia Self-Help Course (FSHC); or (4) a combination of ST and FSHC (ST-FSHC). The primary outcome was change in physical function from baseline to completion of the intervention. Secondary outcomes included social and emotional function, symptoms, and self-efficacy. RESULTS: Improvements in the mean Fibromyalgia Impact Questionnaire score in the 4 groups were -12.7 for the ST-FSHC group, -8.2 for the AE group, -6.6 for the ST group, and -0.3 for the FSHC group. The ST-FSHC group demonstrated greater improvement than the FSHC group (mean difference, -12.4; 95% confidence interval [CI], -23.1 to -1.7). The ST-FSHC (mean difference, 13.6; 95% CI, 2.3 to 24.9) and AE (mean difference, 13.1; 95% CI, 1.6 to 25.6) groups had similar improvements in physical function scores on the 36-Item Short-Form Health Survey. Bodily pain scores on the 36-Item Short-Form Health Survey improved in the ST-FSHC (14.8), AE (13.2), and ST (5.7) groups. Social function, mental health, fatigue, depression, and self-efficacy also improved. The beneficial effect on physical function of exercise alone and in combination with education persisted at 6 months. CONCLUSIONS: Progressive walking, simple strength training movements, and stretching activities improve functional status, key symptoms, and self-efficacy in women with fibromyalgia actively being treated with medication. The

benefits of exercise are enhanced when combined with targeted self-management education. Our findings suggest that appropriate exercise and patient education be included in the treatment of fibromyalgia. Trial Registration clinicaltrials.gov Identifier: NCT00321659.

PMID: 17998491

Rating: 2b

November 19, 2007 — Progressive walking, simple strength training, and stretching improved functional status, key symptoms, and self-efficacy in women with fibromyalgia actively treated with medication, according to the results of a randomized controlled trial reported in the November 12 issue of the Archives of Internal Medicine. Limitations of the study include absence of a control group that received no intervention and dropout of approximately one third of the overall sample. "The findings of this study contribute to the growing body of knowledge on the benefits of exercise and physical activity for improving the health and function of adults with chronic illness," the study authors conclude. "People with rheumatic conditions are even less active than the relatively sedentary general public. Future studies are needed to identify ways of integrating appropriate exercise into the treatment plans of people with fibromyalgia and other chronic illnesses and to promote the adoption and maintenance of a more physically active lifestyle." The Arthritis Foundation and National Institutes of Health supported this study. Dr. Rooks is now employed by the Novartis Institutes for Biomedical Research, Inc, Cambridge, Massachusetts. Four of the study authors have received funding from the Arthritis Foundation and National Institutes of Health. The remaining study authors have disclosed no relevant financial relationships
Clinical Context: Fibromyalgia is a complex disease, characterized by diffuse chronic pain for more than 3 months and bilateral sites of focal tenderness. It is associated with fatigue, sleep dysfunction, stiffness, depression, cognitive disruption, and exercise intolerance. The causes and pathologic mechanisms of fibromyalgia are unknown. Its prevalence is higher in women than men. Treatment usually involves pharmacotherapy; however, it is often insufficient to resolve persistent symptoms or improve functional limitations and quality of life. Self-management has increasingly been recommended as part of standard care for fibromyalgia, but data that assess popular self-management recommendations are scarce.
Study Highlights: Of the 207 participants randomized, 135 (65%) completed the 16-week intervention period and underwent a follow-up assessment. Social function, mental health, fatigue, depression, and self-efficacy also improved in the exercise and the combined groups. The beneficial effect on physical function of exercise alone and in combination with education persisted at 6 months. Limitations of this study included the lack of a no-treatment group and dropout of one third of the sample.

Rosenquist RW, Rosenberg J; United States Veterans Administration. Postoperative pain guidelines. Reg Anesth Pain Med. 2003 Jul-Aug;28(4):279-88.

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BACKGROUND AND OBJECTIVES: Postoperative pain is the expected but nonetheless undesirable byproduct of all surgical procedures. Humanitarian concerns and recent quasi-governmental regulations have heightened awareness about the importance of treating postoperative pain. This guideline builds upon the foundation created by the Agency for Health Care Policy and Research guideline published in 1993, highlights changes that have occurred over the past 10 years, and makes recommendations based on the current scientific evidence. In addition, it takes advantage of the versatile information management inherent in a web-based format to make the information readily available. METHODS: A multidisciplinary group of physicians, dentists, nurses, pharmacists, physical therapists, psychologists, and ethicists from the Veterans Health Administration (VHA) and Department of Defense (DoD) in conjunction with the VHA Office of Quality and Performance and a consultant group developed a postoperative pain algorithm and supporting documentation. The guideline structure and content were determined by a standardized rating of the evidence gleaned from comprehensive electronic searches. RESULTS: An interactive electronic and traditional "paper" guideline with a pre- and postoperative algorithm was developed. A table, which provides a menu of analgesic choices organized by specific operation, was constructed. Preferences for particular analgesic techniques and classes of medications were identified. A postoperative pain interactive pharmacopoeia and printable patient educational materials were also provided. The guideline may be reviewed at the following website: www.oqp.med.va.gov/cpg/cpg.htm. CONCLUSIONS: This postoperative pain guideline provides readily accessible information and evidence-based guidance to a variety of providers. It highlights deficiencies in our understanding of the pain and recovery processes and how they might guide our choices of postoperative analgesic techniques. In combination with the powerful system-wide data collection capabilities of the VHA, there may be improved understanding of what techniques are useful. Finally, it may lead to the development of reliable, individualized analgesic plans for specific surgical procedures that incorporate the full range of pharmacologic and nonpharmacologic techniques.

PMID: 12945020

Rating: 5c

Rosenstock J, Hollander P, Gadde KM, Sun X, Strauss R, Leung A; OBD-202 Study Group. A randomized, double-blind, placebo-controlled, multicenter study to assess the efficacy and safety of topiramate controlled release in the treatment of obese type 2 diabetic patients. Diabetes Care. 2007;30:1480-6.

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OBJECTIVE: This is a randomized, placebo-controlled study of the weight-loss efficacy and safety of a controlled-release (CR) formulation of topiramate in overweight and obese patients with type 2 diabetes treated with diet and exercise alone or in combination with metformin. RESEARCH DESIGN AND METHODS: Patients with type 2 diabetes, BMI > or =27 kg/m2, A1C >6.5 and <11.0%, treated with

diet and exercise alone or in combination with metformin monotherapy were enrolled. Patients were randomized to placebo or topiramate CR titrated up to 175 mg/day. Treatment consisted of a 7-week titration phase followed by a 9-week maintenance phase. RESULTS: A total of 111 subjects were randomized and analyzed. By the end of week 16, patients in the placebo and topiramate groups lost 2.5 and 6.0 kg, which represented 2.3 and 5.8%, respectively, of their baseline body weight ($P < 0.001$ vs. placebo). A1C improved from a baseline of 7.4% in the placebo and 7.6% in the topiramate groups to 7.1 and 6.7%, respectively, representing a 0.4 and 0.9% reduction from baseline, respectively ($P < 0.001$ vs. placebo). Topiramate also significantly reduced blood pressure and urinary albumin excretion. Adverse events were predominantly neuropsychiatric or central and peripheral nervous system related. CONCLUSIONS: Topiramate CR treatment produced significant weight loss and meaningful improvements in A1C and blood pressure in obese patients with type 2 diabetes treated with diet and exercise or in combination with metformin. However, the central nervous system and psychiatric adverse event profile of topiramate CR makes it unsuitable for the treatment of obesity and diabetes.

PMID: 17363756

Rating: 2b

Rousmaniere PF. Pain Medication in Workers Compensation. Risk & Insurance Magazine. April 2002.

Abstract:

Conquest of pain is one of the many holy grails in this age of astonishing medical advances. Opioids can help to relieve pain in many instances. Can they bring workers back to gainful employment and a productive life? If so, they could be the greatest single advance in occupational medicine of this decade. If they do not, they may, as some allege, add 1% to 2%, or $500 million to $1 billion a year to claims costs and leave workers no better off in the end.

According to industry estimates, over 10 % of soft tissue injured workers with at least six months' duration of disability may be on opioids for extended periods. In addition, many physicians appear to be prescribing opioids for brief acute care relief. It is easy to see how use of opioids may grow. First, the potential demand for relief from pain is enormous. Gerry Hendershot, who worked at CDC's National Center for Health Statistics for 25 years, and is now an independent consultant on disability and health statistics, says that between 29% and 48% of working Americans report a recent experience with major, persistent pain. Second, pain is the major issue for claims of long duration. Fred Uehlein, Chairman of Insurance Recovery Group, of Natick, MA, a provider of legal disability services to the property & casualty industry, estimates that chronic pain exists in over half of the long term disability claims and workers comp permanent awards in which his firm is involved.

Publication Type: Review

Rowbotham M, Harden N, Stacey B, Bernstein P, Magnus-Miller L. Gabapentin for the Treatment of Postherpetic Neuralgia. A Randomized Controlled Trial. JAMA 1998;280;1837-42.

UCSF Pain Clinical Research Center, University of California, San Francisco 94115, USA.

Postherpetic neuralgia (PHN) is a syndrome of often intractable neuropathic pain following herpes zoster (shingles) that eludes effective treatment in many patients. A total of 229 subjects were randomized. The study concluded, "Gabapentin is effective in the treatment of pain and sleep interference associated with Postherpetic neuralgia (PHN). Mood and quality of life also improve with gabapentin therapy."

Publication Types: Clinical Trial, Multicenter Study, Randomized Controlled Trial, 229 cases

PMID: 9846778

Rating: 2b

Rowbotham MC. Pharmacologic management of complex regional pain syndrome. Clin J Pain. 2006;22:425-9.

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Few randomized controlled trials of oral pharmacotherapy have been performed in patients with complex regional pain syndrome (CRPS). The prevalence of CRPS is uncertain. Severe and advanced cases of CRPS are easily recognized but difficult to treat and constitute a minority compared with those who meet minimum criteria for the diagnosis. Unsettled disability or liability claims limit pharmaceutical industry interest in the disorder. Many studies are small or anecdotal, or are reported on only via posters at meetings. Targeting the process of bone resorption with bisphosphonate-type compounds such as calcitonin, clodronate, and alendronate has shown efficacy in three published randomized controlled trials. Intravenous phentolamine has been studied both alone and in comparison to intravenous regional blockade or stellate ganglion block. Steroids continue to be administered by multiple routes without large-scale placebo-controlled trials. Topical medications have received little attention. There has been considerable interest in the use of thalidomide and TNF-alpha blockers for CRPS, but no published controlled trials as of yet. Numerous other oral drugs, including muscle relaxants, benzodiazepines, antidepressants, anticonvulsants, and opioids, have been reported on anecdotally. Some therapies have been the subject of early controlled studies, without subsequent follow-up (eg, ketanserin) or without an analogous well-tolerated and equally effective oral treatment (eg, intravenous ketamine). Gabapentin, tricyclic antidepressants, and opioids have been proven effective for chronic pain in disorders other than CRPS. Each has shown a broad enough spectrum of analgesic activity to be cautiously recommended for treatment of CRPS until adequate randomized

controlled trials settle the issue. The relative benefit of oral medications compared with the widely used treatments of intensive physical therapy, nerve blocks, sympathectomy, intraspinally administered drugs, and neuromodulatory therapies (eg, spinal cord stimulation) remains uncertain. In summary, treatment of CRPS has received insufficient study and remains largely empirical.

PMID: 16772796

Rating: 5a

Roxane Laboratories, Inc. Prescribing Information for Methadone. 2006.

Dolophine® Hydrochloride CII (Methadone Hydrochloride Tablets, USP) 5 mg, 10 mg Rx Only

Patient Information Dolophine® Hydrochloride CII

Roy-Byrne PP, Davidson KW, Kessler RC, Asmundson GJ, Goodwin RD, Kubzansky L, Lydiard RB, Massie MJ, Katon W, Laden SK, Stein MB. Anxiety disorders and comorbid medical illness. Gen Hosp Psychiatry. 2008;30:208-25

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OBJECTIVE: To provide an overview of the role of anxiety disorders in medical illness. METHOD: The Anxiety Disorders Association of America held a multidisciplinary conference from which conference leaders and speakers reviewed presentations and discussions, considered literature on prevalence, comorbidity, etiology and treatment, and made recommendations for research. Irritable bowel syndrome (IBS), asthma, cardiovascular disease (CVD), cancer and chronic pain were reviewed. RESULTS: A substantial literature supports clinically important associations between psychiatric illness and chronic medical conditions. Most research focuses on depression, finding that depression can adversely affect self-care and increase the risk of incident medical illness, complications and mortality. Anxiety disorders are less well studied, but robust epidemiological and clinical evidence shows that anxiety disorders play an equally important role. Biological theories of the interactions between anxiety and IBS, CVD and chronic pain are presented. Available data suggest that anxiety disorders in medically ill patients should not be ignored and could be considered conjointly with depression when developing strategies for screening and intervention, particularly in primary care. CONCLUSIONS: Emerging data offer a strong argument for the role of anxiety in medical illness and suggest that anxiety disorders rival depression in terms of risk, comorbidity and outcome. Research programs designed to advance our understanding of the impact of anxiety disorders on medical illness are needed to develop evidence-based approaches to improving patient care.

PMID: 18433653

This article discusses the role of anxiety in chronic pain.

Rating: 5b

Ruane R, Griffiths P, Glucosamine therapy compared to ibuprofen for joint pain, Br J Community Nurs. 2002 Mar;7(3):148-52.

Primary Care and Community Pharmacy, King's College London.

To determine the effectiveness of oral glucosamine with ibuprofen for the relief of joint pain in osteoarthritis a mini-review (Griffiths, 2002) of double-blind randomized controlled trials comparing the two was undertaken. The population was adult patients diagnosed with osteoarthritis at any site. The outcome was arthritic pain reduction. Searches on Medline, Embase, AMED, the Cochrane Library and the Merck index identified four trials. Of these, two studies were obtainable and were included in the review. Both compared 1.2 g ibuprofen daily with 1.5 g glucosamine sulphate daily, in three divided doses. The combined number of participants in the studies was 218. The results of these studies showed glucosamine to be of similar efficacy to ibuprofen. The conclusion is that glucosamine is effective in relieving joint pain associated with osteoarthritis. Glucosamine's pain-relieving effects may be due to its cartilage-rebuilding properties; these disease-modifying effects are not seen with simple analgesics and are of particular benefit. In practice glucosamine can be used as an alternative to anti-inflammatory drugs and analgesics or as a useful adjunct to standard analgesic therapy.

Publication Types:
- Review
- Review Literature

PMID: 11904551
Rating: 1c

Rushton DN, Electrical stimulation in the treatment of pain, Disabil Rehabil. 2002 May 20;24(8):407-15.

Frank Cooksey Rehabilitation Unit, King's College Hospital, Denmark Hill, London SE5 8AZ, UK. david.rushton@kingshc.nhs.uk

PURPOSE: To review the published literature concerning the treatment of painful conditions using devices that deliver electrical stimulation to nervous structures. The review briefly surveys the results obtained using surface electrodes ("TENS") as well as implanted devices. METHOD: The method used is a critical review of the important published literature up to mid-1999. References were obtained using Medline and the keywords "pain", together with "electrical", "stimulation", "neurostimulation" or

"TENS". RESULTS: Electrical stimulation has been found to be of potential benefit in the management of a range of painful conditions. Adequately controlled trials of electrical stimulation are often difficult to achieve. Implanted devices tend to be used in the more severe intractable pain conditions. It is likely that there is more than one mechanism of action. The mechanisms of action are however still often poorly understood, even though historically theoretical and experimental advances in the understanding of pain mechanisms prompted the development of clinical systems and the institution of clinical studies. CONCLUSIONS: TENS has proved to be remarkably safe, and provides significant analgesia in about half of patients experiencing moderate predictable pain. Implanted devices can be more effective, but they carry a risk of device failure, implant infection or surgical complication, and are reserved for the more severe intractable chronic pains. The main implanted devices used clinically are the spinal cord stimulator and the deep brain stimulator.

Publication Types:
- Review
- Review, Tutorial

PMID: 12033995

Rating: 5c

Saarto T, Wiffen PJ. Antidepressants for neuropathic pain. Cochrane Database Syst Rev. 2005 Jul 20;(3):CD005454.

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BACKGROUND: For many years antidepressant drugs have been used to manage neuropathic pain, and are often the first choice treatment. It is not clear, however, which antidepressant is more effective, what role the newer antidepressants can play in treating neuropathic pain, and what adverse effects are experienced by patients. OBJECTIVES: To determine the analgesic effectiveness and safety of antidepressant drugs in neuropathic pain. Migraine and headache studies were not considered. SEARCH STRATEGY: Randomised trials of antidepressants in neuropathic pain were identified in MEDLINE (1966 to Dec 2003); EMBASE (1980 to Dec 2003); the Cochrane Central Register of Controlled Trials (CENTRAL) in The Cochrane Library 2004, Issue 1; and the Cochrane Pain, Palliative and Supportive Care Trials Register (May 2002). Additional reports were identified from the reference list of the retrieved papers, and by contacting investigators. SELECTION CRITERIA: Randomised trials reporting the analgesic effects of antidepressant drugs in adult patients, with subjective assessment of pain of neuropathic origin. Studies that included patients with chronic headache and migraine were excluded. DATA COLLECTION AND ANALYSIS: Two reviewers agreed the included studies, extracted data, and assessed methodological quality independently. Fifty trials of 19 antidepressants were considered eligible (2515 patients) for inclusion. Relative Risk (RR) estimates and Number-Needed-to-Treat

(NNTs) were calculated from dichotomous data for effectiveness and adverse effects. MAIN RESULTS: Tricyclic antidepressants (TCAs) are effective treatments for the treatment of neuropathic pain. Amitriptyline has an NNT of 2 (95%CI 1.7 to 2.5) RR 4.1(95%CI 2.9-5.9) for the achievement of at least moderate pain relief. There is limited evidence for the effectiveness of the newer selective serotonin reuptake inhibitor antidepressant drugs (SSRIs). There were insufficient data for an assessment of evidence of effectiveness for other antidepressants such as St Johns Wort, venlafaxine and L-tryptophan. For diabetic neuropathy the NNT for effectiveness was 1.3 (95%CI 1.2 to 1.5) RR 12.4(95%CI 5.2-29.2) (five studies); for postherpetic neuralgia 2.2 (95%CI 1.7 to 3.1), RR 4.8(95%CI 2.5-9.5)(three studies). There was evidence that TCAs are not effective in HIV-related neuropathies. The number needed to harm (NNH) for major adverse effects defined as an event leading to withdrawal from a study was 16 (95%CI: 10-45). The NNH for minor adverse effects was 4.6 (95%CI 3.3-6.7) AUTHORS' CONCLUSIONS: Antidepressants are effective for a variety of neuropathic pains. The best evidence available is for amitriptyline. There are only limited data for the effectiveness of SSRIs. It is not possible to identify the most effective antidepressant until more studies of SSRIs are conducted.

Publication Types:
Meta-Analysis
Review

PMID: 16034979

Rating: 1a

Saarto T, Wiffen P. Antidepressants for neuropathic pain. Cochrane Database Syst Rev. 2007 Oct 17;(4):CD005454

BACKGROUND: This is an updated version of the original Cochrane review published in Issue 3, 2005 of The Cochrane Library. For many years antidepressant drugs have been used to manage neuropathic pain, and are often the first choice treatment. It is not clear, however, which antidepressant is more effective, what role the newer antidepressants can play in treating neuropathic pain, and what adverse effects are experienced by patients. OBJECTIVES: To determine the analgesic effectiveness and safety of antidepressant drugs in neuropathic pain. SEARCH STRATEGY: Randomised controlled trials (RCTs) of antidepressants in neuropathic pain were identified in MEDLINE (1966 to Oct 2005); EMBASE (1980 to Oct 2005); the Cochrane Central Register of Controlled Trials (CENTRAL) in The Cochrane Library, Issue 3, 2005; and the Cochrane Pain, Palliative and Supportive Care Trials Register (May 2002). Additional reports were identified from the reference list of the retrieved papers, and by contacting investigators. SELECTION CRITERIA: RCTs reporting the analgesic effects of antidepressant drugs in adult patients, with subjective assessment of pain of neuropathic origin. Studies that included patients with chronic headache and migraine were excluded. DATA COLLECTION AND ANALYSIS: Two review authors agreed the included studies, extracted data, and assessed methodological quality independently. Sixty one trials of 20 antidepressants were considered eligible

(3293 participants) for inclusion. Relative Risk (RR) and Number-Needed-to-Treat (NNTs) were calculated from dichotomous data for effectiveness and adverse effects.This update includes 11 additional studies (778 participants). MAIN RESULTS: Sixty one RCTs were included in total. Tricyclic antidepressants (TCAs) are effective and have an NNT of 3.6 (95% CI 3 to 4.5) RR 2.1 (95% CI 1.8 to 2.5) for the achievement of at least moderate pain relief. There is limited evidence for the effectiveness of the newer SSRIs but no studies of SNRIs were found. Venlafaxine (three studies) has an NNT of 3.1 (95% CI 2.2 to 5.1) RR 2.2 (95% CI 1.5 to 3.1). There were insufficient data to assess effectiveness for other antidepressants such as St Johns Wort and L-tryptophan. For diabetic neuropathy the NNT for effectiveness was 1.3 (95% CI 1.2 to 1.5) RR 12.4 (95% CI 5.2 to 29.2) (five studies); for postherpetic neuralgia 2.7 (95% CI 2 to 4.1), RR 2.2 (95% CI 1.6 to 3.1) (four studies). There was evidence that TCAs are not effective in HIV-related neuropathies. The number needed to harm (NNH) for major adverse effects defined as an event leading to withdrawal from a study was 28 (95% CI 17.6 to 68.9) for amitriptyline and 16.2 (95% CI 8 to 436) for venlafaxine. The NNH for minor adverse effects was 6 (95% CI 4.2 to 10.7) for amitriptyline and 9.6 (95% CI 3.5 to 13) for venlafaxine. AUTHORS' CONCLUSIONS: This update has provided additional confirmation on the effectiveness of antidepressants for neuropathic pain and has provided new information on another antidepressant - venlafaxine. There is still limited evidence for the role of SSRIs. Whether antidepressants prevent the development of neuropathic pain (pre-emptive use) is still unclear. Both TCAs and venlafaxine have NNTs of approximately three. This means that for approximately every three patients with neuropathic pain who are treated with either of these antidepressants, one will get at least moderate pain relief. There is evidence to suggest that other antidepressants may be effective but numbers of participants are insufficient to calculate robust NNTs. SSRIs are generally better tolerated by patients and more high quality studies are required.

PMID: 17943857

Review: 1a

Sachs CJ. Oral analgesics for acute nonspecific pain. Am Fam Physician. 2005 Mar 1;71(5):913-8.

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Physicians most often recommend or prescribe oral medication for relief of acute pain. This review of the available evidence supports the use of acetaminophen in doses up to 1,000 mg as the initial choice for mild to moderate acute pain. In some cases, modest improvements in analgesic efficacy can be achieved by adding or changing to a nonsteroidal anti-inflammatory drug (NSAID). The safest NSAID is ibuprofen in doses of 400 mg. Higher doses may offer somewhat greater analgesia but with more adverse effects. Other NSAIDs have failed to demonstrate consistently greater efficacy or safety than ibuprofen. Although they may be more expensive, these alternatives may be chosen for their more convenient dosing. Cyclooxygenase-2 inhibitors provide equivalent efficacy to traditional NSAIDs but

lack a demonstrable safety advantage for the treatment of acute pain. For more severe acute pain, the evidence supports the addition of oral narcotic medications such as hydrocodone, morphine, or oxycodone. Specific oral analgesics that have shown poor efficacy and side effects include codeine, propoxyphene, and tramadol.

PMID: 15768621

Rating: 5b

Sahin F, Yilmaz F, Kotevoglu N, Kuran B. Efficacy of salmon calcitonin in complex regional pain syndrome (type 1) in addition to physical therapy. Clin Rheumatol. 2005 Jun 25.

Department of Physical Medicine and Rehabilitation, Sisli Etfal Education and Research Hospital, Istanbul, Turkey.

The aim of the study was to assess the efficacy of salmon calcitonin, which was suggested as effective in the treatment of complex regional pain syndrome type 1 (CRPS 1). Patients who had suffered trauma to their upper extremities and developed CRPS 1 were included into this randomised, controlled single-blind study. The diagnosis was made according to the clinical examination and scintigraphy. The evaluation parameters were: pain [visual analogue scale (VAS)], the angle of dorsiflexion (DF) and palmar flexion (PF) of the wrist, distance between the fingertip and distal palmar crease (FT-DPC), allodynia, hyperalgesia and trophic changes. One group received paracetamol 1500 m/day and the other group salmon calcitonin 200 IU/day for 2 months. All of the patients participated in a physical therapy and exercise programme. A total of 35 patients were divided into two groups, who were found to be similar for age, body mass index, period of trauma, period of rest in a plaster splint or bandage, the duration of symptoms, VAS, DF and PF angle, FT-DPC, presence of allodynia, hyperalgesia and trophic changes ($p>0.05$). The control examination showed similar results for allodynia, hyperalgesia and trophic changes, whereas remarkable improvement was observed in the rest of the parameters within groups. On the other hand, between the two groups there was no significant difference in any of the parameters ($p>0.05$) This randomised, single-blind study showed that all of the patients with acute CRPS 1 in their upper extremities after trauma, who were treated with either paracetamol or calcitonin along with physical therapy, recovered in all parameters significantly, but without any difference between groups. We can conclude that calcitonin does not make any favourable contribution in the treatment of patients with acute CRPS 1; physical therapy combined with only a simple analgesic is an efficient means of therapy.

PMID: 15980934

Rating: 2b

Salerno SM, Browning R, Jackson JL, The effect of antidepressant treatment on chronic back pain: a meta-analysis, Arch Intern Med. 2002 Jan 14;162(1):19-24.

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BACKGROUND: Back pain is one of the most common problems in primary care. Antidepressant medication is often prescribed, especially for chronic back discomfort, to alleviate pain and restore the patient's ability to conduct activities of daily living. OBJECTIVE: To assess the efficacy of antidepressants in treating back pain in adults. METHODS: We searched the MEDLINE (1966-2000), PsycLit, Cinhal, EMBASE, AIDSLINE, HealthSTAR, CANCERLIT, the Cochrane Library (clinical trials registry and the Database of Systematic Reviews), Micromedex, and Federal Research in Progress databases and references of reviewed articles. Included articles were written in English and dealt with randomized placebo-controlled trials of antidepressant medication use among adults with chronic back pain. Two reviewers abstracted data independently. Two continuous outcomes, change in back pain severity and ability to perform activities of daily living, were measured. Study quality was assessed with the methods used by Jadad and colleagues, and data were synthesized using a random-effects model. RESULTS: Nine randomized controlled trials with 10 treatment arms and 504 patients were included. Seven treatment arms included patients with major depression. Patients had chronic back pain, averaging 10.4 years. Patients treated with antidepressants were more likely to improve in pain severity than those taking placebo (standardized mean difference, 0.41; 95% confidence interval, 0.22-0.61) but not in activities of daily living (standardized mean difference, 0.24; 95% confidence interval, -0.21-0.69). Patients treated with antidepressants experienced more adverse effects (22% vs 14%, P =.01) than those receiving placebo. CONCLUSION: Antidepressants are more effective than placebo in reducing pain severity but not functional status in chronic back pain.

Publication Types:
- Meta-Analysis
- Review
- Review, Tutorial

PMID: 11784215

SAMHSA (Substance Abuse and Mental Health Services Administration). Methadone-Associated Mortality: Report of a National Assessment. Division of Pharmacologic Therapies, Center for Substance Abuse Treatment, DHHS, 5600 Fishers Lane, Rockville, MD 20857. Publication No. 04-3904. Printed 2004

Methadone is a medication valued for its effectiveness in reducing the mortality associated with opioid addiction as well as the various medical and behavioral morbidities associated with addictive disorders.

It also is an inexpensive and increasingly popular analgesic medication suitable for the treatment of even the most severe acute or chronic pain in well-selected patients.

Rating: 6a

Sanders SH, Harden RN, Vicente PJ. Evidence-Based Clinical Practice Guidelines for Interdisciplinary Rehabilitation of Chronic Nonmalignant Pain Syndrome Patients. World Institute of Pain, Pain Practice, Volume 5, Issue 4, 2005 303–315.

Siskin Hospital's Center for Pain Rehabilitation, Chattanooga, Tennessee.

This is an update to evidence-based practice guidelines for chronic nonmalignant pain syndrome patients first published in 1995 and revised in 1999. The current guidelines
recommend interdisciplinary-focused rehabilitation, which is goal-directed and time-limited. Emphasis is placed on educating patients in active self-management techniques that stress maximizing function. Integrated treatment involving medical, psychological/behavioral, physical/occupational therapy, and disability/vocational interventions are recommended on an outpatient basis whenever clinically possible. Patient selection criteria are delineated. Updated references providing evidence-based support for the recommendations are provided, including the use of opioids and sedativehypnotic medications, injection and block procedures, acupuncture, implantable spinal infusion and stimulation devices, and other invasive spinal surgery procedures such as intradiscal electrothermal therapy. Guideline integration and early detection and intervention with chronic pain syndrome patients are encouraged.

Note: This issue of this journal was not accepted into Medline, and therefore it is not part of the primary evidence based used for ODG, but it includes a helpful reference list.

Per Andrew Brylowski, M.D.:
Attached is an article of evidenced based review of interdisciplinary treatment for chronic pain syndrome. Also, I suggest a brief description of the difference between chronic pain and chronic pain syndrome. AMA guides 5th edition is a good place for that. Here is some of it:
AMA guides fifth edition defines chronic pain as: Pain that extends beyond the expected period of healing or is related to a progressive disease. It is usually elicited by an injury or disease but may be perpetuated by factors that are both pathologically and physically remote from the original cause. Because the pain persists, it is likely that environmental and psychological factors interact with the tissue damage, contributing to the persistence of pain and illness behavior. AMA guides fifth edition page 567 defines chronic pain syndrome (CPS) as: "Although not official nomenclature, it is frequently used (chronic pain syndrome) to describe an individual who is markedly impaired by chronic pain with substantial psychological overlay. Chronic pain syndrome is largely a behavioral syndrome that affects a minority of those with chronic pain. It may best be understood as a form of abnormal illness behavior that consists mainly of excessive adoption of the sick role. The term is useful in that it properly directs therapy toward the reversal of regression and away from an exclusive focus on elimination of

nociception (pain). It does not, however, substitute for a careful diagnosis of the physiologic, psychological, and conditioning components that compromise the syndrome. The term CPS must be used with caution, as grouping pain problems together under a generic disorder may mask and leave untreated import and physiologic differences."

Per ODG Reviewers:
... the definition of chronic pain syndrome remains controversial. The challenge for a treatment guideline is to find an operational definition that helps reviewers and treating providers to define whether or not someone has the condition, or not. In that sense, the 5th edition of the Guides may not be as helpful as the 4th edition. In the 4th edition, on pp. 308-309, there is a definition of "8 Ds," of which 4 or more are considered to reliably define the CPS. With regards to the Sanders article… as the Abstract points out, this is the third iteration of this "guideline," and contains updated references… it is published in a relatively low-impact journal of questionable peer review (an uncertain indexing in Index Medicus). This is a "pragmatic guideline," based on a highly selective review of the pain literature. ... it does not focus on chronic pain treatment in workers' compensation, which leaves the usual problems of subjectivity associated with the outcomes.

Saper JR, Mathew NT, Loder EW, DeGryse R, VanDenburgh AM; BoNTA-009 Study Group. A double-blind, randomized, placebo-controlled comparison of botulinum toxin type a injection sites and doses in the prevention of episodic migraine. Pain Med. 2007 Sep;8(6):478-85.

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DESIGN AND METHODS: This was a randomized, double-blind, placebo-controlled study of 232 patients. CONCLUSIONS: In this exploratory study of episodic migraine patients, low-dose injections of BoNTA into the frontal, temporal, and/or glabellar muscle regions were not more effective than placebo.

PMID: 17716321

Rating: 2b

Savage SR. Opioid use in the management of chronic pain. Medical Clinics of North America. 01-May-1999; 83(3): 761-86.
Dartmouth Medical School, Hanover, New Hampshire, USA
Abstract:
Opioids are a necessary and effective component of the management of chronic non-cancer-related pain in some patients. Careful structuring, monitoring, and documentation of care are important, but the therapeutic use of opioids is uncomplicated in the majority of patients using opioids and is gratifying for both the patient and the treating physician when it results in significant reduction in pain, improvement in level of function, and a higher quality of life. Opioid therapy is most often successful when combined

with other pharmacologic and nonpharmacologic interventions as indicated by the type of pain and the context in which it occurs.
Major Subjects:
- Analgesics, Opioid / adverse effects / * therapeutic use
- Opioid-Related Disorders / drug therapy / * etiology
- Pain / * drug therapy

Publication Type: Review
PMID: 10522738

Savage SR. Assessment for addiction in pain-treatment settings. Clin J Pain. 2002 Jul-Aug;18(4 Suppl):S28-38.

Department of Anesthesiology, Dartmouth Medical School, Manchester Veterans Administration Medical Center, New Hampshire Regional Medical Opioid Treatment and Education Project, Bradford, New Hampshire, USA. seddon.savage@dartmouth.edu

The identification of the disease of addiction is important to safe and effective clinical management of pain in persons with addictive disorders. The disease of addiction affects approximately 10% of the general population, and its prevalence may be higher in subpopulations of patients with pain. The presence of active addiction may facilitate the experience of pain. Both active and recovering addiction may complicate the use of medications, such as opioids, important to the management of pain. There is, further, persistent misunderstanding among health care providers, regulators, and the general population regarding the nature and manifestations of addiction that may result in undertreatment of pain and stigmatization of patients using opioids for pain control. The author seeks to clarify understanding of addiction, to underscore the importance of identifying addiction in the context of pain treatment, and to provide a rational approach to assessment for addiction in patients with pain. Current scientific understanding of addiction as a chronic illness is briefly reviewed. Recent definitions related to addiction are presented. The impact of addictive disorders on pain and pain treatment are explored. The roles of medical interview, physical examination, laboratory studies, and standard addiction screening tools in assessing for addiction are outlined. Differential considerations in distinguishing therapeutic use of opioids for analgesia from addictive or other nontherapeutic use of opioids are discussed. In summary, the article provides salient background and a detailed approach to assessment for addictive disorders in the context of pain treatment.

PMID: 12479252

Rating: 5a

Savage SR. Opioid therapy of chronic pain: assessment of consequences. Acta Anaesthesiol Scand. 1999 Oct;43(9):909-17.

Dartmouth Medical School, Hanover, New Hampshire, USA.

This paper will review what is known about key issues of importance in the clinical use of opioids for the treatment of intractable non-cancer related pain, and will attempt to describe the evolving areas of consensus among clinicians who treat pain and addiction regarding various aspects of use of opioids for the treatment of chronic non-cancer pain.

PMID: 10522738

Rating: 5a

Sandroni P, Low PA, Ferrer T, Opfer-Gehrking TL, Willner CL, Wilson PR. Complex Regional Pain Syndrome I (CRPS I): Prospective Study and Laboratory Evaluation. Clin J Pain 1998:282-9.

Department of Neurology, Mayo Clinic, Rochester, Minnesota 55905, USA.

Publication Type: Case Control Study, 102 cases

PMID: 9874005

Sayson SC, Ramamurthy S. Sympathetic Blocks. In. Principles and Practice of Pain Medicine. 2nd ed. Eds. Warfield CA, Bajwa ZH. McGraw-Hill Co., Inc. New York. 2004.

Rating: 9a

Schears RM. Nonbenzodiazepine hypnosedatives. In: Emergency Medicine: A Comprehensive Study Guide, 6th ed. McGraw-Hill 2004.

(American College of Emergency Physicians) Univ. of North Carolina, Chapel Hill.

Comprehensive reference covers the gamut of emergency practice. New to this edition are chapters on bioterrorism and weapons of mass destruction, pharmacology of antimicrobials, drug interactions, antifungals, and more. For physicians and residents.

Rating: 9b

Schmitt R, Gazalle FK, Lima MS, Cunha A, Souza J, Kapczinski F. The efficacy of antidepressants for generalized anxiety disorder: a systematic review and meta-analysis. Rev Bras Psiquiatr. 2005; 27:18-24.

University Hospital, Federal University, RS, Brazil.

OBJECTIVE: To investigate the efficacy and acceptability of antidepressants in the treatment of generalized anxiety disorder. METHODS: All randomized controlled trials assessing the use of antidepressants in generalized anxiety disorder up to May 2002 were included. Non randomized trials and those that included patients with both generalized anxiety disorder and another Axis I co-morbidity were excluded. Relative risks, weighted mean difference and number needed to treat were estimated. People who died or dropped out were regarded as having had no improvement. RESULTS: Antidepressants (imipramine, venlafaxine and paroxetine) were found to be superior to placebo in treating generalized anxiety disorder. The calculated number needed to treat for antidepressants in generalized anxiety disorder was 5.15. Dropout rates did not differ between antidepressants and placebo. CONCLUSION: The available evidence suggests that antidepressants would probably be a reasonable treatment for generalized anxiety disorder patients in the clinical context.
PMID: 15867979

Rating: 1c

Schneier FR. Clinical practice. Social anxiety disorder. N Engl J Med. 2006;355:1029-36.

Anxiety Disorders Clinic, New York State Psychiatric Institute, New York, NY 10032, USA. frs1@columbia.edu

No abstract was given. This is a review of treatment of social anxiety disorder with a discussion of medication management. SSRIs and SNRIs were recommended as first-line treatment.

PMID: 16957148

Rating: 5c

Schnitzer TJ, Ferraro A, Hunsche E, Kong SX. A comprehensive review of clinical trials on the efficacy and safety of drugs for the treatment of low back pain. J Pain Symptom Manage. 2004 Jul;28(1):72-95.

Office of Clinical Research and Training, Northwestern University, Chicago, Illinois, USA.

A systematic review involving 50 randomized controlled trials (4,863 patients) published since 1980 was undertaken with the objective of assessing efficacy and safety of low back pain (LBP) medications. The methodological quality of each trial was evaluated based on a standardized system. Quality scores ranged from 26 to 82 points on a 100-point scale (from 0 to 100), indicating an overall moderate quality of the trials reviewed. Limited evidence was found regarding the effectiveness of drug treatments for LBP and current studies focused on short-term usage of the therapies. Available evidence supported the effectiveness of non-selective nonsteroidal anti-inflammatory drugs (NSAIDs) in acute and chronic LBP, of muscle relaxants in acute LBP, and of antidepressants in chronic LBP; safety results were

heterogeneous. More rigorously designed trials should be implemented to establish comparative efficacy and safety of drugs used to treat chronic and acute LBP.

Publication Types:
- Review
- Review Literature

PMID: 15223086

Rating: 1b

Scholmerich J. Nonsteroidal anti-inflammatory drugs versus selective COX-2 inhibitors in the upper gastrointestinal tract. J Cardiovasc Pharmacol. 2006;47 Suppl 1:S67-71.

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There are enough basic data supporting the use of coxibs with regard to the upper GI tract in patients with the need for continuous treatment of joint pain. The clinical studies available clearly show that coxibs induce fewer lesions and complications in volunteers and in patients when compared with NSAIDs. However, in Helicobacter pylori- positive patients the advantage seems less clear. The combination of NSAID plus PPI is not worse with regard to duodenal ulcers and recurrent clinical complications and is more cost effective than the use of coxibs. Similarly, with the concomitant use of aspirin even in low doses no major advantage of coxibs has been demonstrated. The combination of coxibs and PPI in high-risk patients needs to be studied. It is unclear at the moment how important are the changes in the lower GI tract. Considering the current controversy regarding cardiovascular events, there is no major reason to prefer coxibs to conventional NSAID plus PPI in patients needing long-term treatment.

PMID: 16785832

Rating: 5c

Schonstein E, Kenny D, Keating J, Koes B, Herbert RD. Physical conditioning programs for workers with back and neck pain: a cochrane systematic review. Spine. 2003 Oct 1;28(19):E391-5

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OBJECTIVE: To determine the effect on time lost from work of physical conditioning programs for workers with back and neck pain. DATA SOURCES Randomized trials were located by searching

MEDLINE, EMBASE, CINAHL, PsycINFO, the Cochrane Controlled Trial Register, and PEDro. REVIEW METHODS: Two reviewers independently extracted data and assessed trial quality. Where data could be pooled, meta-analysis was performed. Based on cost considerations, we nominated a mean saving of 10 sick days per year or a number needed to treat to return 1 person to work of 10 as the smallest treatment effects that would be clinically worthwhile. RESULTS: Nineteen trials in 21 publications yielded 23 contrasts relevant to this review. These trials provide evidence that physical conditioning programs that included a cognitive-behavioral approach could produce a clinically worthwhile reduction in the number of sick days taken at 12 months (average of 45 days; 95% confidence interval 3-88) when compared to general practitioner care or advice for workers with chronic back pain. There was little evidence of an effect on time lost from work of specific exercise programs that did not include a cognitive-behavioral component. CONCLUSION: Physical conditioning programs that incorporate a cognitive-behavioral approach reduce the number of sick days for workers with chronic back pain when compared to usual care.

PMID: 14520051

Rating: 1b

Schultz IZ, Crook J, Berkowitz J, Milner R, Meloche GR, Lewis ML. A Prospective Study of the Effectiveness of Early Intervention with High-risk Back-injured Workers-A Pilot Study. J Occup Rehabil. 2008 Jun;18(2):140-51. Epub 2008 Apr 11.

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Introduction: It was postulated that workers, at the sub-acute stage after injury, respond differently to clinical and occupational interventions offered in a workers' compensation environment. Individual worker risk of disability, it was further believed, would influence the effectiveness of early intervention. The objective of the current pilot study was to evaluate return to work (RTW) outcomes following proactive, combined clinical, occupational and case management-based interdisciplinary early intervention, provided in a workers' compensation environment 4-10 weeks of onset of back pain, to workers with medium and high risk for disability. Methods: The project was a controlled study comparing conventional workers' compensation case management with integrated, interdisciplinary and multimodal early intervention (hereinafter referred to as "EI"). At baseline, risk status was determined by a validated Risk for Disability Questionnaire by Carragee et al. (Spine 5(1):24-35, 2005). Seventeen workers at high risk of protracted disability and 20 workers at moderate risk of disability received conventional case management, and 17 workers assessed at high risk of protracted disability and 18 workers at moderate risk of disability received the Early Intervention. Results: At 3 months post back pain onset, no statistically significant differences were identified in RTW outcomes between conventional case management and the Early Intervention. However, by 6 months post back pain onset, workers at high risk of work disability who received the Early Intervention were significantly more

likely to RTW than high risk workers who received conventional case management. In contrast, moderate risk workers continued to exhibit no statistically significant differences in RTW outcomes. Conclusion: Multimodal Early Intervention in the workers' compensation case management context is likely effective for workers with sub-acute back pain who are at high risk of occupational disability. The comprehensive Early Intervention is, however, likely redundant for workers who are not at high risk for disability and should not be applied indiscriminately. Further studies are required to determine longer-term Early Intervention outcomes, and to replicate the findings using a randomized control design. Also, with a larger sample size, it will be possible to determine predictors of occupational outcomes.

PMID: 18404361

Rating: 3b

Scudds RA, Janzen V, Delaney G, Heck C, McCain GA, Russell AL, Teasell RW, Varkey G, Woodbury MG. The use of topical 4% lidocaine in spheno-palatine ganglion blocks for the treatment of chronic muscle pain syndromes: a randomized, controlled trial. Pain. 1995;62:69-77.

Faculties of Applied Health Sciences, University of Western Ontario, London, Canada.
To assess the efficacy of 4% topical lidocaine in spheno-palatine blocks, a randomized controlled trial was carried out on patients with chronic muscle pain syndromes. Sixty-one patients (42 with fibromyalgia (FM) and 19 with myofascial pain syndrome (MPS)) completed the trial. Outcome measures included pain intensity, a daily pain diary, headache frequency, sensitivity to pressure using a dolorimeter, anxiety, depression, and sleep quality. Patients were randomized to receive either 4% lidocaine or sterile water (placebo) 6 times over a 3-week period. Both subjects and investigators were blind to treatment allocation. The results showed that 4% lidocaine had no superiority over placebo in any of the outcome measures. Twenty-one subjects (35%) showed a decrease in pain which was greater than 30% of their baseline value. Of these 21 subjects, 10 received lidocaine and 11 received placebo. These data suggest that, in this population, 4% lidocaine is no better than placebo in the treatment of chronic muscle pain.

PMID: 7478710

Rating: 2c

See S, Ginzburg R. Skeletal muscle relaxants. Pharmacotherapy. 2008; 28:207-13.

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Health care providers prescribe skeletal muscle relaxants for a variety of indications. However, the comparative efficacy of these drugs is not well known. Skeletal muscle relaxants consist of both

antispasticity and antispasmodic agents, a distinction prescribers often overlook. The antispasticity agents-baclofen, tizanidine, dantrolene, and diazepam-aid in improving muscle hypertonicity and involuntary jerks. Antispasmodic agents, such as cyclobenzaprine, are primarily used to treat musculoskeletal conditions. Much of the evidence from clinical trials regarding skeletal muscle relaxants is limited because of poor methodologic design, insensitive assessment methods, and small numbers of patients. Although trial results seem to support the use of these agents for their respective indications, efficacy data from comparator trials did not particularly favor one skeletal muscle relaxant over another. Therefore, the choice of a skeletal muscle relaxant should be based on its adverse-effect profile, tolerability, and cost.

PMID: 18225966

Rating 5c

See S, Ginzburg R. Use of muscle relaxants for musculoskeletal conditions reviewed. Am Fam Physician. August 1, 2008; 78:365-370.

Sharon See, PharmD, BCPS, and Regina Ginzburg, PharmD, from St. John's University College of Pharmacy and Allied Health Professions in Jamaica, New York.

Recommendations for selecting muscle relaxants for musculoskeletal conditions such as low back pain, fibromyalgia, tension headaches, and myofascial pain syndrome are reviewed in an article published in the August 1 issue of American Family Physician. For nonspecific back pain, skeletal muscle relaxants are the most widely prescribed drug class (18.5% of prescriptions vs 16.3% for NSAIDs and 10% for cyclooxygenase-2 inhibitors). The most commonly prescribed antispasmodic agents are carisoprodol, cyclobenzaprine, metaxalone, and methocarbamol. Despite the widespread use of skeletal muscle relaxants for treatment of musculoskeletal conditions, such as low back or neck pain, fibromyalgia, tension headaches, and myofascial pain syndrome, evidence supporting this practice comes mostly from studies with methodologic issues. Therefore, understanding the risks and benefits of skeletal muscle relaxants is of critical importance. Treatment goals for musculoskeletal conditions include relief of muscle pain and improvement in functional ability, allowing return to work or to customary activities. This review offers evidence concerning the use of antispasmodic skeletal muscle relaxants for various musculoskeletal conditions and appropriate choice of agent if a skeletal muscle relaxant is needed. Despite their popularity, skeletal muscle relaxants should not be the primary drug class of choice for musculoskeletal conditions. The American Pain Society and the American College of Physicians recommend using acetaminophen and NSAIDs as first-line agents for acute low back pain and reserving skeletal muscle relaxants as an alternative treatment option. This recommendation is based on available literature, which shows skeletal muscle relaxants are better than placebo, but not more effective than NSAIDs in patients with acute back pain. The 2 main categories of skeletal muscle relaxants are antispastic agents, including baclofen or dantrolene, for conditions such as cerebral palsy and multiple sclerosis and antispasmodic agents for musculoskeletal conditions. Evidence is extremely limited to

support the use of antispastic agents for musculoskeletal conditions, for which an antispasmodic agent is typically more appropriate. Skeletal muscle relaxants are not considered first-line therapy for musculoskeletal conditions. For acute low back pain, skeletal muscle relaxants may be used as adjunctive therapy, and antispasmodic agents should be used short term. Evidence to date does not clearly support the superiority of 1 skeletal muscle relaxant to another for musculoskeletal spasms. Specific drug profile and individual patient situation should guide the choice of skeletal muscle relaxant.

Rating: 5b

Sengupta K, Alluri KV, Satish AR, Mishra S, Golakoti T, Sarma KV, Dey D, Raychaudhuri SP. A double blind, randomized, placebo controlled study of the efficacy and safety of 5-Loxin(R) for treatment of osteoarthritis of the knee. Arthritis Res Ther. 2008 Jul 30;10(4):R85. [Epub ahead of print]

Department of Medicine, Division of Rheumatology, Allergy and Immunology, School of Medicine, U C Davis and VA Medical Center Sacramento, Hospital Way, Mather, California 95655, USA. sraychaudhuri@ucdavis.edu.

ABSTRACT: INTRODUCTION: 5-Loxin(R) is a novel Boswellia serrata extract enriched with 30% 3-O-acetyl-11-keto-beta-boswellic acid (AKBA), which exhibits potential anti-inflammatory properties by inhibiting the 5-lipoxygenase enzyme. A 90-day, double-blind, randomized, placebo-controlled study was conducted to evaluate the efficacy and safety of 5-Loxin(R) in the treatment of osteoarthritis (OA) of the knee. METHODS: Seventy-five OA patients were included in the study. The patients received either 100 mg (n = 25) or 250 mg (n = 25) of 5-Loxin(R) daily or a placebo (n = 25) for 90 days. Each patient was evaluated for pain and physical functions by using the standard tools (visual analog scale, Lequesne's Functional Index, and Western Ontario and McMaster Universities Osteoarthritis Index) at the baseline (day 0), and at days 7, 30, 60 and 90. Additionally, the cartilage degrading enzyme matrix metalloproteinase-3 was also evaluated in synovial fluid from OA patients. Measurement of a battery of biochemical parameters in serum and haematological parameters, and urine analysis were performed to evaluate the safety of 5-Loxin(R) in OA patients. RESULTS: Seventy patients completed the study. At the end of the study, both doses of 5-Loxin(R) conferred clinically and statistically significant improvements in pain scores and physical function scores in OA patients. Interestingly, significant improvements in pain score and functional ability were recorded in the treatment group supplemented with 250 mg 5-Loxin(R) as early as 7 days after the start of treatment. Corroborating the improvements in pain scores in treatment groups, we also noted significant reduction in synovial fluid matrix metalloproteinase-3. In comparison with placebo, the safety parameters were almost unchanged in the treatment groups. CONCLUSION: 5-Loxin(R) reduces pain and improves physical functioning significantly in OA patients; and it is safe for human consumption. 5-Loxin(R) may exert its beneficial effects by controlling inflammatory responses through reducing proinflammatory modulators, and it may improve joint health by reducing the enzymatic degradation of cartilage in OA patients. TRAIL REGISTRATION: (Clinical trial registration number: ISRCTN05212803.).

PMID: 18667054

Rating: 2c

An enriched extract of the 'Indian Frankincense' herb Boswellia serrata has been proven to reduce the symptoms of osteoarthritis. Research published today in BioMed Central's open access journal Arthritis Research & Therapy has shown that patients taking the herbal remedy showed significant improvement in as little as seven days. Osteoarthritis is the most common form of arthritis; it commonly affects weight-bearing joints such as the knees and hips, along with the hands, wrists, feet and spine. The symptoms include pain, stiffness and limited movement. This randomised, double-blinded, placebo-controlled trial of 70 patients will be of great interest to sufferers, especially those who don't get adequate relief from existing treatments. The study was led by Siba Raychaudhuri, a faculty member of the University of California, Davis, in the United States. According to Raychaudhuri, "The high incidence of adverse affects associated with currently available medications has created great interest in the search for an effective and safe alternative treatment". The extract the authors used was enriched with 30% AKBA (3-O-acetyl-11-keto-beta-boswellic acid), which is thought to be the most active ingredient in the plant. Raychaudhuri said, "AKBA has anti-inflammatory properties, and we have shown that B. serrata enriched with AKBA can be an effective treatment for osteoarthritis of the knee". This is a proprietary product developed by Laila Nutraceuticals. B. serrata has been used for thousands of years in the Indian system of traditional medicine known as 'Ayurveda'. This study is the first to prove that an enriched extract of the plant can be used as a successful treatment. The same authors have previously tested the safety of their remedy in animal experiments. They say that, "In this study, the compound was shown to have no major adverse effects in our osteoarthritis patients. It is safe for human consumption and even for long-term use".
Serpell MG; Neuropathic pain study group. Gabapentin in neuropathic pain syndromes: a randomised, double-blind, placebo-controlled trial. Pain. 2002;99:557-66.

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A double-blind, randomised, placebo-controlled 8-week study was conducted to evaluate the efficacy and safety of gabapentin in the treatment of neuropathic pain, using doses up to 2400 mg/day. The study used a novel design that was symptom- rather than syndrome-based; an approach that aimed to reflect the realities of clinical practice. Participants had a wide range of neuropathic pain syndromes, with at least two of the following symptoms: allodynia, burning pain, shooting pain, or hyperalgesia. Patients were randomised to gabapentin (n=153) or placebo (n=152). Gabapentin was given in three divided doses, initially titrated to 900 mg/day over 3 days, followed by two further increases, to a maximum of 2400 mg/day if required by the end of week 5. The primary outcome measure was changed in average daily pain diary score (baseline versus final week). Over the 8 week study, this score decreased (i.e. improved) by 1.5 (21%) in gabapentin treated patients and by 1.0 (14%) in placebo treated patients (P=0.048, rank-based analysis of covariance). Significant differences were shown in favour of

gabapentin (P<0.05) for the Clinician and Patient Global Impression of Change, and some domains of the Short Form-McGill Pain Questionnaire. Improvements were also shown in patient-reported outcomes in quality of life, as seen by significant differences in favour of gabapentin in several domains of the Short-Form-36 Health Survey. Gabapentin was well tolerated and the majority of patients completed the study (79 versus 73% for placebo). The most common adverse events were mild to moderate dizziness and somnolence, most of which were transient and occurred during the titration phase. This study shows that gabapentin reduces pain and improves some quality-of-life measures in patients with a wide range of neuropathic pain syndromes.

PMID: 12406532

Rating: 2b

Severeijns R; Vlaeyen JW; van den Hout MA; Weber WE. Pain catastrophizing predicts pain intensity, disability, and psychological distress independent of the level of physical impairment. Clinical Journal of Pain. 01-Jun-2001; 17(2): 165-72.

Department of Medical Psychology, University Hospital of Maastricht, The Netherlands. r.severeijns@smps.azm.nl

CONCLUSIONS: "It was concluded that for different subgroups of chronic pain patients, catastrophizing plays a crucial role in the chronic pain experience, significantly contributing to the variance of pain intensity, pain-related disability, and psychological distress. Finally, the authors concluded that these results support the validity of a cognitive-behavioral conceptualization of chronic pain-related disability. "

Publication Type: Case Control Study, 211 cases

PMID: 11444718

Shariatmadari ME. Letter: Orphenadrine dependence. Br Med J. 1975;3:486.

This was a case report of orphenadrine dependence.

Rating: 11b

Sharma A, Williams K, Raja SN. Advances in treatment of complex regional pain syndrome: recent insights on a perplexing disease. Curr Opin Anaesthesiol. 2006;19:566-72.

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PURPOSE OF REVIEW: The paper is a critical appraisal of recent advances in the treatment of complex regional pain syndrome. Rapidly changing concepts related to the pathophysiology of this disease has transformed its current management and necessitates an updated review of the literature. RECENT FINDINGS: Chronic regional pain syndrome is a perplexing disease that continues to challenge researchers with respect to its cause and treatment. Recent modification to diagnostic criteria has enabled clinicians to diagnose this disease in a more consistent fashion. Emerging data indicate a possible role of inflammation in the overall pathophysiology and have led to treatment trials with newer anti-inflammatory medications. Certain 'conventional' interventional techniques have been recently scrutinized. A few novel therapeutic options like graded imagery are also outlined. SUMMARY: Enhanced insight into the pathophysiology of chronic regional pain syndrome has modified current clinical practice and the focus of research. Certain 'standard' therapeutic options for chronic regional pain syndrome have failed the test of time while others have prevailed. New options have recently been evaluated and have shown promising early results. Knowledge of recent advances in chronic regional pain syndrome will help pain physicians provide optimal care to these patients.

PMID: 16960493

Rating: 5c

Siddall, P., et al. The efficacy of Intrathecal Morphine and Clonidine in the Treatment of Pain After Spinal Cord Injury. Anesh. Analg, 2000; Number 91:1493-8.

Rating: 2b

Quality: Intermediate. Total Rating: 7.5. Comment: 15 patients were divided into research groups. Found that intrathecal clonidine alone did not perform better than placebo. [CA DWC]

Simon L, Lipman A, et al. Guideline for the Management of Pain in Osteoarthritis, Rheumatoid Arthritis and Juvenile Chronic Arthritis. 2002.
Guideline for the Management of Pain in Osteoarthritis, Rheumatoid Arthritis and Juvenile Chronic Arthritis
Press Release
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Sindrup SH, Otto M, Finnerup NB, Jensen TS. Antidepressants in the treatment of neuropathic pain. Basic Clin Pharmacol Toxicol. 2005 Jun;96(6):399-409.

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Neuropathic pain is due to lesion or dysfunction of the peripheral or central nervous system. Tricyclic antidepressants and anticonvulsants have long been the mainstay of treatment of this type of pain. Tricyclic antidepressants may relieve neuropathic pain by their unique ability to inhibit presynaptic reuptake of the biogenic amines serotonin and noradrenaline, but other mechanisms such as N-methyl-D-aspartate receptor and ion channel blockade probably also play a role in their pain-relieving effect. The effect of tricyclic antidepressants in neuropathic pain in man has been demonstrated in numerous randomised, controlled trials, and a few trials have shown that serotonin noradrenaline and selective serotonin reuptake inhibitor antidepressants also relieve neuropathic pain although with lower efficacy. Tricyclic antidepressants will relieve one in every 2-3 patients with peripheral neuropathic pain, serotonin noradrenaline reuptake inhibitors one in every 4-5 and selective serotonin reuptake inhibitors one in every 7 patients. Thus, based on efficacy measures such as numbers needed to treat, tricyclic antidepressants tend to work better than the anticonvulsant gabapentin and treatment options such as tramadol and oxycodone, whereas the serotonin noradrenaline reuptake inhibitor venlafaxine appears to be equally effective with these drugs and selective serotonin reuptake inhibitors apparently have lower efficacy. Head-to-head comparisons between antidepressants and the other analgesics are lacking.

Contraindications towards the use of tricyclic antidepressants and low tolerability in general of this drug class--many among the antidepressants--favour the use of the serotonin noradrenaline reuptake inhibitors. A recent study on bupropion, which is a noradrenaline and dopamine uptake inhibitor, indicated a surprisingly high efficacy of this drug in peripheral neuropathic pain. In conclusion, antidepressants represent useful tools in neuropathic pain treatment and must still be considered as first line treatments of neuropathic pain. However, without head-to-head comparisons between antidepressants and other analgesics, it is not possible to provide real evidence-based treatment algorithms for neuropathic pain.

Publication Types:
Review

PMID: 15910402

Rating: 5a

Sindrup SH, Jensen TS. Efficacy of pharmacological treatments of neuropathic pain: an update and effect related to mechanism of drug action. Pain. 1999 Dec;83(3):389-400.

Department of Neurology, Odense University Hospital, DK-5000, Odense, Denmark.

Tricyclic antidepressants and carbamazepine have become the mainstay in the treatment of neuropathic pain. Within the last decade, controlled trials have shown that numerous other drugs relieve such pain. We identified all placebo-controlled trials and calculated numbers needed to treat (NNT) to obtain one patient with more than 50% pain relief in order to compare the efficacy with the current treatments, and to search for relations between mechanism of pain and drug action. In diabetic neuropathy, NNT was 1.4 in a study with optimal doses of the tricyclic antidepressant imipramine as compared to 2.4 in other studies on tricyclics. The NNT was 6.7 for selective serotonin reuptake inhibitors, 3.3 for carbamazepine, 10.0 for mexiletine, 3.7 for gabapentin, 1.9 for dextromethorphan, 3.4 for tramadol and levodopa and 5.9 for capsaicin. In postherpetic neuralgia, the NNT was 2.3 for tricyclics, 3.2 for gabapentin, 2.5 for oxycodone and 5.3 for capsaicin, whereas dextromethorphan was inactive. In peripheral nerve injury, NNT was 2.5 for tricyclics and 3.5 for capsaicin. In central pain, NNT was 2.5 for tricyclics and 3. 4 for carbamazepine, whereas selective serotonin reuptake inhibitors, mexiletine and dextromethorphan were inactive. There were no clear relations between mechanism of action of the drugs and the effect in distinct pain conditions or for single drug classes and different pain conditions. It is concluded that tricyclic antidepressants in optimal doses appear to be the most efficient treatment of neuropathic pain, but some of the other treatments may be important due to their better tolerability. Relations between drug and pain mechanisms may be elucidated by studies focusing on specific neuropathic pain phenomena such as pain paroxysms and touch-evoked pain.

Publication Types:

Review

PMID: 10568846

Rating: 1b

Skinner HA, Holt S, Schuller R, Roy J, Israel Y. Identification of alcohol abuse using laboratory tests and a history of trauma. Ann Intern Med. 1984 Dec;101(6):847-51.

In a study involving 68 ambulatory patients with known alcohol problems and 68 social drinkers matched for age and sex, a questionnaire about the patients' history of trauma identified 7 out of 10 subjects with drinking problems. In contrast, abnormal values for gamma-glutamyl transferase, mean corpuscular volume, or high-density lipoproteins had only moderate sensitivity (26% to 40%) for identifying alcohol problems but excellent specificity (88% to 99%) for ruling out cases. Similar rates of sensitivity and specificity were found among 61 family practice patients. Diagnostic accuracy was improved by combining tests results, using computer-based logistic regression analysis. This study suggests that a brief questionnaire on history of trauma is valuable for the earlier detection of problem drinking in ambulatory populations, in contrast to laboratory tests, which appear to have high sensitivity only with more chronic alcoholics.

PMID: 6149716

Rating: 3b

Skouen JS, Grasdal AL, Haldorsen EM, Ursin H. Relative cost-effectiveness of extensive and light multidisciplinary treatment programs versus treatment as usual for patients with chronic low back pain on long-term sick leave: randomized controlled study. Spine. 2002 May 1;27(9):901-9; discussion 909-10.

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STUDY DESIGN: A subgroup of 195 patients with chronic low back pain, being part of a larger study of other musculoskeletal patients, were included in a randomized controlled prospective clinical study. OBJECTIVES: To evaluate the outcome in terms of return to work and cost-effectiveness of a light multidisciplinary treatment program with an extensive multidisciplinary program and treatment as usual initiated by their general practitioner. SUMMARY OF BACKGROUND DATA: Light multidisciplinary programs seem to reduce sick leave in patients with subacute low back pain. There are few, if any, previous studies of the effectiveness of light versus extensive multidisciplinary treatment on return to work in patients with chronic low back pain. METHODS: Patients with chronic low back pain (n = 195), on an average sick-listed for 3 months, were included. The patients were randomized to a light multidisciplinary treatment program, an extensive multidisciplinary program, or treatment as usual by

their primary physician. Full return to work was used as outcome response, and follow-up was 26 months after the end of treatment. Cost-benefit was calculated for the treatment programs. RESULTS: In men significantly better results for full return to work were found for the light multidisciplinary treatment compared with treatment as usual, but no differences were found between extensive multidisciplinary treatment and treatment as usual. No significant differences between any of the two multidisciplinary treatment programs and the controls were found for women. Productivity gains for the society from light multidisciplinary treatment versus "treatment as usual" of 57 male patients with low back pain would during the first 2 years accumulate to U.S. $852.00. CONCLUSIONS: The light multidisciplinary treatment model is a cost-effective treatment for men with chronic low back pain.

PMID: 11979157

Rating: 2b

Skrabek RQ, Galimova L, Ethans K, Perry D. Nabilone for the treatment of pain in fibromyalgia. J Pain. 2008 Feb;9(2):164-73.

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A randomized, double-blind, placebo-controlled trial was conducted to determine the benefit of nabilone in pain management and quality of life improvement in 40 patients with fibromyalgia. After a baseline assessment, subjects were titrated up on nabilone, from 0.5 mg PO at bedtime to 1 mg BID over 4 weeks or received a corresponding placebo. At the 2- and 4-week visits, the primary outcome measure, visual analog scale (VAS) for pain, and the secondary outcome measures, number of tender points, the average tender point pain threshold, and the Fibromyalgia Impact Questionnaire (FIQ), were evaluated. After a 4-week washout period, subjects returned for reassessment of the outcome measures. There were no significant differences in population demographics between groups at baseline. There were significant decreases in the VAS (-2.04, P < .02), FIQ (-12.07, P < .02), and anxiety (-1.67, P < .02) in the nabilone treated group at 4 weeks. There were no significant improvements in the placebo group. The treatment group experienced more side effects per person at 2 and 4 weeks (1.58, P < .02 and 1.54, P < .05), respectively. Nabilone appears to be a beneficial, well-tolerated treatment option for fibromyalgia patients, with significant benefits in pain relief and functional improvement. PERSPECTIVE: To our knowledge, this is the first randomized, controlled trial to assess the benefit of nabilone, a synthetic cannabinoid, on pain reduction and quality of life improvement in patients with fibromyalgia. As nabilone improved symptoms and was well-tolerated, it may be a useful adjunct for pain management in fibromyalgia.

PMID: 17974490

Rating: 2c

"The results are interesting and provocative, and there may very well be a place for this kind of treatment eventually, but I think it would have to be [tested] in a much larger study with a more rigorous methodology," John Kissel, MD, from Ohio State University, in Columbus, who was not involved in the study, speaking on behalf of the American Academy of Neurology, told Medscape Psychiatry. Fibromyalgia, which is characterized by diffuse musculoskeletal pain, affects 2% to 4% of the general population and is up to 7 times more common in women, the group writes. The pathophysiology of fibromyalgia is not clearly understood, and only recently pregabalin (Lyrica, Pfizer) was the first drug approved by the US Food and Drug Administration for this disease. Nabilone is one of 2 orally administered synthetic cannabinoid drugs available in Canada and approved for management of nausea during chemotherapy, and research into its use to manage neuropathic pain has been encouraging, they add. The investigators hypothesized that nabilone would significantly improve pain and quality of life in fibromyalgia patients. Compared with baseline, at week 4, at a nabilone dose of 1 mg twice a day, patients in the nabilone-treatment group had significantly improved VAS, FIQ, and anxiety scores (all P < .02). The nabilone-treated patients had significantly greater improvements in these measures than did the placebo-treated patients. The patients did not have significant improvements in the remaining outcomes, including depression, fatigue, and tender points. Future studies with a longer duration of treatment and a stable dose are still needed, they add. The medication's costs — $4000 a year in Canada — may be prohibitive to some patients, they observe. When interpreting the study results, it is important to note that the study drug was costly, the study was done in a small number of patients, and there was a high dropout rate, Dr. Kissel said. In addition, the dropout patients were not included in an intention-to-treat analysis, which would have resulted in a lower improvement rate. Also, patients in the nabilone group had more adverse effects and likely knew they were taking the study drug. "I don't think this should change at all the way physicians practice right now . . . without this being replicated in a bigger study," he said. The study was supported by an unrestricted research grant from Valeant Canada and a Health Sciences Center Medical Staff Council Fellowship fund.

Smeets RJ, Vlaeyen JW, Hidding A, Kester AD, van der Heijden GJ, van Geel AC, Knottnerus JA. Active rehabilitation for chronic low back pain: Cognitive-behavioral, physical, or both? First direct post-treatment results from a randomized controlled trial. BMC Musculoskelet Disord. 2006 Jan 20;7(1):5.

ABSTRACT: BACKGROUND: The treatment of non-specific chronic low back pain is often based on three different models regarding the development and maintenance of pain and especially functional limitations: the deconditioning model, the cognitive behavioral model and the biopsychosocial model. There is evidence that rehabilitation of patients with chronic low back pain is more effective than no treatment, but information is lacking about the differential effectiveness of different kinds of rehabilitation. A direct comparison of a physical, a cognitive-behavioral treatment and a combination of both has never been carried out so far. METHODS: The effectiveness of active physical, cognitive-behavioral and combined treatment for chronic non-specific low back pain compared with a waiting list control group was determined by performing a randomized controlled trial in three rehabilitation centers.

Two hundred and twenty three patients were randomized, using concealed block randomization to one of the following treatments, which they attended three times a week for 10 weeks: Active Physical Treatment (APT), Cognitive-Behavioral Treatment (CBT), Combined Treatment of APT and CBT (CT), or Waiting List (WL). The outcome variables were self-reported functional limitations, patient's main complaints, pain, mood, self-rated treatment effectiveness, treatment satisfaction and physical performance including walking, standing up, reaching forward, stair climbing and lifting. Assessments were carried out by blinded research assistants at baseline and immediately post-treatment. The data were analyzed using the intention-to-treat principle. RESULTS: For 212 patients, data were available for analysis. After treatment, significant reductions were observed in functional limitations, patient's main complaints and pain intensity for all three active treatments compared to the WL. Also, the self-rated treatment effectiveness and satisfaction appeared to be higher in the three active treatments. Several physical performance tasks improved in APT and CT but not in CBT. No clinically relevant differences were found between the CT and APT, or between CT and CBT. CONCLUSIONS: All three active treatments were effective in comparison to no treatment, but no clinically relevant differences between the combined and the single component treatments were found.

PMID: 16426449

Rating: 2a

Solak O, Turna A, Pekcolaklar A, Metin M, Sayar A, Solak O, Gurses A. Transcutaneous electric nerve stimulation for the treatment of postthoracotomy pain: a randomized prospective study. Thorac Cardiovasc Surg. 2007 Apr;55(3):182-5.

Department of Thoracic Surgery, Afyon Kocatepe University, School of Medicine, Afyonkarahisar, Turkey.

BACKGROUND: Insufficient relief of postthoracotomy pain is a major cause of increased rates of postoperative complications including inadequate coughing, mucous plugging, hypoxia, compromised ventilation or even bacterial lung infection. We aimed to assess the efficacy of transcutaneous electric nerve stimulation (TENS) in patients with postthoracotomy pain. METHODS: Forty patients scheduled to undergo posterolateral thoracotomy were randomly allocated to receive either TENS or patient-controlled intravenous morphine. Postoperative pain was evaluated using a visual analogue scale (VAS) and the Prince Henry pain scale. Pulmonary function was evaluated and an intergroup comparison was done. RESULTS: On the first three days following surgery, the VAS intensity of the TENS group did not differ significantly from that of the morphine group ($P > 0.05$), and on the first two days following thoracotomy, the Prince Henry scale of the TENS group was not statistically significantly different. However, the VAS intensity was significantly lower than that of the control group on the fourth ($P = 0.044$), fifth ($P = 0.016$), sixth ($P = 0.009$), seventh ($P = 0.008$), eighth ($P = 0.004$), ninth ($P = 0.002$), tenth ($P = 0.001$), fifteenth ($P = 0.002$), thirtieth ($P < 0.001$), forty-fifth ($P < 0.001$) and sixtieth ($P < 0.001$) days. The Prince Henry scale of the TENS group was found to be significantly diminished from

the 3rd to the 60th day. TENS significantly reduced the analgesic requirements from day 5 to 60 (P < 0.01). No noticeable side effect was observed in the TENS group during the study period. CONCLUSION: This study demonstrated that TENS provided a better pain relief and comfort compared to PCA from the fourth postoperative day onwards, and this pain-reducing effect continued for at least two months postoperatively.

PMID: 17410506

Rating: 2c

Solomon DH, Schneeweiss S, Glynn RJ, Kiyota Y, Levin R, Mogun H, Avorn J, Relationship between selective cyclooxygenase-2 inhibitors and acute myocardial infarction in older adults, Circulation. 2004 May 4;109(17):2068-73. Epub 2004 Apr 19.

Division of Pharmacoepidemiology and Pharmacoeconomics, Brigham and Women's Hospital, Harvard Medical School, 1620 Tremont St, Suite 3030, Boston, Mass 02120, USA. dhsolomon@partners.org

BACKGROUND: Although cyclooxygenase-2 inhibitors (coxibs) were developed to cause less gastrointestinal hemorrhage than nonselective nonsteroidal antiinflammatory drugs (NSAIDs), there has been concern about their cardiovascular safety. We studied the relative risk of acute myocardial infarction (AMI) among users of celecoxib, rofecoxib, and NSAIDs in Medicare beneficiaries with a comprehensive drug benefit. METHODS AND RESULTS: We conducted a matched case-control study of 54 475 patients 65 years of age or older who received their medications through 2 state-sponsored pharmaceutical benefits programs in the United States. All healthcare use encounters were examined to identify hospitalizations for AMI. Each of the 10 895 cases of AMI was matched to 4 controls on the basis of age, gender, and the month of index date. We constructed matched logistic regression models including indicators for patient demographics, healthcare use, medication use, and cardiovascular risk factors to assess the relative risk of AMI in patients who used rofecoxib compared with persons taking no NSAID, taking celecoxib, or taking NSAIDs. Current use of rofecoxib was associated with an elevated relative risk of AMI compared with celecoxib (odds ratio [OR], 1.24; 95% CI, 1.05 to 1.46; P=0.011) and with no NSAID (OR, 1.14; 95% CI, 1.00 to 1.31; P=0.054). The adjusted relative risk of AMI was also elevated in dose-specific comparisons: rofecoxib < or =25 mg versus celecoxib < or =200 mg (OR, 1.21; 95% CI, 1.01 to 1.44; P=0.036) and rofecoxib >25 mg versus celecoxib >200 mg (OR, 1.70; 95% CI, 1.07 to 2.71; P=0.026). The adjusted relative risks of AMI associated with rofecoxib use of 1 to 30 days (OR, 1.40; 95% CI, 1.12 to 1.75; P=0.005) and 31 to 90 days (OR, 1.38; 95% CI, 1.11 to 1.72; P=0.003) were higher than >90 days (OR, 0.96; 95% CI, 0.72 to 1.25; P=0.8) compared with celecoxib use of similar duration. Celecoxib was not associated with an increased relative risk of AMI in these comparisons. CONCLUSIONS: In this study, current rofecoxib use was associated with an elevated relative risk of AMI compared with celecoxib use and no NSAID use. Dosages of rofecoxib >25 mg were associated with a higher risk than dosages < or =25 mg. The risk was elevated in the first 90 days of use but not thereafter.

PMID: 15096449
Rating: 4a

Sommer HM. The Patient in Jeopardy: How the Low Back Pain Patient Becomes Disabled. Occupational Medicine 1998;(13)1:23-31.
Department of Medical Psychology, University Hospital of Maastricht, The Netherlands. r.severeijns@smps.azm.nl
Abstract:
Dr. Sommer divides the low back pain episode into four stages that can lead to patient disablement. Contributing factors include: suboptimal training for the diagnosis and management of musculoskeletal disorders and resultant physician anxiety; a compensation system that demands proof; physician wariness of chronic pain patients; transformation of worker from person to patient to claimant; and the complexities of determining impairment and disability.
Publication Type: Review
PMID: 11444718

Soomro GM, Altman D, Rajagopal S, Oakley-Browne M. Selective serotonin re-uptake inhibitors (SSRIs) versus placebo for obsessive compulsive disorder (OCD). Cochrane Database Syst Rev. 2008;(1):CD001765.

St. George's Hospital Medical School, Department of Psychiatry, University of London, Cranmer Terrace, London, UK SW17 0RE. gms357@hotmail.com

BACKGROUND: Obsessive compulsive disorder is a common and disabling disorder. A significant proportion of patients manifest a chronic course. Individual randomised controlled trials (RCTs) have shown that selective serotonin re-uptake inhibitors (SSRIs) are effective in this condition. Previous systematic reviews or meta-analyses summarising the evidence are methodologically problematic or limited in the scope of their analysis. OBJECTIVES: To examine the efficacy and adverse effects of serotonin re-uptake inhibitors (SSRIs) versus placebo for obsessive compulsive disorder (OCD) in adults. SEARCH STRATEGY: CCDANCTR-Studies and CCDANCTR-References were searched on 12/11/2007. Reference lists were checked. Experts in the field were contacted. SELECTION CRITERIA: All RCTs and quasi-RCTs examining the efficacy of SSRIs compared with placebo for OCD in adults were eligible for inclusion. DATA COLLECTION AND ANALYSIS: Selection of studies and data extraction were carried out by two review authors independently, and quality assessment of studies was undertaken. Data analysis was conducted using Review Manager software. Summary measures were produced using the weighted mean difference (WMD) for continuous data and relative risk (RR) for dichotomous data, with 95% confidence intervals (CI). SSRIs were examined as an overall group of drugs, and as individual drugs. MAIN RESULTS: Seventeen studies were included in the review, involving 3097 participants. Based on all 17 studies, SSRIs as a group were more effective

than placebo in reducing the symptoms of OCD between 6 and 13 weeks post-treatment, measured using the Yale-Brown Obsessive Compulsive Scale (YBOCS) (WMD -3.21, 95% CI -3.84 to -2.57). The WMD for individual SSRI drugs were similar and not statistically different. Based on 13 studies (2697 participants), SSRIs were more effective than placebo in achieving clinical response at post-treatment (RR 1.84, 95% CI 1.56 to 2.17). The pooled RR was shown to be similar between individual SSRI drugs. Although reported adverse effects data were more limited, with few exceptions, the overall and individual adverse effects for the different SSRIs were always worse than for placebo and, in the majority of cases, the difference was statistically significant. Nausea, headache and insomnia were always reported amongst the most common adverse effects in trials of each of the drugs. AUTHORS' CONCLUSIONS: SSRIs are more effective than placebo for OCD, at least in the short-term, although there are differences between the adverse effects of individual SSRI drugs. The longer term efficacy and tolerability of different SSRI drugs for OCD has yet to be established.

PMID: 18253995

Rating: 1c

Spence SH, Sharpe L, Newton-John T, Champion D. Effect of EMG biofeedback compared to applied relaxation training with chronic, upper extremity cumulative trauma disorders. Pain. 1995 Nov;63(2):199-206.

Department of Psychology, University of Queensland, Brisbane, Australia.

This study examined the relative effectiveness of EMG biofeedback, applied relaxation training and a combined procedure in the management of chronic, upper extremity cumulative trauma disorder. Forty-eight patients with a history of about 5-6 years of upper extremity pain were randomly assigned to 1 of 4 treatment conditions, namely applied relaxation training, EMG biofeedback, a combined approach or a wait-list control. Treatments were conducted on an individual basis, twice per week for 4 weeks. Patients in all 3 treatment conditions showed significant short-term reductions in pain and psychopathology in comparison to the wait-list group who showed minimal change. Six-month follow-up data were obtained for patients in the treatment conditions, but not the wait-list group. There was some evidence of relapse on measures of depression, anxiety and pain beliefs for treated patients during the 6-month follow-up period, although measures remained significantly below pre-treatment levels for most outcome indices. Self-monitored pain continued to decrease for the treatment groups through follow-up. Contrary to predictions, however, the strongest short-term treatment benefits were shown by patients receiving applied relaxation training on measures of pain, distress, interference in daily living, depression and anxiety. By 6-month follow-up, differences between treatment groups were no longer evident.

PMID: 8628585

Rating: 2c

Spruce MC, Potter J, Coppini DV. The pathogenesis and management of painful diabetic neuropathy: a review. Diabet Med. 2003 Feb;20(2):88-98.

Department of Diabetes, Poole General Hospital, Poole, Dorset, UK. mcs2@soton.ac.uk

Painful diabetic neuropathy has always been a challenging complication of diabetes mellitus. Emerging theories suggest that early dysaesthesia associated with painful neuropathy may act as a marker for the development of the 'at risk' foot, allowing preventative clinical strategies to be undertaken. The mechanisms of neuropathic pain are complex. The authors' intentions are to help members of the diabetes care team better understand and appreciate the diverse symptoms reported by patients. The various treatments available for painful neuropathy are discussed in detail. Robust comparative studies on such treatments are, however, unavailable and the authors have designed a logical approach to management based on best current evidence and their own clinical experience.

PMID: 12581259

Rating: 5c

Staats PS. Pain, depression and survival. American Family Physician . 01-Jul-1999; 60(1): 42, 44.
Department of Medical Psychology, University Hospital of Maastricht, The Netherlands.
r.severeijns@smps.azm.nl
Abstract:
Adequate pain relief has an obvious positive effect on a patient's quality of life. However, recent data suggest that pain control also improves morbidity and mortality, that pain relief administered before surgery and during the postoperative period improves clinical outcomes, and that depression, anxiety and poor coping skills are independently associated with mortality and, therefore, are important factors to address. Whether the correlation between improved analgesia and increased life expectancy is the result of biomedical or psychosocial factors is unclear. However, several recent studies support the contention that pain causes increased severity of disease and mortality. Therefore, providing pain relief is not only a humane gesture but also a medical necessity.
Publication Type: Review
PMID: 11444718

Stacey BR, Dworkin RH, Murphy K, Sharma U, Emir B, Griesing T. Pregabalin in the Treatment of Refractory Neuropathic Pain: Results of a 15-Month Open-Label Trial. Pain Med. 2008 Mar 11.

Departments of Comprehensive Pain Center, Anesthesiology and Peri-Operative Medicine, Oregon Health & Science University, Portland, Oregon, USA.

Objective. Neuropathic pain associated with postherpetic neuralgia (PHN) and painful diabetic peripheral neuropathy (DPN) can be intractable and may not respond to commonly used treatments, such as tricyclic antidepressants (TCAs) and opioids. This long-term, open-label study was a preliminary evaluation of pregabalin for patients whose pain had been judged refractory to other treatments for neuropathic pain. Design. Patients had previously participated in double-blind, placebo-controlled, randomized trials of pregabalin in DPN and PHN. They had moderate to severe neuropathic pain despite treatment with gabapentin, a TCA, and a third medication (e.g., other anticonvulsants, opioid, selective serotonin reuptake inhibitor, tramadol). Flexible-dosage pregabalin 150-600 mg/day was taken for 3-month periods followed by 3- to 28-day pregabalin "drug holidays," with an analysis up to 15 months (five treatment cycles). Pain intensity was measured using the visual analog scale of the Short-Form McGill Pain Questionnaire. Results. In total, 81 patients were included in this analysis. Pregabalin 150-600 mg/day was associated with clinically meaningful and sustained pain reduction during each treatment cycle. During pregabalin "drug holidays," pain quickly returned to baseline levels; it was reduced again when pregabalin was reinstated. Conclusions. These results suggest that pregabalin may be beneficial in patients with neuropathic pain who have had an unsatisfactory response to treatment with other medications.

PMID: 18346060

Rating: 4c

Stanos S, Houle TT. Multidisciplinary and interdisciplinary management of chronic pain. Phys Med Rehabil Clin N Am. 2006 May;17(2):435-50, vii.

Department of Physical Medicine and Rehabilitation, Northwestern University, Feinberg Medical School, Ward Building, 3-130, 303 E. Chicago Avenue, Chicago, IL 60611, USA. sstanos@ric.org

Multidisciplinary and interdisciplinary pain management programs incorporate a biopsychosocial model in assessing and treating pain and result in pain reduction, improved quality of life, and psychosocial functioning. Additionally, return-to-work and vocational outcomes may be seen in selected patients. Treatment teams may include a physiatrist, a physical or occupational therapist, a pain psychologist, a relaxation (biofeedback) therapist, vocational and therapeutic recreational therapists, social workers, and nurses. The key component to program success is collaborative ongoing communication among team members, the patient, and the case manager.

Rating: 5c

Stanton-Hicks M, Janig W, Hassenbusch S, Haddox JD, Boas R, Wilson P. Reflex sympathetic dystrophy: changing concepts and taxonomy. Pain. 1995 Oct;63(1):127-33.

Pain Management Center, Cleveland Clinic Foundation, OH 44195, USA.

We present a revised taxonomic system for disorders previously called reflex sympathetic dystrophy (RSD) and causalgia. The system resulted from a special consensus conference that was convened on this topic and is based upon the patient's history, presenting symptoms, and findings at the time of diagnosis. The disorders are grouped under the umbrella term CRPS: complex regional pain syndrome. This overall term, CRPS, requires the presence of regional pain and sensory changes following a noxious event. Further, the pain is associated with findings such as abnormal skin color, temperature change, abnormal sudomotor activity, or edema. The combination of these findings exceeds their expected magnitude in response to known physical damage during and following the inciting event. Two types of CRPS have been recognized: type I, corresponds to RSD and occurs without a definable nerve lesion, and type II, formerly called causalgia refers to cases where a definable nerve lesion is present. The term sympathetically maintained pain (SMP) was also evaluated and considered to be a variable phenomenon associated with a variety of disorders, including CRPS types I and II. These revised categories have been included in the 2nd edition of the IASP Classification of Chronic Pain Syndromes.

Publication Types:
Consensus Development Conference
Review

PMID: 8577483

Rating: 5a

Stanton-Hicks M. Complex Regional Pain Syndrome. In: Warfield CA, Bajwa JH. Principles and Practice of Pain Medicine. 2nd ed. McGraw-Hill; 2004.

Rating 9a

State of Colorado Department of Labor and Employment, Division of Workers' Compensation. Chronic Pain Disorder (Evaluation and Management) Medical Treatment Guidelines. 7/30/03. Revised: September 29, 2005. Effective: January 1, 2006.
MANUAL THERAPY is generally accepted, well-established and widely used in the treatment of musculoskeletal pain. The intended goal or effect of Manual Medicine is the achievement of positive symptomatic or objective gains that facilitate progression in the patient's therapeutic exercise program and return to productive activities.
Manual Medicine addresses dysfunctions of the musculoskeletal system in order to reduce pain, restore maximal biomechanical function, and improve postural balance. The commonly used term "manipulation" is a general term that applies to all Manual Medicine procedures, although it is often confused to be synonymous with "thrust-type" procedures. Some of the commonly used Manual Medicine procedures are:

a. High-Velocity, Low-Amplitude Thrust (Mobilization with Impulse, Adjustment, Grade V Joint Mobilization)
b. Joint Mobilization (Articulatory Technique)
c. Soft Tissue Mobilization
d. Myofascial Release
e. Muscle Energy
f. Counterstrain
g. Functional
h. Balance and Hold G38
i. Craniosacral
j. Lymphatic Drainage
k. Neural Tension Release
l. Trigger Point Therapy
m. Visceral Manipulation
n. Therapeutic Massage
o. Manual Traction
Treatment Parameters:
a. Time to produce effect: 3-5 treatments
b. Frequency: 1-5 supervised treatments per week the first 2 weeks, decreasing to 1-3 times per week for the next 6 weeks, then 1-2 times per week for the next 4 weeks, if necessary. Daily treatment is not indicated in chronic or outlier patients
c. Optimum duration: 2-3 months
d. Maximum duration: treatment beyond 8 weeks must be documented with respect to need and ability to facilitate positive symptomatic or functional gains. Such palliative care should be reevaluated and documented at each treatment session. Continued monitoring and supportive treatment may be appropriate within the following guideline if the worker is working or is participating in a work-hardening, functional restoration or supervised reconditioning program: up-to-3 months of biweekly visits followed by up-to-3 months of monthly visits Publication Type: State Treatment Guideline
State of Colorado Department of Labor and Employment, Division of Workers' Compensation. Reflex Sympathetic Dystrophy/Complex Regional Pain Syndrome Medical Treatment Guidelines. 15-Mar-1998.
Abstract:
Not available.
Publication Type: State Treatment Guideline

State of Colorado Department of Labor and Employment, Division of Workers' Compensation. Colorado Rule XVII, Exhibit 7, Complex Regional Pain Syndrome Medical Treatment Guideline. 01/01/06

Complex Regional Pain Syndrome (CRPS Types I and II) describes painful syndromes, which were formerly referred to as Reflex Sympathetic Dystrophy (RSD) and causalgia. CRPS conditions usually follow injury that appears regionally and have a distal predominance of abnormal findings, exceeding the expected clinical course of the inciting event in both magnitude and duration and often resulting in significant impairment of limb function

CRPS-I (RSD) is a syndrome that usually develops after an initiating noxious event, is not limited to the distribution of a single peripheral nerve, and is apparently disproportionate to the inciting event. It is associated at some point with evidence of edema, changes in skin blood flow, abnormal sudomotor activity in the region of the pain, allodynia or hyperalgesia. The site is usually in the distal aspect of an affected extremity or with a distal to proximal gradient. The peripheral nervous system and possibly the central nervous system are involved.

CRPS-II (Causalgia) is the presence of burning pain, allodynia, and hyperpathia usually in the hand or foot after partial injury to a nerve or one of its major branches. Pain is within the distribution of the damaged nerve but not generally confined to a single nerve.

Stages seen in CRPS-I are not absolute and in fact, may not all be observed in any single patient. In some patients, stages may be missed or the patient may remain for long periods of time in one stage.

Stage 1 - Acute (Hyperemic)

Starts at the time of injury or even weeks later. Associated with spontaneous pain, aching, burning. Typically restricted to the distal extremity. Hyperpathia, allodynia, hypoesthesia or hyperesthesia may be present. Initially, hair and nail growth may be increased but later decrease. Skin may be warm or cold.

Stage 2 - Dystrophic (Ischemic)

Spontaneous burning and/or aching pain, more pronounced hyperpathia and or allodynia. Signs of chronic sympathetic overactivity include (a) reduced blood flow; (b) sudomotor changes; (c) increased edema; (d) cyanotic skin; (e) muscle wasting; (f) decreased hair and nail growth; and (g) osteoporosis.

Stage 3 - Atrophic

Signs and symptoms of this stage include (a) pain may be less prominent; (b) decreased hyperpathia and/or allodynia; (c) reduction in blood flow; (d) skin temperature and sweating may be increased or decreased; (e) irreversible trophic changes in skin and integument; and (f) pronounced muscle atrophy with contractures.

Education

Education of the patient and family, as well as the employer, insurer, policy makers and the community should be the primary emphasis in the treatment of chronic pain. Currently, practitioners often think of education last, after medications, manual therapy and surgery. Practitioners must develop and implement an effective strategy and skills to educate patients, employers, insurance systems, policy makers and the community as a whole. An education-based paradigm should always start with inexpensive communication providing reassuring information to the patient. More in-depth education currently exists within a treatment regime employing functional restorative and innovative programs of prevention and rehabilitation. No treatment plan is complete without addressing issues of individual and/or group patient education as a means of facilitating self-management of symptoms and prevention.

Return-to-Work
Return-to-work is therapeutic, assuming the work is not likely to aggravate the basic problem or increase long-term pain. Even if there is residual chronic pain, return-to-work is not necessarily contraindicated.

Diagnostic Criteria for CRPS
a. CRPS-I (RSD)
1) Patient complains of pain, usually diffuse burning or aching;
2) Patient has physical findings on examination of at least vasomotor and/or sudomotor signs. Allodynia and/or trophic changes add strength to the diagnosis of CRPS-I; and
3) At least two diagnostic testing procedures are positive. Even the most sensitive tests can have false negatives. The patient can still have CRPS-I, if clinical signs are strongly present. In patients with continued signs and symptoms of CRPS-I, further diagnostic testing may be appropriate.
b. CRPS-II (causalgia)
1) Patient complains of pain;
2) Documentation of peripheral nerve injury with pain initially in the distribution of the injured nerve;
3) Patient has physical findings on examination of at least vasomotor and/or sudomotor signs. Allodynia and/or trophic changes add strength to the diagnosis of CRPS-II; and
4) At least two diagnostic testing procedures are positive. Even the most sensitive tests can have false negatives. The patient can still have CRPS-II, if clinical signs are strongly present. In patients with continued signs and symptoms of CRPS-II, further diagnostic testing may be appropriate.
c. Sympathetically Mediated Pain (SMP)
1) Patient complains of pain;
2) Usually does not have clinically detectable vasomotor or sudomotor signs; and

3) Has pain relief with sympathetic blocks.
d. Not CRPS
1) Patient complains of pain;
2) May or may not have vasomotor or sudomotor signs;
3) No relief with sympathetic blocks; and
4) No more than one other diagnostic test procedure is positive.

Publication Type: State Treatment Guideline

Rating: 7a

Staiger TO, Gaster B, Sullivan MD, Deyo RA, Systematic review of antidepressants in the treatment of chronic low back pain, Spine. 2003 Nov 15;28(22):2540-5

Department of Medicine, University of Washington, Seattle, WA, USA. staiger@u.washington.edu

BACKGROUND: Three previous reviews have reached conflicting conclusions regarding the efficacy of antidepressants for patients with back pain. OBJECTIVES: To systematically review the efficacy of antidepressants for the treatment of patients with back pain and to determine whether there is evidence that outcomes vary between classes of antidepressants. MATERIALS AND METHODS: Best evidence synthesis of randomized, placebo-controlled trials of oral antidepressive agents in patients with back pain. Studies were identified by searching MEDLINE, PsycINFO, and the Cochrane Controlled Trials Registry. Two independent reviewers performed data extraction and assessed included studies with a 22-point methodologic quality assessment scale. Effect sizes were calculated if sufficient data were available. RESULTS: Twenty-two trials of antidepressants for the treatment of back pain were identified, of which seven studies of chronic low back pain met inclusion criteria. Among studies using antidepressants that inhibit norepinephrine reuptake (tricyclic or tetracyclic antidepressants), four of five found significant improvement in at least one relevant outcome measure. Assessment of these agents' impact on functional measures produced mixed results. No benefit in pain relief or functional status was found in three studies of antidepressants that do not inhibit norepinephrine reuptake. CONCLUSIONS: Based on a small number of studies, tricyclic and tetracyclic antidepressants appear to produce moderate symptom reductions for patients with chronic low back pain. This benefit appears to be independent of depression status. SSRIs do not appear to be beneficial for patients with chronic low back pain. There is conflicting evidence whether antidepressants improve functional status of patients with chronic low back pain.

PMID: 14624092

Rating: 1b

Stanton-Hicks M. Complex regional pain syndrome: manifestations and the role of neurostimulation in its management. J Pain Symptom Manage. 2006 Apr;31(4 Suppl):S20-4.

Department of Pain Management, The Cleveland Clinic Foundation, Ohio, USA. stanton@ccf.org

The hallmark of complex regional pain syndrome (CRPS) is excruciating pain (aching, burning, pricking, or shooting). Diagnosis should be established as soon as possible, as response to treatment is adversely affected by any delay. Treatment of CRPS is aimed at improving function, using an interdisciplinary, time-dependent, patient-dependent approach that encompasses rehabilitation, psychological therapy, and pain management. If no response to conventional treatment (e.g., pharmacotherapy) is noted within 12-16 weeks, a more interventional technique such as spinal cord stimulation (SCS) should be used. SCS has been shown to be highly effective in the treatment of CRPS type I, resulting in a significant, long-term reduction in pain and improvement in quality of life. SCS is particularly effective at helping to restore function in affected extremities, especially if applied early in the course of the disease. SCS is also cost effective and improves health-related quality of life.

PMID: 16647591

Rating: 5b

Stein C. What is wrong with opioids in chronic pain? Current Opinion in Anesthesiology 13(5):557-559, October 2000.

Stein, Christoph

References: 1 Savage SR. Opioid therapy of chronic pain: assessment of consequences. Acta Anaesthesiol Scand 1999; 43:909-917. 2 Bruera E, Walker P, Lawlor P. Opioids in cancer pain. In: Opioids in pain control - basic and clinical aspects. Edited by Stein C. Cambridge: Cambridge University Press; 1999: 309-324. 3 Stein C. Opioid treatment of chronic nonmalignant pain. Anesth Analg 1997; 84:912-914. 4 Schofferman J. Long-term use of opioid analgesics for the treatment of chronic pain of nonmalignant origin. J Pain Symptom Manage 1993; 8:279-288. 5 Dellemijn P. Are opioids effective in relieving neuropathic pain? Pain 1999; 80:453-462. 6 Portenoy RK. Chronic opioid therapy in nonmalignant pain. J Pain Symptom Manage 1990; 5(Suppl):46-62. 7 Arkinstall W, Sandler A, Goughnour B, et al. Efficacy of controlled-release codeine in chronic non-malignant pain: a randomized, placebo-controlled clinical trial. Pain 1995; 62:169-178. 8 Dellemijn PL, Vanneste JA. Randomised double-blind active-placebo-controlled crossover trial of intravenous fentanyl in neuropathic pain. Lancet 1997; 349:753-758. 9 Moulin DE, Iezzi A, Amireh R, et al. Randomised trial of oral morphine for chronic non-cancer pain. Lancet 1996; 347:143-147. 10 Watson CP, Babul N. Efficacy of oxycodone in neuropathic pain: a randomized trial in postherpetic neuralgia. Neurology 1998; 50:1837-1841. 11 Caldwell JR, Hale ME, Boyd RE, et al. Treatment of osteoarthritis pain with controlled release oxycodone or fixed combination oxycodone plus acetaminophen added to nonsteroidal antiinflammatory drugs: a double blind, randomized, multicenter, placebo controlled trial. J Rheumatol 1999; 26:862-869. 12 Peloso PM, Bellamy N, Bensen W, et al. Double blind randomized placebo control trial of controlled release codeine in the treatment of osteoarthritis of the hip or knee. J Rheumatol 2000; 27:764-771. 13 Turk DC. Assess the person, not just the pain. Pain. Clinical Updates 1993; 1:1-4. 14 Fordyce WE. Opioids and treatment targets. Am Pain Soc Bull 1991; 1:1-4. 15 Clark

AJM. Chronic pain: is anything new? Can J Anaesth 1995; 42:R55-R61. 16 Fordyce WE. Learned pain: pain as behavior. In: The management of pain. Bonica JJ (editor). Philadelphia: Lea and Febiger; 1990: 291-299.

Rating: 5c

Note: Current Opinion in Anesthesiology was not accepted into Medline until 2005, so this article is not available on Medline.

Stein DJ, Bandelow B, Hollander E, Nutt DJ, Okasha A, Pollack MH, Swinson RP, Zohar J; World Council of Anxiety. WCA Recommendations for the long-term treatment of posttraumatic stress disorder. CNS Spectr. 2003 Aug;8(8 Suppl 1):31-9.

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Posttraumatic stress disorder (PTSD) is a common and disabling condition. In addition to combat-related PTSD, the disorder occurs in civilians exposed to severe traumatic events, with the community prevalence rate for the combined populations reaching as high as 12%. If left untreated, PTSD may continue for years after the stressor event, resulting in severe functional and emotional impairment and a dramatic reduction in quality of life, with negative economic consequences for both the sufferer and society as a whole. Although PTSD is often overlooked, diagnosis is relatively straightforward once a triggering stressor event and the triad of persistent symptoms-reexperiencing the traumatic event, avoiding stimuli associated with the trauma, and hyperarousal have been identified. However, comorbid conditions of anxiety and depression frequently hamper accurate diagnosis. Treatment for PTSD includes psychotherapy and pharmacotherapy. The latter includes selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressants, and monoamine oxidase inhibitors. Only SSRIs have been proven effective and safe in long-term randomized controlled trials. Current guidelines from the Expert Consensus Panel for PTSD recommend treatment of chronic PTSD for a minimum of 12-24 months.

PMID: 14767396

Rating: 5a

Stein DJ, Ipser JC, Seedat S. Pharmacotherapy for post traumatic stress disorder (PTSD). Cochrane Database Syst Rev. 2006;(1):CD002795.

University of Cape Town, Dept of Psychiatry, Anzio Road, Rondebosch, Cape Town, South Africa, 7700. djs2@sun.ac.za

MAIN RESULTS: 35 short-term (14 weeks or less) RCTs were included in the analysis (4597 participants). Symptom severity for 17 trials was significantly reduced in the medication groups, relative to placebo (weighted mean difference -5.76, 95% confidence intervals (CI) -8.16 to -3.36, number of participants (N) = 2507). Similarly, summary statistics for responder status from 13 trials demonstrated overall superiority of a variety of medication agents to placebo (relative risk 1.49, 95% CI 1.28 to 1.73, number needed to treat = 4.85, 95% CI 3.85 to 6.25, N = 1272). Medication and placebo response occurred in 59.1% (N = 644) and 38.5% (628) of patients, respectively. Of the medication classes, evidence of treatment efficacy was most convincing for the SSRIs. Medication was superior to placebo in reducing the severity of PTSD symptom clusters, comorbid depression and disability. Medication was also less well tolerated than placebo. A narrative review of 3 maintenance trials suggested that long term medication may be required in treating PTSD. AUTHORS' CONCLUSIONS: Medication treatments can be effective in treating PTSD, acting to reduce its core symptoms, as well as associated depression and disability. The findings of this review support the status of SSRIs as first line agents in the pharmacotherapy of PTSD, as well as their value in long-term treatment. However, there remain important gaps in the evidence base, and a continued need for more effective agents in the management of PTSD.

PMID: 16437445

Rating: 1c

Stewart W, 10th IASP World Congress on Pain, San Diego, 8/21/2002
Ouch! Pain Costs Employers $80 Billion Annually
Kathleen Doheny | Reuters Health | 08/21/2002
SAN DIEGO, CA -- Pain from common conditions such as headaches and back ache costs US employers about $80 billion a year in lost productivity, according to a report presented here at the 10th World Congress on Pain.

But the bulk of the loss, or about $64 billion, is largely invisible to employers because it occurs not when workers take sick days but rather when they are on the job but in too much pain to perform up to par.

The survey is "the first to really measure the cost of pain," lead author Walter Stewart, a researcher at the Center for Work and Health at AdvancePCS in Hunt Valley, Maryland, told Reuters Health. AdvancePCS provides information on health improvement services.

"People are at work but not performing as well as they would were they pain-free," said Judith Ricci, another member of the research team.

To arrive at the estimate, the researchers conducted an ongoing telephone survey, from July 2001 to July 2002, including more than 29,000 employed and more than 1600 unemployed people ranging from 18 to

65 years old. They described pain complaints from headache, arthritis, backache and other musculoskeletal conditions as well as work absences and reduced work performance.

The researchers converted the subjects' lost productive time to dollars per worker per week, using self-reported annual salary.

"I was surprised at how pervasive pain is," Ricci says. "Over half the people we interviewed who were working reporting being in pain at least once in the past two weeks," Ricci says. Even more pain reports were received from the unemployed respondents.

The researchers conclude that pain is the most prevalent health condition in the US work force and the most costly in terms of productive work time. Headache and back pain account for the majority of on-the-job pain complaints. Pain has the most impact on the job for men, those 35 to 40 years, those with less education, African Americans and workers with high demand jobs over which they have little control

"The critical finding here is that pain is common in the workforce," Stewart says. "People bring it to work and they don't function well. And it's invisible to employers."
Rating: 9b

Stewart WF, Ricci JA, Chee E, Morganstein D, Lipton R, Lost productive time and cost due to common pain conditions in the US workforce, JAMA. 2003 Nov 12;290(18):2443-54.

AdvancePCS Center for Work and Health, Hunt Valley, Md, USA. wfstewart@geisinger.edu

This was a cross-sectional study using survey data from the American Productivity Audit (a telephone survey that uses the Work and Health Interview) of working adults between August 1, 2001, and July 30, 2002, using a random sample of 28,902 working adults in the United States. The findings were that 13% of the total workforce experienced a loss in productive time during a 2-week period due to a common pain condition. Headache was the most common (5.4%) pain condition resulting in lost productive time. It was followed by back pain (3.2%), arthritis pain (2.0%), and other musculoskeletal pain (2.0%). Workers who experienced lost productive time from a pain condition lost a mean of 4.6 hours/week. Workers who had a headache had a mean loss in productive time of 3.5 hr/wk. Workers who reported arthritis or back pain had mean lost productive times of 5.2 hr/wk. Other common pain conditions resulted in a mean loss in productive time of 5.5 hr/wk. Lost productive time from common pain conditions among active workers costs an estimated $61.2 billion annually. The majority (76.6%) of the lost productive time was explained by reduced performance while at work and not work absence. The study concluded, "Pain is an inordinately common and disabling condition in the US workforce. Most of the pain-related lost productive time occurs while employees are at work and is in the form of reduced performance."

PMID: 14612481

Rating: 4b

Stitik TP, Altschuler E, Foye PM. Pharmacotherapy of osteoarthritis. Am J Phys Med Rehabil. 2006;85:S15-28; quiz S29-31.

Department of Physical Medicine and Rehabilitation, University of Medicine and Dentistry of New Jersey-New Jersey Medical School, Newark, New Jersey 07103, USA.

PMID: 17079975

No abstract was given. This was a review article in a supplement issue that described current treatment of osteoarthritis of the knee and hip. The article was sponsored by Sanori-Aventis.

Rating: 5c

Stojanovic MP. Stimulation methods for neuropathic pain control. Curr Pain Headache Rep. 2001 Apr;5(2):130-7.

MGH Pain Center, Department of Anesthesia and Critical Care, Massachusetts General Hospital, Boston, MA 02114, USA. mstojanovic@partners.org

Neurostimulation methods for control of chronic neuropathic pain have recently gained in popularity. The reasons for this are multifactorial. As opposed to nerve ablation, these methods are minimally invasive and reversible. The improvements in hardware design simplified implantation techniques and prolonged equipment longevity. Stimulation trials have become less invasive, allowing patients to test its effects before final implantation. Finally, the scientific evidence has shown good outcomes of neurostimulation methods for chronic neuropathic pain control. Recent research efforts have revealed new potential mechanisms of action of neurostimulation. Whereas its action was widely explained by gate control theory in the past, it seems that neuromodulation acts also by modulation of neurotransmitters in the central nervous system. Three neurostimulation methods are currently used in clinical practice: spinal cord stimulation (SCS), peripheral nerve stimulation (PNS), and deep brain stimulation (DBS). The SCS and PNS are excellent treatment choices for certain forms of neuropathic pain. The new indications for SCS are end-stage peripheral vascular disease and ischemic heart disease, whereas PNS is used for the treatment of occipital neuralgia and chronic pelvic pain. DBS is reserved for carefully selected patients in whom the other treatment modalities have failed. In a minority of patients the "tolerance" to neurostimulation develops after long-term use. Further research is needed to establish better outcome predictors to neurostimulation and possibly improve patient selection criteria.

Publication Types:

- Review
- Review, Tutorial

PMID: 11252147

Rating: 5b

Stuckey SJ, Jacobs A, Goldfarb J. EMG biofeedback training, relaxation training, and placebo for the relief of chronic back pain. Percept Mot Skills. 1986 Dec;63(3):1023-36.

24 patients with chronic low back pain were randomly assigned to three treatment conditions: EMG biofeedback, relaxation training, and a placebo condition. Patients were seen for eight sessions and were evaluated before Session 1 and after Session 8. Eight analyses of covariance which were adjusted for age and pretest scores were computed on the final scores to find which variables could detect significant difference between treatments. Age was included as a covariate because the differences in age between conditions were significant. Four variables with significant and nearly significant differences were chosen for analysis. The second set of analyses identified the nature of the differences among the three conditions. These included a priori planned comparisons among conditions, and paired t tests. Relaxation-trained subjects were significantly superior to subjects in the placebo condition, in decreasing pain during the function test, increasing relaxation, and decreasing Upper Trapezius EMG. They were superior to EMG Biofeedback training in increasing reported activity. Both Relaxation and EMG trained subjects were able to reduce Upper Trapezius EMG by Session 8. Relaxation-trained subjects showed significant change on eight of the 14 possible comparisons for each treatment condition. EMG biofeedback training showed significant favorable results in only one condition; the placebo condition showed no significant results. Relaxation training gave better results in reducing EMG and pain, and in increasing relaxation and activity than either EMG biofeedback alone or a placebo condition.

PMID: 2949196

Rating: 2c

Sullivan MJ, Ward LC, Tripp D, French DJ, Adams H, Stanish WD. Secondary prevention of work disability: community-based psychosocial intervention for musculoskeletal disorders. J Occup Rehabil. 2005 Sep;15(3):377-92.

Department of Psychology, University of Montreal, Montreal, Quebec, Canada.
michael.jl.sullivan@umontreal.ca

INTRODUCTION: One objective of the present research was to examine the degree to which psychological risk factors could be reduced through participation in a community-based psychosocial

intervention for work-related musculoskeletal disorders. A second objective was to examine whether psychosocial risk reduction had an effect on the probability of return to work. METHODS: Participants were 215 Workers Compensation Board claimants with work-related musculoskeletal disorders who had been absent from work for an average of approximately 7 months (M = 28.8 weeks, range = 4-100 weeks) and were referred to a community-based multidisciplinary secondary prevention program in Nova Scotia, Canada. RESULTS: In the current sample, 63.7% of participants returned to work within 4 weeks of treatment termination. The percentage reductions in targeted risk factors from pretreatment to posttreatment were as follows: catastrophizing (32%), depression (26%), fear of movement/re-injury (11%), and perceived disability (26%). Logistic regression indicated that elevated pretreatment scores on fear of movement and re-injury (OR = 0.58, 95% CI = 0.35-0.95) and pain severity (OR = 0.64, 95% CI = 0.43-0.96) were associated with a lower probability of return to work. A second logistic regression addressing the relation between risk factor reduction and return to work revealed that only reductions in pain catastrophizing (OR = 0.17, 95% CI = 0.07-0.46) were significant predictors of return to work. CONCLUSIONS: The results of the present study provide further evidence that risk factor reduction can impact positively on short term return to work outcomes. SIGNIFICANCE: Outcomes of rehabilitation programs for work disability might be improved by incorporating interventions that specifically target catastrophic thinking. Community-based models of psychosocial intervention might represent a viable approach to the management of work disability associated with musculoskeletal disorders.

PMID: 16119228

Rating: 4b

Sundaraj SR, Johnstone C, Noore F, Wynn P, Castro M. Spinal cord stimulation: a seven-year audit. J Clin Neurosci. 2005 Apr;12(3):264-70.

Pain Management Unit, Nepean Teaching Hospital, Sydney University, Penrith, NSW, Australia. sunderaj@bigpond.net.au

OBJECTIVE: To evaluate the outcome and complications of spinal cord stimulation (SCS) for chronic neuropathic pain in an Australian population. MATERIALS AND METHODS: An independent researcher retrospectively examined the records of 138 patients trialing SCS between 1995 and 2002 at our institution. Information collected included pain relief, ability to perform activities of daily living (ADLs), return to work and reduction in opiate analgesia. Clinical, psychological, demographic and financial data were also collected. RESULTS: Of 138 patients who trialed SCS, 103 (74.7%) achieved a greater than 50% reduction in their pain and proceeded to permanent implantation. At 1 year following permanent implantation, 84.4% of these still had a reduction in their pain by greater than 50%. The majority of patients, 59.1%, stated that their analgesia was good (50-74% pain reduction). All patients required opiate analgesics prior to SCS implantation, but this fell to 54.6% after SCS implantation. Additionally, 73.6% had a significant improvement in their ability to perform ADLs and 24% of patients were able to return to work. CONCLUSION: SCS is an effective treatment in the control of chronic

neuropathic pain, particularly in combination with comprehensive medical management within a multidisciplinary pain management centre.

Publication Type:
Cohort Study

PMID: 15851079

Rating: 3b

Swigris JJ, Olin JW, Mekhail NA, Implantable spinal cord stimulator to treat the ischemic manifestations of thromboangiitis obliterans (Buerger's disease), J Vasc Surg. 1999 May;29(5):928-35

Department of Vascular Medicine, Cleveland Clinic Foundation, Ohio, USA.

Thromboangiitis obliterans (Buerger's disease) is a segmental inflammatory vasculitis that involves the small-sized and medium-sized arteries, veins, and nerves. It is causally related to tobacco use. The diagnosis is usually made on the basis of the presence of distal arterial disease in individuals who smoke and in whom other disease entities have been excluded. The most effective treatment for Buerger's disease is smoking cessation. Without strict adherence to tobacco avoidance, disease progression is likely. Methods to control ischemic pain include medications, sympathectomy, or surgical revascularization. The effect of sympathectomy is unpredictable, and the chances of a successful revascularization procedure are rare because distal target vessels often are extensively diseased. Herein, we describe a patient whose condition did not respond to the usual conservative therapy but did respond dramatically to the implantation of a permanent spinal cord stimulator. Although these devices have been used for more than 20 years in various other peripheral arterial diseases, their use in Buerger's disease has been limited.

Publication Types:
- Case Reports

PMID: 10231644

Rating: 11b

Taricco, M., et al. Pharmacological interventions for spasticity following spinal cord injury: results of a Cochrane systematic review. Eura Medicophys. 2006; Volume 42: 5-15.

Rating: 1c

Quality: N/A. Total Rating: N/A. Comment: Does not meet inclusion criteria for evidence-based review. [CA DWC]

Tassone DM, Boyce E, Guyer J, Nuzum D. Pregabalin: a novel gamma-aminobutyric acid analogue in the treatment of neuropathic pain, partial-onset seizures, and anxiety disorders. Clin Ther. 2007:29:26-48.

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BACKGROUND: The US Food and Drug Administration (FDA) approved pregabalin in December 2004 for the treatment of neuropathic pain associated with diabetic peripheral neuropathy and postherpetic neuralgia. Pregabalin is the first drug approved in the United States and in Europe for both conditions. In June 2005, pregabalin was approved as an adjunctive treatment in adults with partial-onset seizures. The FDA currently is considering the approval of pregabalin as adjunctive therapy in adults with generalized anxiety disorder (GAD) or social anxiety disorder (SAD). OBJECTIVES: The goals of this review were to summarize the pharmacology, pharmacokinetics, efficacy, and tolerability of pregabalin; review its approved uses in the management of neuropathic pain and refractory partial-onset seizures; and investigate its potential use in patients with GAD or SAD. METHODS: Relevant English-language literature was identified through a search of MEDLINE (1993-June 2006) and International Pharmaceutical Abstracts (2000-June 2006). The search terms included pregabalin, Lyrica, S-(+)-3 isobutyl-gaba, PN, DPN, diabetic peripheral neuropathy, PHN, postherpetic neuralgia, partial seizures, epilepsy, generalized anxiety disorder, and CI-1008. RESULTS: In 4 clinical trials in a total of 1068 patients with diabetic peripheral neuropathy, the patients receiving pregabalin 300 to 600 mg/d had significantly greater improvement in mean pain scores than placebo recipients (P < or = 0.01). Patients with postherpetic neuralgia receiving pregabalin 450 to 600 mg/d had significantly greater improvement in relief of pain and pain-related sleep interference than placebo recipients (P < or = 0.002). Patients with refractory partial-onset seizures who received pregabalin 150 to 600 mg/d (divided into 2 or 3 doses) concomitantly with antiepileptic drugs had significantly fewer seizures than placebo recipients (P < or = 0.001). In the 3 studies that evaluated the efficacy of pregabalin in patients with GAD or SAD, the patients receiving pregabalin 200 to 600 mg/d (divided into 2 or 3 daily doses) had a significantly greater reduction in mean pain scores on the Hamilton Anxiety Scale than placebo recipients (P < or = 0.01). Across all the reviewed clinical trials, the most commonly reported adverse effects (AEs) were those affecting the central nervous system, including somnolence (< or =50%), dizziness (< or =49%), and headache (< or =29%). AEs resulted in withdrawal from the study in < or =32% of patients. CONCLUSIONS: Pregabalin appears to be an effective therapy in patients with diabetic peripheral neuropathy, postherpetic neuralgia, and adults with refractory partial-onset seizures. The available data suggest that pregabalin may be beneficial as an adjunctive therapy in adult patients with GAD or SAD.

PMID: 17379045

Rating: 5a

Taylor WD, Doraiswamy PM. A Systematic Review of Antidepressant Placebo-Controlled Trials for Geriatric Depression: Limitations of Current Data and Directions for the Future, Neuropsychopharmacology. 2004 Sep 1

Department of Psychiatry, Duke University Medical Center, Durham, NC, USA.

Depression in the elderly is a major public health problem as untreated depression adversely impacts comorbid illnesses. It is important to develop safe and effective antidepressant therapies for older individuals. We performed a systematic review of all published randomized, placebo-controlled antidepressant medication trials in populations over age 55 years. Papers were obtained via MEDLINE (1966-August 2003) and PSYCINFO (1872-August 2003). Unpublished trials, trials examining nonpharmacologic interventions, and papers reporting post hoc analyses were not included in this review unless they provided new insights. A total of 18 placebo-controlled trials examining acute efficacy met our criteria. The combined sample size in these studies was 2252. The mean sample size was 51 (range 20-728) and mean trial duration was 7 weeks. A total of 12 trials examined tricyclic antidepressants (TCAs), five trials examined selective serotonin reuptake inhibitors (SSRIs), two trials examined bupropion, and one trial examined mirtazapine. There were no published trials of venlafaxine or nefazodone. In all, 71.5% of trials reported significantly greater efficacy with drug than placebo. In conclusions, there is a paucity of published controlled antidepressant trials in the elderly. Most published studies examine small sample sizes and do not include common comorbid conditions. Efficacy studies examining relapse prevention are lacking. Large placebo response rates, lack of controlled head to head comparisons, and other methodological design differences make crosstrial comparisons difficult. Large simple studies are urgently needed to address the unmet needs for data on safety and efficacy of antidepressants in this population. Neuropsychopharmacology advance online publication, 1 September 2004; doi:10.1038/sj.npp.1300550

PMID: 15340391
Rating: 1b

Taylor RS, Buyten JP, Buchser E. Spinal cord stimulation for complex regional pain syndrome: A systematic review of the clinical and cost-effectiveness literature and assessment of prognostic factors. Eur J Pain. 2006 Feb;10(2):91-101.

Department of Public Health and Epidemiology, University of Birmingham, Edgbaston, Birmingham B15 2TT, UK.

OBJECTIVE: To review the clinical and cost-effectiveness of spinal cord stimulation (SCS) in the management of patients with complex regional pain syndrome (CRPS) and identify the potential predictors of SCS outcome. DESIGN: Systematic review of the literature and meta-regression.

METHODS: Electronic databases were searched for controlled and uncontrolled studies and economic evaluations relating to the use of SCS in patients with either CRPS type I or II. RESULTS: One randomised controlled trial, 25 case series and one cost-effectiveness study were included. In the randomised controlled trial in type I CRPS patients, SCS therapy lead to a reduction in pain intensity at 24 months of follow-up (mean change in VAS score -2.0), whereas pain was unchanged in the control group (mean change in VAS score 0.0) ($p<0.001$). In the case series studies, 67% (95% CI 51%, 84%) of type I and type II CRPS patients implanted with SCS reported pain relief of at least 50% over a median follow-up period of 33 months. No statistically significant predictors of pain relief with SCS were observed in multivariate meta-regression analysis across studies. An economic analysis based on the randomised controlled trial showed a lifetime cost saving of approximately 58,470 (US$60,800) with SCS plus physical therapy compared with physical therapy alone. The mean cost per quality-adjusted life-year at 12-month follow-up was 22,580 (US$23,480). CONCLUSIONS: SCS appears to be an effective therapy in the management of patients with CRPS type I (Level A evidence) and type II (Level D evidence). Moreover, there is evidence to demonstrate that SCS is a cost-effective treatment for CRPS type I.

PMID: 16310712

Rating: 1c

Taylor RJ, Taylor RS. Spinal cord stimulation for failed back surgery syndrome: a decision-analytic model and cost-effectiveness analysis. Int J Technol Assess Health Care. 2005 Summer;21(3):351-8.

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OBJECTIVES: The aim of this study was to develop a decision-analytic model to assess the cost-effectiveness of spinal cord stimulation (SCS), relative to nonsurgical conventional medical management (CMM), for patients with failed back surgery syndrome (FBSS). METHODS: A decision tree and Markov model were developed to synthesize evidence on both health-care costs and outcomes for patients with FBSS. Outcome data of SCS and CMM were sourced from 2-year follow-up data of two randomized controlled trials (RCTs). Treatment effects were measured as levels of pain relief. Short- and long-term health-care costs were obtained from a detailed Canadian costing study in FBSS patients. Results are presented as incremental cost per quality adjusted life year (QALY) and expressed in 2003 Euros. Costs were discounted at 6 percent and outcomes at 1.5 percent. RESULTS: Over the lifetime of the patient, SCS was dominant (i.e., SCS is cost-saving and gives more health gain relative to CMM); a finding that was robust across sensitivity analyses. At a 2-year time horizon, SCS gave more health gain but at an increased cost relative to CMM. Given the uncertainty in effectiveness and cost parameters, the 2-year cost-effectiveness of SCS ranged from 30,370 Euros in the base case to 63,511 Euros in the worst-case scenario. CONCLUSIONS: SCS was found to be both more effective and less costly than CMM, over the lifetime of a patient. In the short-term, although SCS is potentially cost-

effective, the model results are highly sensitive to the choice of input parameters. Further empirical data are required to improve the precision in the estimation of short-term cost-effectiveness.

Publication Type:
Meta-Analysis

PMID: 16110715

Rating: 1b
Teichman PG. A tool for safely treating chronic pain. Family Practice Management. 2001 Nov-Dec; 8(10): 47-9
Harpers Ferry Rural Family Medicine Residency, West Virginia University in Harpers Ferry, W.Va., USA.
Abstract:
Two competing high-pressure systems have converged over medical care. A gale of headlines bewails the rampant diversion of prescription drugs onto America's streets. Meanwhile, a tempest of advocates, reviewers, defenders and regulators bemoans the under-treatment of chronic pain conditions in our communities. From the eye of the storm, physicians may find it difficult to balance these boisterous fronts and accomplish our goal of maximizing patients' social and physical functions via safe pain relief. Confronted with the pain care needs of our patients and the attendant hazards of effective analgesic medications, our practice implemented a "medication use agreement" that charts a clear course of treatment and shelters our community from medication misuse.
Publication Type: Review
PMID: 11757239

Thompson JC, Dunbar E, Laye RR. Treatment challenges and complications with ziconotide monotherapy in established pump patients. Pain Physician. 2006 Apr;9(2):147-52.

Pain Control Network, Louisville, KY 40205, USA. jim.thompson@insightbb.com

BACKGROUND: The U.S. Food and Drug Administration (FDA) recently approved Ziconotide intrathecal infusion for the management of severe chronic pain in patients for whom intrathecal therapy is warranted, and who are intolerant of, or refractory to, other methods of treatment, including intrathecal morphine. Ziconotide is approved as a monotherapy, but there are challenges associated with the decision to wean intrathecal opioids for Ziconotide alone. Maintaining adequate analgesia and managing opioid withdrawal symptoms may be difficult. Additionally, a variety of adverse physiological, cognitive and psychiatric events may be associated with this new drug. Patients with pretreatment psychiatric disorders may be at increased risk for treatment complications. OBJECTIVE: To present a report of a case series describing treatment challenges and complications associated with the decision to convert established pump patients from intrathecal opioid therapy to Ziconotide monotherapy. DESCRIPTION OF CASES: Three established pump patients, refractory to intrathecal

opioid therapy, were converted to Ziconotide monotherapy. All of these patients experienced significant emotional distress or psychological symptoms that threatened the success of the treatment. Achieving adequate analgesia, reducing Ziconotide to mitigate adverse physiological effects, managing opioid withdrawal symptoms, and supportive psychological consultation were combined to achieve successful outcomes in two of our three patients. CONCLUSION: This report describes challenges associated with the decision to convert established pump patients from intrathecal opioid therapy to Ziconotide monotherapy. Inadequate analgesia, adverse medication effects, and opioid withdrawal symptoms can precipitate a stressful situation that may be perceived as dangerous or threatening by patients who are predisposed to anxiety. Screening patients for psychiatric disorders, anxiety-proneness and/or vulnerability to stress should be considered to reduce the risk of treatment complications. A multimodal approach is strongly advocated, including rapid responses of treating physicians and nurses along with strong psychological support.

PMID: 16703976

Rating: 4c

Thorlacius S. Fibromyalgia and Chronic Fatigue Syndrome. Disability Medicine. American Board of Independent Medical Examiners. Vol. 1, No. 1. January-March 2001.

Abstract:

Neither fibromyalgia or chronic fatigue syndrome can be confirmed with reliable, objective tests and the related symptoms could often be part of an anxiety or mood disorder. Due to prejudices against psychological disorders, a label of fibromyalgia or chronic fatigue syndrome is usually given to the condition, not always leading to direct and optimal treatment.

Ticknor CB, Pharmacologic considerations in treating depression: a patient-centered approach. J Manag Care Pharm. 2004 Mar;10(2 Suppl):S8-15.

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OBJECTIVE: To review the tricyclic antidepressants, selective serotonin reuptake inhibitors, and dually acting antidepressants and their economic and treatment implications. SUMMARY: Major depressive disorder.s cost to the U.S. economy is staggering, but the selection of drugs available to treat it has expanded to include drugs that have better side-effect profiles. Regardless, remission rates are high, and, often, patients are not treated aggressively enough. Somatic presentations are more common than previously thought, and pain, in particular, may be associated with depression. Pain and depression are both regulated by serotonin and norepinephine, and several studies suggest that using dual-action antidepressants may be helpful in patients who have an element of pain to their disorder. Titration to an

adequate dose of any antidepressant is important, as is sustaining treatment for months to years, depending on the patient.s history. CONCLUSION: Increasingly, the mental health community is realizing that the goal of treatment for patients with major depressive disorder must be sustained remission.

Publication Types:
- Review
- Review, Tutorial

PMID: 15046545

Rating: 5b

Tofferi JK, Jackson JL, O'Malley PG, Treatment of fibromyalgia with cyclobenzaprine: A meta-analysis, Arthritis Rheum. 2004 Feb 15;51(1):9-13.

Walter Reed Army Medical Center, Washington, DC, USA.

OBJECTIVE: To systematically review the effectiveness of cyclobenzaprine in the treatment of fibromyalgia. METHODS: Articles describing randomized, placebo-controlled trials of cyclobenzaprine in people with fibromyalgia were obtained from Medline, EMBase, Psyclit, the Cochrane Library, and Federal Research in Progress Database. Unpublished literature and bibliographies were also reviewed. Outcomes, including global improvement, treatment effects on pain, fatigue, sleep, and tender points over time, were abstracted. RESULTS: Five randomized, placebo-controlled trials were identified. The odds ratio for global improvement with therapy was 3.0 (95% confidence interval [95% CI] 1.6-5.6) with a pooled risk difference of 0.21 (95% CI 0.09-0.34), which calculates to 4.8 (95% CI 3.0-11) individuals needing treatment for 1 patient to experience symptom improvement. Pain improved early on, but there was no improvement in fatigue or tender points at any time. CONCLUSION: Cyclobenzaprine-treated patients were 3 times as likely to report overall improvement and to report moderate reductions in individual symptoms, particularly sleep.

PMID: 14872449

Rating: 1c

Tomas-Carus P, Häkkinen A, Gusi N, Leal A, Häkkinen K, Ortega-Alonso A. Aquatic training and detraining on fitness and quality of life in fibromyalgia. Med Sci Sports Exerc. 2007 Jul;39(7):1044-50.

Fitness and Lifequality Laboratory, Faculty of Sports Sciences, University of Extremadura, Cáceres, Spain.

PURPOSE: To evaluate the effects of a 12-wk period of aquatic training and subsequent detraining on health-related quality of life (HRQOL) and physical fitness in females with fibromyalgia. METHODS: Thirty-four females with fibromyalgia were randomly assigned into two groups: an exercise group, who exercised for 60 min in warm water, three times a week (N = 17); and a control group, who continued their habitual leisure-time activities (N = 17). HRQOL was assessed using the Short Form 36 questionnaire and the Fibromyalgia Impact Questionnaire. Physical fitness was measured using the following tests: Canadian Aerobic Fitness, hand grip dynamometry, 10-m walking, 10-step stair climbing, and blind one-leg stance. Outcomes were measured at baseline, after treatment, and after 3 months of detraining. RESULTS: After 12 wk of aquatic exercise, significant positive effects of aquatic training were found in physical function, body pain, general health perception, vitality, social function, role emotional problems and mental health, balance, and stair climbing. After the detraining period, only the improvements in body pain and role emotional problems were maintained. CONCLUSION: The present water exercise protocol improved some components of HRQOL, balance, and stair climbing in females with fibromyalgia, but regular exercise and higher intensities may be required to preserve most of these gains.

PMID: 17596770

Rating: 2b

Toth PP, Urtis J. Commonly used muscle relaxant therapies for acute low back pain: a review of carisoprodol, cyclobenzaprine hydrochloride, and metaxalone. Clin Ther. 2004;26:1355-67.

Department of Family and Community Medicine, University of Illinois School of Medicine, Peoria, USA.

BACKGROUND: Low back pain is a leading reason for primary care visits. Many treatment options are available, but some lack scientific support. OBJECTIVE: The aim of this review was to discuss the etiology of low back pain and the relative risks and benefits of muscle relaxants commonly prescribed for the management of back pain. METHODS: We searched Intercontinental Marketing Services data for January 2003 through January 2004 to determine the most commonly prescribed agents for the management of musculoskeletal pain. Carisoprodol, cyclobenzaprine hydrochloride, and metaxalone represented >45% of all such prescriptions. Cochrane Library, MEDLINE, and EMBASE databases were searched (time frame: 1960 through January 2004; search terms: back pain, carisoprodol, cyclobenzaprine, metaxalone, muscle relaxants, and pharmacotherapy) and reference lists of identified articles were hand-searched. RESULTS: Three trials of carisoprodol (N = 197) were located in the Cochrane Library database. Two double-blind, randomized, placebo-controlled trials evaluating the safety and efficacy of cyclobenzaprine hydrochloride (N = 1405) were identified in the literature. Three double-blind, placebo-controlled trials were identified for metaxalone (N = 428) in 2 reports. The types of adverse events seen with these agents involved the central nervous system, including drowsiness/sedation, fatigue, and dizziness. However, the efficacy of cyclobenzaprine hydrochloride

was shown to be independent of its sedative effects, which were dose related. The potential for abuse with carisoprodol is of growing concern. CONCLUSIONS: Analgesic pain management for low back pain due to muscle spasm may be combined with a muscle relaxant. Cyclobenzaprine hydrochloride has the most recent and largest clinical trials demonstrating its benefit, but carisoprodol and metaxalone also appear to be effective. However, carisoprodol's usefulness is mitigated by its potential for abuse.

PMID: 15530999

Ranking: 5a

Towheed TE, Anastassiades TP, Shea B, Houpt J, Welch V, Hochberg MC, Glucosamine therapy for treating osteoarthritis, Cochrane Database Syst Rev. 2001;(1):CD002946.

Medicine, Community Health and Epidemiology, Queen's University, Room 2066 Etherington Hall, Queen's University, Kingston, Ontario, Canada, K7L 3N6. tt5@post.queensu.ca

BACKGROUND: Osteoarthritis (OA) is the most common form of arthritis, and it is often associated with significant disability and an impaired quality of life. OBJECTIVES: To review all randomized controlled trials (RCTs) evaluating the effectiveness and toxicity of glucosamine in osteoarthritis (OA). SEARCH STRATEGY: We searched MEDLINE, Embase, and Current Contents up to November 1999, and the Cochrane Controlled Trials Register. We also wrote letters to content experts, and hand searched reference lists of identified RCTs and pertinent review articles. SELECTION CRITERIA: Relevant studies met the following criteria: 1) RCTs evaluating the effectiveness and safety of glucosamine in OA, 2) Both placebo based and comparative studies were eligible, 3) Both single blinded and double-blinded studies were eligible. DATA COLLECTION AND ANALYSIS: Data abstraction was performed independently by two investigators and the results were compared for degree of agreement. Gotzsche's method and a validated tool (Jadad 1995) were used to score the quality of the RCTs. Continuous outcome measures were pooled using standardized mean differences. Dichotomous outcome measures were pooled using Peto Odds Ratios. MAIN RESULTS: Collectively, the 16 identified RCTs provided evidence that glucosamine is both effective and safe in OA. In the 13 RCTs in which glucosamine was compared to placebo, glucosamine was found to be superior in all RCTs, except one. In the four RCTs in which glucosamine was compared to an NSAID, glucosamine was superior in two, and equivalent in two. REVIEWER'S CONCLUSIONS: Further research is necessary to confirm the long term effectiveness and toxicity of glucosamine therapy in OA. Most of the trials reviewed only evaluated the Rotta preparation of glucosamine sulfate. It is not known whether different glucosamine preparations prepared by different manufacturers are equally effective in the therapy of OA.

Publication Types:
- Review
- Review, Academic

PMID: 11279782

Rating: 1b

Towheed TE, Maxwell L, Judd MG, Catton M, Hochberg MC, Wells G. Acetaminophen for osteoarthritis. Cochrane Database Syst Rev. 2006 ;(1):CD004257.

Queen's University, Medicine and of Community Health and Epidemiology, Etherington Hall-Room 2066, Kingston, Ontario, Canada, K7L 3N6. tt5@post.queensu.ca

RESULTS: In the comparator-controlled RCTs, acetaminophen was less effective overall than NSAIDs in terms of pain reduction, global assessments and in terms of improvements in functional status. No significant difference was found overall between the safety of acetaminophen and NSAIDs, although patients taking traditional NSAIDS were more likely to experience an adverse GI event (RR 1.47, (95% CI 1.08 to 2.00). 19% of patients in the traditional NSAID group versus 13% in the acetaminophen group experienced an adverse GI event. CONCLUSIONS: The evidence to date suggests that NSAIDs are superior to acetaminophen for improving knee and hip pain in people with OA. The size of the treatment effect was modest, and the median trial duration was only six weeks, therefore, additional considerations need to be factored in when making the decision between using acetaminophen or NSAIDs. In OA subjects with moderate-to-severe levels of pain, NSAIDs appear to be more effective than acetaminophen.

PMID: 16437479

Rating: 1c

Townsend CO, Bruce BK, Hooten WM, Rome JD. The role of mental health professionals in multidisciplinary pain rehabilitation programs. J Clin Psychol. 2006 Aug 25; [Epub ahead of print]

Mayo Clinic Comprehensive Pain Rehabilitation Center.

The traditional roles of psychologists and mental health therapists are challenged by the comprehensive treatment necessary for patients being treated in multidisciplinary pain rehabilitation programs (MPRPs). Mental health professionals within MPRPs provide direct clinical care but also guide the biopsychosocial model of pain management and cognitive-behavioral interventions for multiple disciplines. Illustrated by a case example of a patient who has complex chronic pain, this article discusses the biopsychosocial approach to pain treatment, structure of multidisciplinary care, major roles of mental health professionals in MPRPs, complexities of treating patients who have pain, and challenges in collaborating with multiple disciplines. (c) 2006 Wiley Periodicals, Inc. J Clin Psychol: In Session.

PMID: 16937355

Rating: 5b

Tracz MJ, Sideras K, Bolona ER, Haddad RM, Kennedy CC, Uraga MV, Caples SM, Erwin PJ, Montori VM. Testosterone use in men and its effects on bone health. A systematic review and meta-analysis of randomized placebo-controlled trials. J Clin Endocrinol Metab. 2006;91:2011-6.

Knowledge and Encounter Research Unit, Department of Medicine, Mayo Clinic College of Medicine, Rochester, Minnesota 55905, USA.

CONTEXT: Androgen-deficient men are at increased risk of osteoporosis. The extent to which testosterone can prevent and treat osteoporosis in men remains unclear. OBJECTIVE AND DESIGN: We performed a systematic review and meta-analysis of randomized placebo-controlled trials in men to estimate the effect of testosterone use on bone health outcomes. DATA SOURCES: The review encompassed librarian-designed search strategies using MEDLINE (1966 to March 2005), EMBASE (1988 to March 2005), and Cochrane CENTRAL (inception to March 2005); a review of reference lists from included studies; and content expert files. DATA COLLECTION: Independently and in duplicate, we assessed the methodological quality of the eligible trials and collected data on bone mineral density and bone fractures at the longest point of complete follow-up. DATA SYNTHESIS: We included eight trials enrolling 365 patients. Two trials followed patients for more than 1 yr. Meta-analysis of these trials showed that, compared with placebo, im testosterone was associated with an 8% (95% confidence interval, 4%, 13%) gain in lumbar bone mineral density and transdermal testosterone had no significant impact. Testosterone use was associated with a nonsignificant 4% (95% confidence interval, -2%, 9%) gain in femoral neck bone mineral density with unexplained differences in results across trials (26% of these differences were not explained by chance alone). No trials measured or reported the effect of testosterone on fractures. CONCLUSIONS: Intramuscular testosterone moderately increased lumbar bone density in men; the results on femoral neck bone density are inconclusive. Without bone fracture data, the available trials offer weak and indirect inferences about the clinical efficacy of testosterone on osteoporosis prevention and treatment in men.

PMID: 16720668

Rating: 1a

Tulder MW van, Cherkin DC, Berman B, Lao L, Koes BW. Acupuncture for low back pain (Cochrane Review). In: The Cochrane Library, Issue 2, 2002. Oxford: Update Software.

Institute for Research in Extramural Medicine, Vrije Universiteit, van der Boechorststraat 7, Amsterdam, Netherlands, 1081 BT. mw.van_tulder.emgo@med.vu.nl.

Abstract:
Background: Although low back pain is usually a self-limiting and benign disease that tends to improve spontaneously over time, a large variety of therapeutic interventions are available for the treatment of low back pain.
Objectives: The objective of this review was to assess the effects of acupuncture for the treatment of non-specific low back pain.
Search strategy: We searched the Cochrane Complementary Medicine Field trials register, the Cochrane Controlled Trials Register (1997, issue 1), Medline (1966 - 1996), Embase (1988 - 1996), Science Citation Index and reference lists of articles.
Selection criteria: Randomised trials of all types of acupuncture treatment that involves needling for subjects with non-specific low back pain.
Data collection and analysis: Two reviewers blinded with respect to authors, institution and journal independently assessed trial quality and extracted data.
Main results: Eleven trials were included. The methodological quality was low. Only two trials were of high quality. Three trials compared acupuncture to no treatment, which were of low methodological quality and provide conflicting evidence. There was moderate evidence from two trials that acupuncture is not more effective than trigger point injection or transcutaneous electrical nerve stimulation (TENS). There was limited evidence from eight trials that acupuncture is not more effective than placebo or sham acupuncture for the treatment of chronic low back pain.
Reviewers' conclusions: The evidence summarised in this systematic review does not indicate that acupuncture is effective for the treatment of back pain.
Publication Type: Meta-Analysis
PMID: 10796434
Tulder MW van, Esmail R, Bombardier C, Koes BW. Back schools for non-specific low back pain (Cochrane Review). In: The Cochrane Library, Issue 2, 2002. Oxford: Update Software.
Abstract:
Background: Since the introduction of the Swedish back school in 1980, the content of back schools has changed and appears to vary widely today. Back schools are frequently used in the treatment of low back pain patients.
Objectives: The objective of this systematic review was to assess the effects of back schools for patients with non-specific low back pain.
Search strategy: We searched the Medline and Embase databases up to December 1997 and the Cochrane Controlled Trials Register up to December 1998 if reported in English, Dutch, French or German. We also screened references given in relevant reviews and identified randomised trials.
Selection criteria: Only randomised trials that reported on any type of back school for non-specific low back pain were included.

Data collection and analysis: Two reviewers blinded with respect to authors, institution and journal independently extracted the data and assessed trial quality. Our preset "high quality" level was 6 or more out of 11 internal validity criteria with positive scores.
As data were statistically and clinically too heterogeneous, a qualitative review (best evidence synthesis) was performed. The evidence was classified into 4 levels (strong, moderate, limited or no evidence) taking into account the methodological quality of the studies.
Main results: Fifteen RCTs were included in our systematic review. Overall, the methodological quality was low. Only 3 trials were considered high quality. It was not possible to make relevant subgroup analyses for radiation versus no radiation or to have a relevant subgroup of studies reporting on acute low back pain only. The results indicate that there is moderate evidence that back schools have better short-term effects than other treatments for chronic low back pain, and that there is moderate evidence that back schools in an occupational setting are more effective compared to 'placebo' or waiting list controls.
Reviewers' conclusions: Back schools may be effective for patients with recurrent and chronic low back pain in occupational settings, but little is known about the cost-effectiveness of back schools.
Publication Type: Meta-Analysis
Tulder MW van, Malmivaara A, Esmail R, Koes BW. Exercise therapy for low back pain (Cochrane Review). In: The Cochrane Library, Issue 2, 2002. Oxford: Update Software.
Abstract:
Background: Exercise therapy is a widely used treatment for low back pain.
Objectives: The objective of this review was to assess the effectiveness of exercise therapy for low back pain with regard to pain intensity, functional status, overall improvement and return to work.
Search strategy: We searched the Cochrane Controlled Trials Register (1999, issue 1), MEDLINE (1966 - April 1999), EMBASE (1988 - September 1998), PsycLIT (from 1984 to April 1999) and reference lists of articles.
Selection criteria: Randomised trials of all types of exercise therapy for subjects with non-specific low back pain with or without radiation into the legs.
Data collection and analysis: Two reviewers independently extracted data and assessed trial quality. Because trials were considered heterogeneous with regard to study populations, interventions and outcomes, we decided not to perform a meta-analysis but to summarise the results using a rating system of four levels of evidence (strong, moderate, limited or no evidence).
Main results: 39 RCTs were identified. There is strong evidence that exercise therapy is not more effective than inactive or other active treatments it has been compared with for acute low back pain. There is conflicting evidence on the effectiveness of exercise therapy compared with inactive treatments for chronic low back pain. Exercise therapy was more effective than usual care by the general practitioner and equally effective as conventional physiotherapy for chronic low back pain.
Reviewers' conclusions: The evidence summarised in this systematic review does not indicate that specific exercises are effective for the treatment of acute low back pain. Exercises may be helpful for chronic low back pain patients to increase return to normal daily activities and work.
Publication Type: Meta-Analysis

Turk DC and Okifuji A. Assessment of Patients' Reporting of Pain: An Integrated Perspective. Lancet 1999;53:1784-88.

Department of Anesthesiology, University of Washington, Seattle 98195, USA.

Publication Type: Review

PMID: 10348007

Turner JA, Loeser JD, Bell KG, Spinal cord stimulation for chronic low back pain: a systematic literature synthesis, Neurosurgery. 1995 Dec;37(6):1088-95; discussion 1095-6

Department of Psychiatry, School of Medicine, University of Washington, Seattle, USA.

A systematic literature synthesis was performed to analyze the long-term risks and benefits of spinal cord stimulation for patients with failed back surgery syndrome. Relevant articles were identified through a MEDLINE search (January 1966-June 1994), bibliography reviews, searches of personal files, and literature supplied by a stimulator manufacturer. Two investigators independently reviewed each article to determine whether it met the following study inclusion criteria: 1) original data on return to work, pain, medication use, reoperations, functional disability, or stimulator use after permanent implantation of spinal cord stimulators in patients with chronic low back or leg pain despite previous back surgery; and 2) follow-up > or = 30 days for all patients. Articles were excluded if data from patients with other diagnoses were mixed with (and could not be separated from) data from patients with chronic low back or leg pain, or if their data were redundant with those reported in an included article. Articles written in languages other than English or French were excluded. Thirty-nine studies, all case studies, were analyzed. At follow-up (mean, 16 mo; range, 1-45 mo), an average of 59% of patients had > or = 50% pain relief (range, 15-100% of patients). Complications occurred in 42% of patients but were generally minor. It seems that approximately 50 to 60% of patients with failed back surgery syndrome report > 50% pain relief with the use of spinal cord stimulation at follow-up; the lack of randomized trials precludes conclusions concerning the effectiveness of spinal cord stimulation relative to other treatments, placebo, or no treatment.

Publication Types:
- Meta-Analysis

PMID: 8584149

Rating: 1c

Turner JA, Loeser JD, Deyo RA, Sanders SB. Spinal cord stimulation for patients with failed back surgery syndrome or complex regional pain syndrome: a systematic review of effectiveness and complications. Pain. 2004 Mar;108(1-2):137-47.

Department of Psychiatry and Behavioral Sciences, University of Washington School of Medicine, Seattle, WA 98195, USA. jturner@u.washington.edu

We conducted a systematic review of the literature on the effectiveness of spinal cord stimulation (SCS) in relieving pain and improving functioning for patients with failed back surgery syndrome and complex regional pain syndrome (CRPS). We also reviewed SCS complications. Literature searches yielded 583 articles, of which seven met the inclusion criteria for the review of SCS effectiveness, and 15 others met the criteria only for the review of SCS complications. Two authors independently extracted data from each article, and then resolved discrepancies by discussion. We identified only one randomized trial, which found that physical therapy (PT) plus SCS, compared with PT alone, had a statistically significant but clinically modest effect at 6 and 12 months in relieving pain among patients with CRPS. Similarly, six other studies of much lower methodological quality suggest mild to moderate improvement in pain with SCS. Pain relief with SCS appears to decrease over time. The one randomized trial suggested no benefits of SCS in improving patient functioning. Although life-threatening complications with SCS are rare, other adverse events are frequent. On average, 34% of patients who received a stimulator had an adverse occurrence. We conclude with suggestions for methodologically stronger studies to provide more definitive data regarding the effectiveness of SCS in relieving pain and improving functioning, short- and long-term, among patients with chronic pain syndromes.

Publication Types:
- Review
- Review Literature

PMID: 15109517

Rating: 1c

Turner JA, Sears JM, Loeser JD. Programmable intrathecal opioid delivery systems for chronic noncancer pain: a systematic review of effectiveness and complications. Clin J Pain. 2007;23:180-95.

Department of Psychiatry and Behavioral Sciences, University of Washington School of Medicine, Seattle, WA 98195, USA. jturner@u.washington.edu

OBJECTIVES: We conducted a systematic review of the literature on the effectiveness and complications of programmable intrathecal opioid and ziconotide drug delivery systems (IDDS) for patients with chronic noncancer pain. METHODS: We searched MEDLINE, Cochrane, and other

bibliographic databases to identify English-language journal articles reporting programmable IDDS complications or effects on pain or functioning. Additional study methodology criteria were applied for the effectiveness review. Two authors independently abstracted data from each included article. RESULTS: Six articles met the inclusion criteria for the effectiveness and complications reviews, and 4 others met the criteria only for the complications review; none were randomized trials or of ziconotide. All 6 articles reviewed for effectiveness reported improvement in pain and functioning on average among patients who received a permanent IDDS. Two articles reported the proportion of patients with > or =50% improvement in pain at 6 months (38%, 56%) and 2 at longer follow-ups (30%, 44%). Intrathecal morphine-equivalent doses increased over time. The most commonly reported permanent IDDS drug side effects were nausea/vomiting (mean rate weighted by sample size=33%), urinary retention (24%), and pruritus (26%). Catheter problems were also reported commonly. Rare but serious complications included intrathecal catheter tip granulomas. CONCLUSIONS: The studies reviewed found improvement in pain and functioning on average among patients with chronic noncancer pain who received permanent IDDS. However, their methodologic limitations preclude conclusions concerning the effectiveness of this technology long-term and as compared with other treatments. Drug side effects and hardware complications were common. Suggestions are made for methodologic improvements in future studies.

PMID: 17237668

Rating: 1c

Turturro MA, Paris PM, Larkin GL. Tramadol versus hydrocodone-acetaminophen in acute musculoskeletal pain: a randomized, double-blind clinical trial. Ann Emerg Med. 1998 Aug;32(2):139-43.

Department of Emergency Medicine, The Mercy Hospital of Pittsburgh, PA, USA. turturro+@pitt.edu

STUDY OBJECTIVE: To evaluate the efficacy of an oral tramadol preparation versus that of an oral hydrocodone-acetaminophen preparation in acute musculoskeletal pain. METHODS: A randomized, prospective, double-blind clinical trial was conducted in an urban teaching emergency department with an annual census of 41,000. Participants comprised a convenience sample of 68 adult ED patients with acute musculoskeletal pain caused by minor trauma. Thirty-three patients received tramadol (100 mg), and 35 patients received hydrocodone-acetaminophen (5 mg hydrocodone with 500 mg acetaminophen). The drugs were prepared in identical-appearing capsules. Pain was evaluated by a 100-mm visual analog scale (VAS) at baseline and at 30, 60, 90, 120, and 180 minutes after dosing. VAS scores were analyzed by 2-way repeated-measures ANOVA, and nominal data were analyzed by Fisher's exact test. RESULTS: Mean pain scores did not differ at baseline (tramadol, 68.3+/-21.8; hydrocodone-acetaminophen, 69.1+/-17.8; P=NS) but were significantly lower in the hydrocodone-acetaminophen group beginning at 30 minutes through 180 minutes. There were 6 dropouts as a result of reported inadequate analgesia, 3 in each group (P=NS). The discharge diagnoses and prevalence of side effects

did not differ significantly between groups. CONCLUSION: Tramadol provides inferior analgesia to hydrocodone-acetaminophen in ED patients with acute musculoskeletal pain.

PMID: 9701294

Rating: 2b

Tutak U, Doleys DM. Intrathecal infusion systems for treatment of chronic low back and leg pain of noncancer origin. South Med J. 1996 Mar;89(3):295-300.

Department of Anesthesiology and Pain Management Services, HealthSouth Medical Center, Birmingham, Ala, USA.

In this study, 26 patients (average age, 44.3 years) with chronic noncancer pain averaging 115 months' duration had implantation of an infusion pump with intrathecal catheter placement. In general, preservative-free morphine sulfate was used. Average follow-up was 23 months. Measurements of pain reduction, activity improvement, oral medication use, and overall satisfaction by patient, spouse, and clinic staff were obtained. Of the 26 patients, 20 noted a good or excellent outcome. Average daily dosage of intrathecal morphine increased over time by approximately sevenfold. Subjective pain levels decreased an average of 59%, and daily functioning increased 50%. No postoperative complications were noted, but 11 patients required additional surgery (9 for catheter complications). These data support chronic spinal opiate therapy as an option for safe and long-term management of noncancer pain.

Publication Type:
Clinical Trial

PMID: 8604459

Rating: 2c

Ubbink DT, Vermeulen H, Spinal cord stimulation for non-reconstructable chronic critical leg ischaemia, Cochrane Database Syst Rev. 2003;(3):CD004001.

Vascular Surgery, Academic Medical Centre Amsterdam, Meibergdreef 9, P.O. Box 22700, Amsterdam, Netherlands.

BACKGROUND: Patients suffering from inoperable chronic critical leg ischaemia (NR-CCLI), face amputation of the leg. Spinal cord stimulation (SCS) has been proposed as a helpful treatment in addition to standard conservative treatment. OBJECTIVES: To find evidence for an improvement of limb salvage, pain relief and clinical situation by means of SCS over conservative treatment alone.

SEARCH STRATEGY: The reviewers searched the Cochrane Peripheral Vascular Diseases Group Specialised Register, (last searched November 2002), the Cochrane Central Register of Controlled Trials (CENTRAL) (last searched Issue 4, 2002). Additional data were obtained from research institutes. SELECTION CRITERIA: Controlled studies comparing additional SCS with any form of conservative treatment in patients with NR-CCLI. DATA COLLECTION AND ANALYSIS: Two reviewers (DU, HV), independently assessed the quality of the studies and extracted the data. MAIN RESULTS: Six studies comprising nearly 450 patients were included. In general the quality of the studies was good, although none of them was blinded due to the nature of the intervention. Limb salvage after 12 months was significantly higher in the SCS group (RR 0.71, 95%CI: 0.56 to 0.90; RD -0.13, 95%CI: -0.22 to -0.04). Significant pain relief occurred in both treatment groups, but was more prominent in the SCS group, in which the patients required significantly less analgesics. In the SCS group significantly more patients reached Fontaine stage II than in the conservative group (RR 4.9, 95%CI: 2.0 to 11.9; RD 0.33, 95%CI: 0.19 to 0.47). Overall, no significantly different effect on ulcer healing was observed between the two treatments. Complications of SCS treatment consisted of implantation problems (9%; 95%CI: 4 to 15%) and changes in stimulation requiring reintervention, (15%; 95%CI: 10 to 20%). Infections of the lead or pulse generator pocket occurred less frequently (3%; 95%CI: 0 to 6%). The overall risk of complications of additional SCS treatment was 17%, 95%CI: 12 to 22%, indicating a number needed to harm of six (95%CI: 5 to 8). A cost comparison was made in only one study. The average overall costs at two years were 36,500 euros, in the SCS group and 28,600 euros, in the conservative group. The difference (7,900 euros) was significant (p<0.009). REVIEWER'S CONCLUSIONS: There is evidence to favour SCS over standard conservative treatment to improve limb salvage and clinical situation in patients with NR-CCLI. The benefits of SCS against the possible harm of relatively mild complications, and costs must be considered.

Publication Types:
- Review
- Review, Academic

PMID: 12917998

Rating: 1c

Uher EM, Vacariu G, Schneider B, Fialka V. Comparison of manual lymph drainage with physical therapy in complex regional pain syndrome, type I. A comparative randomized controlled therapy study. Wien Klin Wochenschr. 2000 Feb 11;112(3):133-7.

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Sympathetic blockage and physiotherapy are among the most effective treatment approaches for the complex regional pain syndrome (CRPS). It is important to institute the treatment as early as possible in

order to avoid major functional limitations of the affected limb. Unfortunately, there is a paucity of vigorously applied randomised or placebo-controlled trials for these therapeutic approaches. A prospective randomised study of 35 outpatient clinic patients with type I complex regional pain syndrome of the lower extremities lasting less than 6 months is described. One of two treatments, exercise alone or exercise in combination with manual lymph drainage, was applied for six weeks, three times a week, to the affected limb. Clinical and subjective parameters for pain, swelling, temperature, and range of motion were evaluated. Manual lymph drainage was chosen as adequate therapy for oedema reduction, whereas exercise was applied as standard therapy for contracture prophylaxis in reflex sympathetic dystrophy. Both groups were asked not to use analgesics but received extensive instructions for avoiding pain. Significant improvements in clinical parameters were observed in both groups, but no significant effect between treatment groups was found. Pain measurement alone with a verbal rating scale showed a tendency towards greater pain reduction in the group receiving lymph drainage. The results indicate that, during the first 6 months of complex regional pain syndrome type I, manual lymph drainage provides no additional benefit when applied in conjunction with an intensive exercise program.

PMID: 10729965

Rating: 2c

United Health Care. Technology Assessment: Intrathecal Pump for Chronic Nonmalignant Pain. Number 2005T0060C, Approved By Medical Technology Assessment Committee 11/17/2005.

An implantable infusion pump is covered when used to administer opioid drugs (e.g., morphine) intrathecally or epidurally for treatment of severe chronic intractable pain of malignant or nonmalignant origin in patients who have a life expectancy of at least 3 months, and who have proven unresponsive to less invasive medical therapy as determined by the following criteria:

- The patient's history must indicate that he/she would not respond adequately to noninvasive methods of pain control, such as systemic opioids (including attempts to eliminate physical and behavioral abnormalities which may cause an exaggerated reaction to pain); and
- A preliminary trial of intraspinal opioid drug administration must be undertaken with a temporary intrathecal/epidural catheter to substantiate adequately acceptable pain relief and degree of side effects (including effects on the activities of daily living) and patient acceptance.

Determinations may be made on coverage of other uses of implanted infusion pumps if the contractors medical staff verifies that:

- The drug is reasonable and necessary for the treatment of the individual patient;
- It is medically necessary that the drug be administered by an implanted infusion pump; and,
- The Food and Drug Administration (FDA)-approved labeling for the pump must specify that the drug being administered and the purpose for which it is administered is an indicated use for the pump.

The implantation of an infusion pump is contraindicated in the following patients:

- With a known allergy or hypersensitivity to the drug being used (e.g., oral baclofen, morphine, etc.);
- Who have an infection;
- Whose body size is insufficient to support the weight and bulk of the device; and,
- With other implanted programmable devices since crosstalk between devices may inadvertently change the prescription.

Payment may also be made for drugs necessary for the effective use of an implantable infusion pump as long as the drug being used with the pump is itself reasonable and necessary for the patients treatment.

Coverage Rationale

Intrathecal Administration of Analgesic Medication is proven when delivered by a FDA-approved implantable infusion pump and all of the following situations apply:

- Life expectancy of greater than 3 months
- Unsatisfactory response to less invasive methods of pain control, including oral opioid trials and inadequate response to therapy to eliminate physical and behavioral abnormalities, which may cause an exaggerated reaction to pain.
- Positive response to intrathecal drug administration prior to pump implantation.
- The pain is not primarily of psychological origin.
- Patient is not an active abuser of chemicals or chemically dependent.

Clinical Recommendations

Note: This section provides detailed information about the clinical intended use for the treatment that is the topic of this Technology Assessment. The detailed information provided in this section is NOT used to decide whether or not a service is paid for. Rather, it provides background information and rationale about the scientifically appropriate use of the treatment, for discussion purposes with providers. See "Coverage" section to determine what procedure(s) are covered/non-covered (i.e., paid for where such benefits are available). Clinical evidence supports the use of intrathecal pump for chronic nonmalignant pain when delivered by a FDA-approved implantable infusion pump and all of the following situations apply:

- Life expectancy of greater than 3 months
- Unsatisfactory response to less invasive methods of pain control, including oral opioid trials and inadequate response to therapy to eliminate physical and behavioral abnormalities, which may cause an exaggerated reaction to pain.
- Positive response to the drug in intrathecal administration drug prior to pump implantation.
- The pain is not primarily of psychological origin.
- Patient not an active abuser of chemicals or chemically dependent.
- An intrathecal pump should be used in caution in individuals with a past history of substance abuse.
- Implantation of intrathecal pumps should be done by a physician and in a facility with experience and expertise in this procedure.

Clinical Precautions
Before patients begin long-term spinal analgesic infusion, they must
1. Undergo a comprehensive psychological evaluation
2. Have knowledge of the risks involved
3. Have been reviewed for efficacy of a definitive surgical surgical treatment
4. Have been reviewed for efficacy of oral pharmacotherapy and
5. Complete the McGill Pain Questionnaire to provide a complete description of their pain.7

Use of implantable intrathecal infusion pumps is contraindicated in the following situations:
- Patients who have another implanted device, such as cardiac pacemaker (due to lack of research in patients with other implanted devices)
- Infection at the pump site
- Patients in whom the pump cannot be implanted less than 2.5 cm from the surface of the skin
- Patients who are not large enough to accept pump bulk and weight
- Patients who have a contraindication to the drug

Intrathecal administration of morphine may result in a number of short-term side effects, including pruritus, dysphoria,histamine release, sedation, respiratory depression, gastrointestinal hypomotility, impotence abnormal body temperature regulation, nausea and vomiting, urinary retention, and constipation.
These side effects are usually amenable to symptomatic treatment. A number of significant complications related to device failure or the implantation procedure have been reported in up to 39% of patients with implanted infusion pumps; these include cessation or change in therapy due to battery depletion or pump failure, pocket seroma, hematoma, erosion or infection, complete or partial catheter occlusion, kinking, breakage, leakage or disconnection, catheter dislodgement or migration, bleeding, arachnoiditis, meningitis, and spinal headache. Device-related complications may require an additional surgical procedure to replace or remove the pump. Although the development of tolerance to morphine can potentially limit the usefulness of intrathecal opioid therapy, most studies have shown only a gradual increase in effective dose, and many patients show no decrease in responsiveness to morphine over time. For those who do develop tolerance, pain can often be managed effectively by supplementation with oral nonnarcotic analgesics, or by use of intrathecal hydromorphone or hydromorphone plus bupivacaine combinations in place of morphine.

Rating: 6b

U.S. Department of Veterans Affairs, Technology Assessment Program (VATAP). Transcutaneous electrical nerve stimulation. Bibliography. Boston, MA: VATAP; November 2001.

The current medical literature is inconclusive regarding the effectiveness of
TENS units for pain management. The quality and scope of the evidence is generally
insufficient, or results with TENS were equivocal with respect to alternative modalities.

Rating: 8a

VA/DoD Clinical Practice Guideline Working Group, Veterans Health Administration, Department of Veterans Affairs and Health Affairs, Department of Defense (DoD). Management of Opioid Therapy for Chronic Pain. Washington, DC: Office of Quality and Performance publication 10Q-CPG/OT-03. August 2003

The Opioid Therapy for Chronic Pain Guideline was developed by and written for clinicians by the Department of Veterans Affairs, and Department of Defense, An experienced moderator facilitated the multidisciplinary working group that included anesthesiologists, internists, nurses, psychiatrists, substance use and addictions specialists, pharmacists, and expert consultants in the field of guideline and algorithm development. The guideline draws heavily from the Guideline for Medical Management for Chronic Non-Malignant Pain (Canadian Pain Society and the College of Physicians Ontario, Canada). The guideline integrates the recommendations developed by VHA's Medical Advisory Panel (MAP) and the Pharmacy Benefits Management Strategic Health Group.
GOALS/OBJECTIVES.
To promote evidence-based management of individuals with chronic pain
To identify the critical decision points in management of patients with chronic pain who are candidates for opioid therapy
To allow flexibility so that local policies or procedures, such as those regarding referrals to or consultation with substance use specialty, can be accommodated.
To decrease the development of complications
To improve patient outcome, i.e., reduce pain, decrease complications, increase functional status and enhance the quality of life.
MAJOR RECOMMENDATIONS
The guideline is presented in an algorithmic format that allows the practitioner to follow in the recognition and treatment of chronic pain with the use of opioids. Recommendations are made with regard to the intent to establish verifiable treatment objectives for patients with chronic pain that will lead to a reduction in pain, increase in function and quality of life

Rating: 6a

Van Buyten JP, Van Zundert J, Vueghs P, Vanduffel L, Efficacy of spinal cord stimulation: 10 years of experience in a pain centre in Belgium, Eur J Pain. 2001;5(3):299-307

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Spinal cord stimulation is a minimally invasive mode of treatment in the management of certain forms of chronic pain that do not respond to conventional pain therapy. Several authors have reported

encouraging findings with this technique. Over a 10-year period in a single centre, 254 patients were subjected to a trial period of spinal cord stimulation with an externalized pulse generator. Two hundred and seventeen of the patients showed satisfactory results justifying permanent implantation of a spinal cord stimulation system. In 1998, an independent physician invited 153 patients (155 pain cases), who still had the system in place and who could be contacted, for an interview. The aim of this study was to evaluate the efficacy of an implanted spinal cord stimulation system in terms of pain relief and quality of life and to assess the accuracy of the patient selection criteria. The results of this study demonstrate a high success rate as evaluated by the patients' own assessments--68% of the patients rated the result of the treatment as excellent to good after an average follow-up of almost 4 years. The resumption of work by 31% of patients who had been working before the onset of pain supports these positive findings. Copyright 2001 European Federation of Chapters of the International Association for the study of Pain.

Publication Types:
- Meta-Analysis

PMID: 11558985

Rating: 4b

Van Buyten, Jean-Pierre, MD, for The Itrel 3 Study Group, The Performance and Safety of an Implantable Spinal Cord Stimulation System in Patients with Chronic Pain: A 5-Year Study, Neuromodulation, Volume 6 Issue 2 Page 79 - April 2003

Reliability and ease of use of the Itrel 3 System (Medtronic Inc., Minneapolis, MN) were prospectively assessed over 5 years in patients with a range of pain syndromes (mainly low back and/or leg pain, or ischemic pain due to peripheral vascular disease). The longevity of the implantable pulse generator (IPG) battery, the frequency with which system settings were changed, and the ease of use of the EZ patient programmer were assessed. Data on adverse events, pain relief, and patient satisfaction with therapy were also collected. Following a screening procedure, 85 systems were implanted in 84 patients. Twenty-four patients were withdrawn prematurely and, in an additional 32 cases, end of battery life was reached before the end of the study. The survival curve for the IPG batteries showed that approximately 50% are expected to last up to the sixth year. No device failures or unanticipated device-related adverse events were reported. At least 90% of patients considered the EZ patient programmer easy to use. System settings were stable over time. The intensity and duration of pain were reduced significantly and patient satisfaction with therapy was high. We conclude that the Itrel 3 System performed well over 5 years and was easy to use. Its safety and effectiveness for the relief of chronic intractable pain of the trunk or limbs were also confirmed.

Note: Significant conflict of interest.

Rating: 4c

van Hilten BJ, van de Beek WJ, Hoff JI, Voormolen JH, Delhaas EM. Intrathecal baclofen for the treatment of dystonia in patients with reflex sympathetic dystrophy. N Engl J Med. 2000 Aug 31;343(9):625-30.

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BACKGROUND AND METHODS: Patients with reflex sympathetic dystrophy (also known as the complex regional pain syndrome) may have dystonia, which is often unresponsive to treatment. Some forms of dystonia respond to the intrathecal administration of baclofen, a specific gamma-aminobutyric acid-receptor (type B) agonist that inhibits sensory input to the neurons of the spinal cord. We evaluated this treatment in seven women who had reflex sympathetic dystrophy with multifocal or generalized tonic dystonia. First, we performed a double-blind, randomized, controlled crossover trial of bolus intrathecal injections of 25, 50, and 75 microg of baclofen and placebo. Changes in the severity of dystonia were assessed by the woman and by an investigator after each injection. In the second phase of the study, six of the women received a subcutaneous pump for continuous intrathecal administration of baclofen and were followed for 0.5 to 3 years. RESULTS: In six women, bolus injections of 50 and 75 microg of baclofen resulted in complete or partial resolution of focal dystonia of the hands but little improvement in dystonia of the legs. During continuous therapy, three women regained normal hand function, and two of these three women regained the ability to walk (one only indoors). In one woman who received continuous therapy, the pain and violent jerks disappeared and the dystonic posturing of the arm decreased. In two women the spasms or restlessness of the legs decreased, without any change in the dystonia. CONCLUSIONS: In some patients, the dystonia associated with reflex sympathetic dystrophy responds markedly to intrathecal baclofen.

Publication Types:
Clinical Trial
Randomized Controlled Trial

PMID: 10965009

Rating: 2c

van Lankveld W, Naring G, van't Pad Bosch P, et al. The Negative Effect of Decreasing the Level of Activity in Coping with Pain in Rheumatoid Arthritis: An Increase in Psychological Distress and Disease Impact. Journal of Behav Med 2000;23(4):377-391.

Abstract:

The objective of this study was to analyze the effect of coping with pain in rheumatoid arthritis (RA) on subsequent changes in psychological distress and disease impact. A sample of 109 randomly selected

RA patients was asked to participate in a longitudinal study. Patients were measured at baseline and after 3 years. Both measurements were completed in 80 patients. At each assessment the following variables were assessed: disease activity, pain, physical and psychological distress, disease impact, and coping. The relation between coping with pain at baseline and subsequent changes in psychological distress and disease impact was analyzed using stepwise regression. Disease status variables assessed at baseline and after 3 years were entered in the regression analysis as control variables. Results show that cognitive coping with pain at baseline was not related to subsequent changes in psychological distress or disease impact. On the other hand, behavioral pain coping assessed at baseline was related to subsequent changes in psychological distress and disease impact. "Decreasing activity" was related to an increase in self-reported psychological distress and disease impact after controlling for disease status at both assessments. It was concluded that cognitive pain coping did not predict any subsequent changes in psychological distress or disease impact. "Decreasing activity" as a behavioral pain coping style has a negative effect on subsequent changes in psychological distress and disease impact.

Publication Type: Case Control, 109 cases
van Tulder M, Koes B, Bouter L. Conservative Treatment of Acute and Chronic Nonspecific Low Back Pain: A Systematic Review of Randomized Controlled Trials of the Most Common Interventions. Spine 1997; 22(18):2128-2156. (Includes Letter to the Editor and Response in Spine 1998; 23(11): 1288-1291, and Table A: Content of 12 Multidisciplinary Interventions for the Treatment of Chronic Low Back Pain tested in 10 Randomised Controlled Trials
http://www.bmj.com/cgi/content/full/322/7301/1511/DC1.htm (accessed 8/2/01)).

Institute for Research in Extramural Medicine, Vrije Universiteit, Amsterdam, The Netherlands.

Abstract:

STUDY DESIGN: A systematic review of randomized controlled trials. OBJECTIVES: To assess the effectiveness of the most common conservative types of treatment for patients with acute and chronic nonspecific low back pain. SUMMARY OF BACKGROUND DATA: Many treatment options for acute and chronic low back pain are available, but little is known about the optimal treatment strategy. METHODS: A rating system was used to assess the strength of the evidence, based on the methodologic quality of the randomized controlled trials, the relevance of the outcome measures, and the consistency of the results. RESULTS: The number of randomized controlled trials identified varied widely with regard to the interventions involved. The scores ranged from 20 to 79 points for acute low back pain and from 19 to 79 points for chronic low back pain on a 100-point scale, indicating the overall poor quality of the trials. Overall, only 28 (35%) randomized controlled trials on acute low back pain and 20 (25%) on chronic low back pain had a methodologic score of 50 or more points, and were considered to be of high quality. Various methodologic flaws were identified. Strong evidence was found for the effectiveness of muscle relaxants and nonsteroidal anti-inflammatory drugs and the ineffectiveness of exercise therapy for acute low back pain; strong evidence also was found for the effectiveness of manipulation, back schools, and exercise therapy for chronic low back pain, especially for short-term

effects. CONCLUSIONS: The quality of the design, execution, and reporting of randomized controlled trials should be improved, to establish strong evidence for the effectiveness of the various therapeutic interventions for acute and chronic low back pain.

Publication Type: Meta-Analysis

PMID: 9322325

van Tulder MW, Scholten RJ, Koes BW, Deyo RA, Nonsteroidal anti-inflammatory drugs for low back pain: a systematic review within the framework of the Cochrane Collaboration Back Review Group, Spine. 2000 Oct 1;25(19):2501-13.

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STUDY DESIGN: A systematic review of randomized and double-blind controlled trials was performed. SUMMARY OF BACKGROUND DATA: Nonsteroidal anti-inflammatory drugs are the most frequently prescribed medications worldwide and are widely used for patients with low back pain. OBJECTIVES: To assess the effects of nonsteroidal anti-inflammatory drugs in the treatment of nonspecific low back pain with or without radiation, and to assess which type of nonsteroidal anti-inflammatory drug is most effective. METHODS: For this study, the Cochrane Controlled Trials Register, Medline and Embase, and reference lists of articles were searched. Two reviewers blinded with respect to authors, institution, and journal independently extracted data and assessed the methodologic quality of the studies. If data were considered clinically homogeneous, a meta-analysis was performed. If data were considered clinically heterogeneous, a qualitative analysis was performed using a rating system with four levels of evidence: strong, moderate, limited, and no evidence. RESULTS: This review involved 51 trials and 6057 patients. Of these trials, 16 (31%) were of high quality. The pooled relative risk for global improvement after 1 week was 1.24 (95% confidence interval [CI] = 1.10-1.41), and for additional analgesic use was 1.29 (95% CI = 1.05-1.57), indicating a statistically significant but small effect in favor of nonsteroidal anti-inflammatory drugs as compared with a placebo. The results of the qualitative analysis showed that there is conflicting evidence (Level 3) that nonsteroidal anti-inflammatory drugs are more effective than paracetamol for acute low back pain, and that there is moderate evidence (Level 2) that nonsteroidal anti-inflammatory drugs are not more effective than other drugs for acute low back pain. There is strong evidence (Level 1) that various types of nonsteroidal anti-inflammatory drugs are equally effective for acute low back pain. CONCLUSIONS: The evidence from the 51 trials included in this review suggests that nonsteroidal anti-inflammatory drugs are effective for short-term symptomatic relief in patients with acute low back pain. Furthermore, there does not seem to be a specific type of nonsteroidal anti-inflammatory drug that is clearly more effective than others. Sufficient evidence on chronic low back pain still is lacking.

Publication Types:

- Review
- Review, Academic

PMID: 11013503

Rating: 1a

van Tulder MW, Koes B, Malmivaara A. Outcome of non-invasive treatment modalities on back pain: an evidence-based review. Eur Spine J. 2006 Jan;15 Suppl 1:S64-81.

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At present, there is an increasing international trend towards evidence-based health care. The field of low back pain (LBP) research in primary care is an excellent example of evidence-based health care because there is a huge body of evidence from randomized trials. These trials have been summarized in a large number of systematic reviews. This paper summarizes the best available evidence from systematic reviews conducted within the framework of the Cochrane Back Review Group on non-invasive treatments for non-specific LBP. Data were gathered from the latest Cochrane Database of Systematic Reviews 2005, Issue 2. The Cochrane reviews were updated with additional trials, if available. Traditional NSAIDs, muscle relaxants, and advice to stay active are effective for short-term pain relief in acute LBP. Advice to stay active is also effective for long-term improvement of function in acute LBP. In chronic LBP, various interventions are effective for short-term pain relief, i.e. antidepressants, COX2 inhibitors, back schools, progressive relaxation, cognitive-respondent treatment, exercise therapy, and intensive multidisciplinary treatment. Several treatments are also effective for short-term improvement of function in chronic LBP, namely COX2 inhibitors, back schools, progressive relaxation, exercise therapy, and multidisciplinary treatment. There is no evidence that any of these interventions provides long-term effects on pain and function. Also, many trials showed methodological weaknesses, effects are compared to placebo, no treatment or waiting list controls, and effect sizes are small. Future trials should meet current quality standards and have adequate sample size.

PMID: 16320031

Rating: 1b

van Tulder MW, Touray T, Furlan AD, Solway S, Bouter LM; Cochrane Back Review Group. Muscle relaxants for nonspecific low back pain: a systematic review within the framework of the Cochrane collaboration. Spine. 2003;28:1978-92.

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STUDY DESIGN: A systematic review of randomized and/or double-blinded controlled trials. SUMMARY OF BACKGROUND DATA: The use of muscle relaxants in the management of nonspecific low back pain is controversial. It is not clear if they are effective, and concerns have been raised about the potential adverse effects involved. OBJECTIVES: The aim of this review was to determine if muscle relaxants are effective in the treatment of nonspecific low back pain. METHODS: A computer-assisted search of the Cochrane Library (Issue 2, 2002), MEDLINE (1966 up to October 2001), and EMBASE (1988 up to October 2001) was carried out. These databases were searched using the algorithm recommended by the Cochrane Back Review Group. References cited in the identified articles and other relevant literature were screened. Randomized and/or double-blinded controlled trials, involving patients diagnosed with nonspecific low back pain, treated with muscle relaxants as monotherapy or in combination with other therapeutic methods, were included for review. Two reviewers independently carried out the methodologic quality assessment and data extraction of the trials. The analysis comprised not only a quantitative analysis (statistical pooling) but also a qualitative analysis ("best evidence synthesis"). This involved the appraisal of the strength of evidence for various conclusions using a rating system based on the quality and outcomes of the studies included. Evidence was classified as "strong," "moderate," "limited," "conflicting," or "no" evidence. RESULTS: Thirty trials met the inclusion criteria. Twenty-three trials (77%) were of high quality; 24 trials (80%) were on acute low back pain. Four trials studied benzodiazepines, 11 nonbenzodiazepines, and 2 antispasticity muscle relaxants in comparison with placebo. Results showed that there is strong evidence that any of these muscle relaxants are more effective than placebo for patients with acute low back pain on short-term pain relief. The pooled relative risk for nonbenzodiazepines versus placebo after 2 to 4 days was 0.80 (95% confidence interval: 0.71 to 0.89) for pain relief and 0.49 (95% confidence interval: 0.25 to 0.95) for global efficacy. Adverse events, however, with a relative risk of 1.50 (95% confidence interval: 1.14 to 1.98) were significantly more prevalent in patients receiving muscle relaxants and especially the central nervous system adverse effects (relative risk 2.04; 95% confidence interval: 1.23 to 3.37). The various muscle relaxants were found to be similar in performance. CONCLUSIONS: Muscle relaxants are effective in the management of nonspecific low back pain, but the adverse effects require that they be used with caution. Trials are needed that evaluate if muscle relaxants are more effective than analgesics or nonsteroidal anti-inflammatory drugs.

PMID 12973146

Rating: 1a

Varrassi G, Paladini A, Marinangeli F, Racz G. Neural modulation by blocks and infusions. Pain Pract. 2006;6:34-8.

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Neural blockade is widely used in clinical practice to alleviate acute or chronic pain, including neuropathic pain. However, to date there is little controlled evidence to confirm the efficacy of nerve blocks in neuropathic pain. The most common indication for nerve blocks, especially sympathetic blockade, is complex regional pain syndrome, in which success rates of up to 38% have been achieved, depending on the type of the block used. Greater efficacy has been achieved by combining a nerve block with patient-controlled analgesia. Sympathectomy is recommended for the treatment of neuropathic pain only after careful consideration of its usefulness, effectiveness, and risk of adverse effects. Current evidence and clinical experience suggest that neural blockade could be a useful adjunct in the management of refractory neuropathic pain, but further well-controlled studies would be of great benefit to support this type of therapy.

PMID: 17309707

Rating: 5c

Varenna M, Zucchi F, Ghiringhelli D, Binelli L, Bevilacqua M, Bettica P, Sinigaglia L. Intravenous Clodronate in the Treatment of Reflex Sympathetic Dystrophy Syndrome. A Randomized, Double Blind, Placebo Controlled Study. J Rheumatol 2000;27:1477-83.

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Abstract:

OBJECTIVE: To evaluate the efficacy of intravenous (i.v.) clodronate in patients with reflex sympathetic dystrophy syndrome (RSDS) and to assess the urinary excretion of type I collagen crosslinked N-telopeptide (NTx) before and after the treatment. METHODS: Thirty-two patients with RSDS were randomized to receive either i.v. clodronate 300 mg daily for 10 consecutive days or placebo. Forty days later, the placebo treated patients received the clodronate treatment. Outcome measures included as a primary endpoint the visual analog scale of pain (VAS, range 0-100); secondary endpoints were a clinical global assessment (CGA, range 0-3) and an efficacy verbal score (EVS, range 0-3). Clinical and biochemical assessments were performed before the treatment, 40 (T40), 90 (T90), and 180 (T180) days later. RESULTS: At T40 the 15 patients randomized to clodronate treatment showed significant decreases of VAS and CGA ($p = 0.002$, $p = 0.001$, respectively). Compared with the placebo group (17 patients), significant differences were found in all clinical variables (VAS: $p = 0.001$; CGA: $p = 0.001$; EVS: $p<0.0001$). A further clinical improvement was observed throughout the study. Pooling the results of all 32 patients after clodronate treatment, at T180 the overall percentage decrease of VAS was 93.2+/-15.6%, with 30 patients significantly improved or asymptomatic. Significant inverse correlations between baseline NTx values and decreases of VAS were found at T90 ($p = 0.03$) and T180 ($p = 0.01$). No adverse events related to treatment occurred. CONCLUSION: A 10 day i.v. clodronate course is better than placebo and effective in the treatment of RSDS. NTx seems to be a predictive factor for clodronate efficacy.

Conclusion:

IV clodronate is better than placebo and induces lasting improvement of RSD

Publication Type: RCT, 32 cases

PMID: 10852274

Villavicencio AT, Leveque JC, Rubin L, Bulsara K, Gorecki JP, Laminectomy versus percutaneous electrode placement for spinal cord stimulation, Neurosurgery. 2000 Feb;46(2):399-405; discussion 405-6.

Division of Neurosurgery, Duke University Medical Center, Durham, North Carolina 27712, USA.

OBJECTIVE: The purpose of this study was to compare the long-term effectiveness of spinal cord stimulation using laminectomy-style electrodes versus that using percutaneously implanted electrodes. METHODS: Forty-one patients underwent an initial trial period of spinal cord stimulation with temporary electrodes at Duke Medical Center between December 1992 and January 1998. A permanent system was implanted if trial stimulation reduced the patient's pain by more than 50%. Median long-term follow-up after permanent electrode placement was 34 months (range, 6-66 mo). Severity of pain was determined postoperatively by a disinterested third party using a visual analog scale and a modified outcome scale. RESULTS: Twenty-seven (66%) of the 41 patients participating in the trial had permanent electrodes placed. Visual analog scores decreased an average of 4.6 among patients in whom electrodes were placed via laminectomy in the thoracic region (two-tailed t test, $P < 0.0001$). Patients who underwent percutaneous placement of thoracic electrodes had an average decrease of 3.1 in their visual analog scores (two-tailed t test, $P < 0.001$). Electrodes placed through laminectomy furnished significantly greater long-term pain relief than did those placed percutaneously, as measured by a four-tier outcome grading scale ($P = 0.02$). CONCLUSION: Spinal cord stimulation is an effective treatment for chronic pain in the lower back and lower extremities that is refractory to conservative therapy. Electrodes placed via laminectomy in the thoracic region appear to be associated with significantly better long-term effectiveness than are electrodes placed percutaneously.

PMID: 10690729

Rating: 3c

Vlaeyen JW, Haazen IW, Schuerman JA, Kole-Snijders AM, van Eek H. Behavioural rehabilitation of chronic low back pain: comparison of an operant treatment, an operant-cognitive treatment and an operant-respondent treatment. Br J Clin Psychol. 1995 Feb;34 (Pt 1):95-118.

Institute for Rehabilitation Research, Hoensbroek, The Netherlands.

Seventy-one chronic low back pain patients were assigned to one of three behavioural rehabilitation treatments or a waiting-list condition. The first intervention consisted of an operant treatment, aimed at increasing health behaviours and activity levels and at reducing pain and illness behaviours. In the second intervention, a cognitive treatment, aimed at the reinterpretation of catastrophizing pain cognitions and at enhancing self-control, was combined with an operant treatment. The third intervention consisted of the combination of the operant approach and a respondent treatment. During the respondent treatment, patients were taught to decrease muscle tension levels, using the 'applied relaxation' technique supported by EMG-biofeedback and graded exposure to tension-eliciting situations. A repeated measurements design included observer rating of pain behaviours, observer ratings of mood, self-reported depression, residual health behaviours, pain cognitions and experienced pain intensity. Follow-up assessment occurred at six months and one year after termination of treatment. Results suggest that, for the sample as a whole, improvements are found on measures of pain behaviours, health behaviours, pain cognitions and affective distress and that these improvements are maintained at six months and one year follow-up. During the treatment the three treatment groups improved significantly more than the waiting-list control group on most of the measures. Further, the results of this study provide evidence that the operant-cognitive and operant-respondent conditions are more efficacious in decreasing pain behaviours and in increasing health behaviours and efficacy expectations than operant treatment alone. This differential effect among the conditions is maintained at follow-up. Patients who received the OC and OR treatments catastrophize less than OP patients, and OC patients showed better scores on outcome-efficacy than OR patients. In general, the results suggest that behavioural rehabilitation programmes for chronic low back pain are effective and that the effects of an operant treatment are magnified when self-control techniques are added.

PMID: 7757046

Rating: 2c

Voerman GE, Vollenbroek-Hutten MM, Hermens HJ. Changes in pain, disability, and muscle activation patterns in chronic whiplash patients after ambulant myofeedback training. Clin J Pain. 2006 Sep;22(7):656-63.

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OBJECTIVE: The aim of this exploratory study was to investigate changes in pain, disability, and muscle activation patterns in patients with chronic whiplash-associated disorder (WAD) after 4 weeks of myofeedback training. METHODS: Eleven WAD patients received ambulatory myofeedback training, during which upper trapezius muscle activation and relaxation were continuously recorded and processed for 4 weeks. Feedback was provided when muscle relaxation was insufficient. Pain in neck,

shoulders, and upper back (Visual Analogue Scale), disability (Neck Disability Index), and muscle activation patterns during rest, typing, and stress tasks (surface electromyography) were assessed before and after the 4 weeks of training. RESULTS: Pain intensity decreased after 4 weeks of training. Clinically relevant changes were found with regard to pain in the neck and upper back region (55% of the patients), right shoulder (64%), and left shoulder (18%). A trend for decreased disability was found which was clinically relevant in 36% of the patients. A remarkable reduction was found in the Neck Disability Index items concerning headache and lifting weights. Overall, muscle activation was lower and muscle relaxation was higher after the training period with the largest differences during rest. Clinically relevant changes in surface electromyography parameters were found in a minority of patients. CONCLUSION: Four weeks of ambulant training may be beneficial in reducing pain and disability levels and normalizing muscle activation patterns in chronic WAD patients. A randomized-controlled study is recommended to further explore the effects of myofeedback training.

PMID: 16926582

Rating: 4c
Waara-Wolleat KL, Hildebrand KR, Stewart GR. A review of intrathecal fentanyl and sufentanil for the treatment of chronic pain. Pain Med. 2006;7:251-9.

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Intrathecal infusion of morphine using implantable pumps is an accepted practice for long-term management of chronic pain. Despite clinical benefit, development of tolerance and side-effects associated with intrathecal morphine has prompted investigators to explore alternative opioids such as the potent anilinopiperidine analogs, fentanyl, and sufentanil. Relevant preclinical and clinical literature from the MEDLINE database was used primarily for this review. In vitro, both compounds are stable in solution, but studies have not been conducted using implantable pumps under simulated use conditions (e.g., long-term stability at body temperature). Preclinical studies of limited duration have demonstrated efficacy, but safety-toxicology studies have been limited to intermittent boluses of sufentanil only. Few clinical reports on the use of intrathecal sufentanil or fentanyl for chronic pain are available. Although results confirm potency and efficacy with intrathecal administration, further studies are needed to support the long-term use of either opioid in chronic pain management.

PMID: 16712626

Rating: 5b

Wafford KA, Ebert B. Emerging anti-insomnia drugs: tackling sleeplessness and the quality of wake time. Nat Rev Drug Discov. 2008;7:530-40. Epub 2008 May 23.

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Sleep is essential for our physical and mental well being. However, when novel hypnotic drugs are developed, the focus tends to be on the marginal and statistically significant increase in minutes slept during the night instead of the effects on the quality of wakefulness. Recent research on the mechanisms underlying sleep and the control of the sleep-wake cycle has the potential to aid the development of novel hypnotic drugs; however, this potential has not yet been realized. Here, we review the current understanding of how hypnotic drugs act, and discuss how new, more effective drugs and treatment strategies for insomnia might be achieved by taking into consideration the daytime consequences of disrupted sleep.

Rating: 5c

Warfield CA, Bajwa ZH, editors. Principles and practice of pain medicine. 2nd ed. New York: McGraw-Hill; 2004.

This major, North American text is aimed at the pain specialist. The editors have brought together many experts and produced a concise textbook.

Rating: 9a

Waknine Y. Duloxetine HCl (Cymbalta) Approved for Management of Fibromyalgia. Medscape, LLC. Release Date: June 19, 2008.

June 19, 2008 — The US Food and Drug Administration (FDA) has approved duloxetine HCl delayed-release capsules for the management of fibromyalgia. Previously, only pregabalin (Lyrica; Pfizer, Inc) was approved to treat this painful condition. On June 13, the FDA approved a new indication for duloxetine HCl delayed-release capsules (Cymbalta; Eli Lilly and Company), allowing their use for the management of fibromyalgia in adults. Approximately 2% to 4% of the US population is affected by fibromyalgia, which occurs primarily in women and is characterized by chronic widespread muscular pain, fatigue, and tenderness. Although there is no known cure for the condition, its symptoms can be managed with a multidimensional approach that includes patient education, medication, and lifestyle changes. The approval was based on data from 2 pivotal double-blind, fixed-dose, randomized, phase-3 clinical trials of patients meeting the American College of Rheumatology criteria for primary fibromyalgia, including a history of widespread pain for 3 months and pain present at 11 or more of the 18 specific tender point sites. Study 1 enrolled women only (n = 354) and was 3 months in duration; study 2 enrolled both men and women (n = 520) for a period of 6 months. Both studies compared duloxetine 60 mg or 120 mg once daily (as divided doses in study 1 and a single dose in study 2) with placebo; study 2 also evaluated the benefit of duloxetine therapy at 20 mg/day vs placebo during the initial 3 months of the 6-month study. The mean baseline pain score was 6.5 on an 11-point Brief Pain Inventory (BPI) 24-hour average pain scale ranging from 0 (no pain) to 10 (worst possible pain); approximately 25% of participants had a comorbid diagnosis of major depressive disorder. For the first

study, results at 3 months showed that treatment with duloxetine 60 mg/day yielded clinically significant pain relief, defined as a 30% or greater reduction in BPI scores from baseline (55% vs placebo, 33%; P < .001). No additional benefit was observed in patients receiving 120 mg vs 60 mg of duloxetine daily (55% vs 54%). These findings were supported by those of the second study, which showed that duloxetine 60 and 120 mg/day was similarly effective for achieving a 30% or greater reduction in BPI scores from baseline at 3 months (50.7% and 52.1% vs placebo, 36%; P = .016 and P = .008) and for achieving a 50% or greater decrease at 6 months (32.6% and 35.9% vs 21.6%, P = .045 and P = .0009). The FDA notes that although duloxetine was effective for reducing pain in patients with and without major depressive disorder, the degree of pain relief may have been greater in those with comorbid depression. Benefits were also observed with respect to secondary endpoints, which included improvement from baseline as evaluated with the Patient Global Impression of Improvement scale and the Fibromyalgia Impact Questionnaire total score, which is used to assess and evaluate disease impact on health and functioning. Neither study demonstrated an additional benefit for the 120-mg vs the 60-mg daily dose of duloxetine, and the higher dose was associated with a significantly increased risk for adverse events leading to discontinuation of treatment (study 2, 26.5% vs 15.3%; placebo, 13.2%). Therefore, the recommended dose for duloxetine is 60 mg administered once daily. Treatment should be initiated at 30 mg once daily for 1 week to allow patients to adjust to the medication before increasing to 60-mg/day dosing. In clinical studies, some patients experienced a decrease in pain as early as week 1, which persisted throughout the study. According to data pooled from 4 studies of fibromyalgia, the most commonly observed adverse events in duloxetine-treated patients (incidence ≥ 5% and occurring at least twice as often vs placebo) were similar to that observed in other studies and included nausea (29% vs placebo, 11%), dry mouth (18% vs 5%), constipation (15% vs 4%), decreased appetite (11% vs 2%), somnolence (11% vs 3%), hyperhidrosis (7% vs 1%), and agitation (6% vs 2%). Duloxetine previously was approved for the treatment of diabetic peripheral neuropathic pain, depression, and generalized anxiety disorder.
Pearls for Practice: Data from 2 large placebo-controlled clinical trials have revealed that more than 51% to 55% of patients receiving duloxetine HCl 60 mg/day achieved a 30% or greater reduction in pain at 3 months; 32.6% of patients had a 50% or greater reduction in pain at 6 months. Significant benefit was also observed in well-being and functioning. Treatment of fibromyalgia with duloxetine should be initiated at 30 mg/day for 1 week and then uptitrated to the recommended 60-mg dose. The 120-mg/day dose does not confer added benefit and increases the risk for adverse events and discontinuation of treatment. Some patients may respond to treatment during the first week.

Rating: 5b

Walach H, Guthlin C, Konig M. Efficacy of massage therapy in chronic pain: a pragmatic randomized trial. J Altern Complement Med. 2003 Dec;9(6):837-46.

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BACKGROUND: Although classic massage is used widely in Germany and elsewhere for treating chronic pain conditions, there are no randomized controlled trials (RCT). DESIGN: Pragmatic RCT of classic massage compared to standard medical care (SMC) in chronic pain conditions of back, neck, shoulders, head and limbs. OUTCOME MEASURE: Pain rating (nine-point Likert-scale; predefined main outcome criterion) at pretreatment, post-treatment, and 3 month follow-up, as well as pain adjective list, depression, anxiety, mood, and body concept. RESULTS: Because of political and organizational problems, only 29 patients were randomized, 19 to receive massage, 10 to SMC. Pain improved significantly in both groups, but only in the massage group was it still significantly improved at follow-up. Depression and anxiety were improved significantly by both treatments, yet only in the massage group maintained at follow-up. CONCLUSION: Despite its limitation resulting from problems with numbers and randomization this study shows that massage can be at least as effective as SMC in chronic pain syndromes. Relative changes are equal, but tend to last longer and to generalize more into psychologic domains. Because this is a pilot study, the results need replication, but our experiences might be useful for other researchers.

Publication Types:
Clinical Trial
Randomized Controlled Trial

PMID: 14736355

Rating: 2c

Wallace M, Schulteis G, Atkinson JH, Wolfson T, Lazzaretto D, Bentley H, Gouaux B, Abramson I. Dose-dependent Effects of Smoked Cannabis on Capsaicin-induced Pain and Hyperalgesia in Healthy Volunteers. Anesthesiology. 107(5):785-796, November 2007.

Background: Although the preclinical literature suggests that cannabinoids produce antinociception and antihyperalgesic effects, efficacy in the human pain state remains unclear. Using a human experimental pain model, the authors hypothesized that inhaled cannabis would reduce the pain and hyperalgesia induced by intradermal capsaicin. Methods: In a randomized, double-blinded, placebo-controlled, crossover trial in 15 healthy volunteers, the authors evaluated concentration-response effects of low-, medium-, and high-dose smoked cannabis (respectively 2%, 4%, and 8% 9-[delta]-tetrahydrocannabinol by weight) on pain and cutaneous hyperalgesia induced by intradermal capsaicin. Capsaicin was injected into opposite forearms 5 and 45 min after drug exposure, and pain, hyperalgesia, tetrahydrocannabinol plasma levels, and side effects were assessed. Results: Five minutes after cannabis exposure, there was no effect on capsaicin-induced pain at any dose. By 45 min after cannabis exposure, however, there was a significant decrease in capsaicin-induced pain with the medium dose and a significant increase in capsaicin-induced pain with the high dose. There was no effect seen with the low dose, nor was there an effect on the area of hyperalgesia at any dose. Significant negative correlations between pain perception and plasma [delta]-9-tetrahydrocannabinol levels were found after adjusting for the overall dose effects.

There was no significant difference in performance on the neuropsychological tests. Conclusions: This study suggests that there is a window of modest analgesia for smoked cannabis, with lower doses decreasing pain and higher doses increasing pain.

Rating: 2c

October 31, 2007 — One of the first dose-response studies of cannabis in humans has found a window of efficacy within which healthy volunteers experienced relief from experimentally induced pain. But although mid-range doses provided some pain relief, high doses appeared to exacerbate pain."This study suggests that there is a window of modest analgesia for smoked cannabis, with lower doses decreasing pain and higher doses increasing pain," the researchers, with first author Mark Wallace, MD, professor of anesthesiology at the University of California, San Diego (UCSD), conclude in their report. The study included 15 male and female occasional pot smokers (they had been exposed to cannabis in the past 6 months but not in the past 30 days). In 4 separate sessions, the volunteers randomly smoked a low-, medium-, and high-dose marijuana cigarette (2%, 4%, and 8% respectively of delta-9-tetrahydrocannabinol [THC] by weight) or a placebo cigarette that smelled and tasted like marijuana but did not contain THC. Five minutes after subjects smoked each cigarette, Dr. Wallace injected capsaicin, a derivative of hot chili pepper, under the skin of each volunteer's right arm. Capsaicin mimics neuropathic pain — a brief, intense pain followed by a longer-lasting secondary pain — that plagues many patients with HIV/AIDS, diabetes, and shingles. He then took blood samples, pain reports (spontaneous and elicited), and other data from the subjects. Forty-five minutes after smoking, subjects were "stung" again on their left arm and the same information was collected. There was no effect on pain levels 5 minutes after smoking, regardless of the dose, although patients tended to report a fair degree of "highness," said Dr. Wallace, who is also program director for the UCSD Center for Pain Medicine. After 45 minutes, volunteers reported lower levels of highness and varying degrees of pain relief. "The low dose had no effect — there was no difference from placebo, while the medium dose reduced their pain and the high dose increased their pain," he told Medscape Neurology & Neurosurgery. Dr. Wallace said he is not sure why the volunteers reported more pain with higher THC blood levels. "Maybe the high doses were causing a little more paranoia," which counteracted the analgesic effects, he said. Or the cannabis may contain a compound not measured in the study that led to pain at the higher dose. Dr. Wallace also did not know whether the pain relief would have eventually kicked in with the high dose, because subjects were tested only to 45 minutes. Researchers for this study also looked at neuropsychological functioning in the 15 subjects. "Although patients were reporting highness, there were no significant effects on their neurocognitive functioning," said Dr. Wallace. This, he noted, would be an advantage over currently marketed pain relievers that have mind-altering effects or, like opioids, come with a myriad of problems related to abuse, dependence, and withdrawal. For this and other reasons, Dr. Wallace said, cannabis is a valuable tool in modern pain control. But he was critical of the current system that allows cannabis for medicinal purposes but does not involve pharmacists in dispensing it. "Cannabis is a medicine that should be in the hands of a pharmacist," said Dr. Wallace, "I'm not comfortable prescribing it, not because I think it's harmful or don't think it's useful, but I wouldn't prescribe any medication if I didn't know where it came from." The cannabis that Dr.

Wallace used in his study came from government sources. "I knew exactly what I was giving them. I knew the concentration of each cigarette, the exact dose," he said.

Walsh JK, Krystal AD, Amato DA, Rubens R, Caron J, Wessel TC, Schaefer K, Roach J, Wallenstein G, Roth T. Nightly treatment of primary insomnia with eszopiclone for six months: effect on sleep, quality of life, and work limitations. Sleep. 2007;30:959-68.

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STUDY OBJECTIVES: To evaluate 6 months' eszopiclone treatment upon patient-reported sleep, fatigue and sleepiness, insomnia severity, quality of life, and work limitations. DESIGN: Randomized, double blind, controlled clinical trial. SETTING: 54 research sites in the U.S. PATIENTS: 830 primary insomnia patients who reported mean nightly total sleep time (TST) < or = 6.5 hours/night and/or mean nightly sleep latency (SL) >30 min. INTERVENTION: Eszopiclone 3 mg or matching placebo. MEASUREMENTS: Patient-reported sleep measures, Insomnia Severity Index, Medical Outcomes Study Short-Form Health Survey (SF-36), Work Limitations Questionnaire, and other assessments measured during baseline, treatment Months 1-6, and 2 weeks following discontinuation of treatment. RESULTS: Patient-reported sleep and daytime function were improved more with eszopiclone than with placebo at all months (P <0.001). Eszopiclone reduced Insomnia Severity Index scores to below clinically meaningful levels for 50% of patients (vs 19% with placebo; P <0.05) at Month 6. SF-36 domains of Physical Functioning, Vitality, and Social Functioning were improved with eszopiclone vs placebo for the Month 1-6 average (P < 0.05). Similarly, improvements were observed for all domains of the Work Limitations Questionnaire with eszopiclone vs placebo for the Month 1-6 average (P <0.05). CONCLUSIONS: This is the first placebo-controlled investigation to demonstrate that long-term nightly pharmacologic treatment of primary insomnia with any hypnotic enhanced quality of life, reduced work limitations, and reduced global insomnia severity, in addition to improving patient-reported sleep variables.

Rating: 2b

Washington State Department of Labor and Industries. Guidelines for outpatient prescription of oral opioids for injured workers with chronic, noncancer pain. Olympia (WA): Washington State Department of Labor and Industries; 2002 Aug.

Guidelines for Outpatient Prescription of Oral Opioids for Injured Workers with Chronic, Noncancer Pain

1. How do I assess whether a formal trial of opioids for chronic pain is indicated?
You should address several questions to decide if a formal trial of opioids for chronic pain is indicated:

1) Are there reasonable alternatives other than opioids? 2) Is the patient likely to improve with opioids? and 3) Is the patient likely to abuse opioids or have other adverse outcomes? Beyond 2-4 months of acute/subacute opioid use, the following assessment is strongly recommended:
a) Perform a baseline history and physical, including pain history and the impact of pain on the patient, a complete exam, review of previous diagnostic and therapeutic results and an assessment of coexisting conditions.
b) Obtain relevant baseline clinical or laboratory studies and/or urine drug screen, as indicated.
c) Based on the results of your assessment, identify the pain diagnosis. (See Table 1.)
d) Baseline pain and functional assessments should be documented.
e) Assess the worker's ability to participate in a return-to-work program, for example, workhardening and vocational services.
f) Assess likelihood the patient can be weaned from
opioids in the event there is no improvement in pain and function.
g) Decide whether you have the expertise to conduct a formal opioid trial for chronic pain. If not, make an appropriate referral.

2. How should I manage a formal trial of opioids for chronic pain?
The following general parameters should guide the attending physician's plan of care:
a) Second opinion: Consider a second opinion before planning the trial of opioids to assess whether a trial is indicated, and if so, how it should be conducted.
b) Documentation: Using the one-page Opioid Progress Report Supplement will also serve as a step-by-step guide to remind you and your patient to address a number of key issues, such as the treatment agreement, screening for addiction, return-to-work efforts, assessment of functional progress, consultations, medication history, treatment plan, etc.
c) Contingency plan: Plan ahead of time for both of these possibilities:
1) The patient needs to be weaned from opioids because there has been no improvement in pain and function.
2) Continuation of opioids beyond maximum medical improvement is indicated, and other forms of payment for the medications will be needed.
d) Treatment agreement: You and your patient should together sign a treatment agreement that outlines: the risks and benefits of opioid use, the conditions under which opioids will be prescribed, the physician's need to document overall improvement in function, and worker responsibilities. Safety risks: Patients should especially be warned about potential side effects of opioids such as increased reaction time, clouded judgment, drowsiness and tolerance. Also, they should be warned about the possible danger associated with the use of opioids while operating heavy equipment or driving.
e) Helping your patient return to work: You should participate in a team conference with your patient, the employer (or potential new employers), the claim manager, the vocational counselor and others (preferably face-to-face) to explore return-to-work options. Which parties need to be involved will vary with each situation. Phone conferences often work well.
f) Principles for prescription of opioids: You should follow these general principles:

1) Single prescribing physician: There should be a single prescribing physician for all controlled substances.
2) Single pharmacy: You should use a single pharmacy for prescription filling (whenever possible).
3) Lowest possible dose: The lowest possible effective dose should be used to initiate therapy, and should be titrated, as needed to minimize both pain and medication side effects and maximize pain management and increased functioning.
4) Appearance of misuse of medications: Be sure to watch out for and document any appearance of misuse of medications. Acquisition of drugs from other physicians, uncontrolled dose escalation or other aberrant behaviors must be carefully assessed. In all such patients, opioid use should be reconsidered and additional, more rigid guidelines applied if opioids continue. In some cases, tapering and discontinuation of opioid therapy will be necessary.
g) Visit frequency: Visits initially at least every 2 weeks for the first 2-4 months of the trial, then at least once every 6-8 weeks while receiving opioids.
h) Consultations: You should request a consultation if:
1) A dose in excess of 100-150 mg of oral morphine daily or its equivalent (for example, 45 mg of MS Contin every 8 hours) is being used;
2) Pain and functional status have not substantially improved after 3 months of opioid treatment;
3) A patient has a history of chemical dependency; or
4) A patient appears to have significant problems with depression, anxiety or irritability (a psychologic consultation may be indicated in these cases).
i) Laboratory studies and drug screens: Remember to order relevant ongoing clinical or laboratory studies (especially liver or kidney function screens), including drug screens, as indicated.
j) Discontinuation vs. continuation of opioids: After 6 months of a well-designed opioid trial, a physician should determine whether opioid therapy is appropriate for the patient, in accordance with the following:
1) If there has not been an overall improvement in function, opioids should usually be discontinued. (If there are extenuating circumstances that justify further use of opioids after 6 months of an opioid trial, these should be described in detail.)
2) If the patient has returned to work or has demonstrated substantial improvement both in function and reported pain level during a 6- month opioid trial, reasonable doses of opioids could continue. However, you and your patient should understand that state law forbids L&I from paying for opioids once the patient reaches maximum medical improvement. You should speak with your patient about other sources of payment for opioids when L&I can no longer pay. With this in mind, you should re-evaluate the need for opioids every two months, using techniques such as weaning and/or substitution of alternative treatments.
3) Weaning time: Weaning can be done safely by way of a slow taper. Patients who undergo intensive treatment programs in a pain center or a drug rehabilitation center can be tapered off opioids in 1-2 weeks. Patients being treated in an office-based practice should be tapered more slowly, but the taper should never take more than 3 months.
1. What should I do if I have a patient who has already been on opioids for 6 months or more and is not back at work (or if I accept a new patient like this)?

If a patient has already received opioids for six months or more, you should do the following: a) Re-assess: Perform a thorough re-assessment of the patient to see if anything has been missed.
1) Is the original diagnosis still present? Are there additional diagnoses that may contribute to the pain?
2) Has the patient been given other medications for management of pain? If so, how effective were they, what side effects were experienced and how severe were the side effects?
3) Has the patient tried other treatment methods or consulted with other specialists? If so, what alternative methods have been tried, length of alternative treatments, effectiveness, and/or specialist recommendations and effectiveness of those recommendations?
4) Has there been functional improvement since opioids were started? Try to quantify the improvement.
5) Would a psychological or psychiatric evaluation, completed by a psychiatrist or psychologist experienced in evaluating chronic pain patients, be helpful or necessary for you to determine effective pain management for this patient? Or has the patient completed a similar evaluation within the last 3-6 months? Psychosocial issues include motivation, attitude about pain/work, return-to-work options, home life, etc.
6) Has screening for elements of addiction been completed? Special caution should be exercised in patients with a history of substance abuse that cannot be attributed to a past mistaken diagnosis of addiction because this patient previously used opiates for pain management. Have you reviewed prior medical records, including L&I medical records and drug summaries? A drug summary may be obtained from the claim manager.
7) Review Sections A2, C1 and C2 for guidance on re-assessment and documentation. The essential material in these sections, particularly the treatment plan and its relationship to recovery, should be covered in your summary.
b) Summarize: Provide the insurer and others involved in the patient's care with a written summary of the case. Special attention should be given to the history of opioid use (how long, in what doses, etc.). Give a clear statement of your rationale if you think opioid treatment should continue.
c) Help the patient return to work: You should participate in a team conference with the patient, the employer (or potential new employers), the claim manager, the vocational counselor and others (preferably face-to-face) to explore returnto- work options. Which parties need to be involved will vary with each situation. Phone conferences sometimes work well.
d) Triage: If the patient has been treated with opioids for 6 months or more, you should automatically review the case as described in a) through d). At that point the physician should choose one of three pathways:
1) Modify the treatment plan to achieve optimum opioid benefit. Many patients like this will be taking combinations of medications that don't offer optimal pain control.
2) Discontinue opioid therapy.
3) Continue in opioid therapy.
1. What precautions should I take when prescribing opioids?
a) DO NOT USE: Opioids in combination with sedative-hypnotics (such as benzodiazepines or barbiturates) for chronic, noncancer pain. (There may be specific indications for such combinations, such as the co-existence of spasticity. In such cases, a consultation is strongly recommended.)
b) Use of these medications is NOT RECOMMENDED:

1. Meperidine, which should not be prescribed for chronic pain.
2. Tramadol (Ultram) in combination with other opioids.
3. Carisoprodol (Soma).
4. Combination agonists and mixed agonists/antagonists. Mixed agonists/antagonists include such drugs as butorphanol (Stadol); dezocine (Dalgan), nalbuphine (Nubain) and pentazocine (Talwin).
5. Barbiturates (except if used to treat a seizure disorder).
6. Outpatient prescriptions of parenteral dosage forms of any drug.

c) Use caution when prescribing:
1. Acetaminophen in doses greater than 4 grams (including, for example, combinations of drugs that include both an opioid and acetaminophen).
2. Cyclobenzaprine (Flexeril) in combination with tricyclic antidepressants (both share the same toxic potential).
3. Nonopioid drugs concomitantly with combination opioids (e.g., Tylenol given with Percocet).
4. Tramadol (Ultram) to patients at risk for seizures and/or who are also taking drugs which can precipitate seizures (e.g., SSRI antidepressants, tricyclic antidepressants).
5. Opioids, including tramadol, to patients with a prior or active history of chemical dependency. d) Other recommendations include:

% Drug therapy should be individualized to the patient's specific pain condition and chosen on the basis of each drug's pharmacologic activity.
% Maintain patients on as few medications as possible. Drug interactions and adverse events increase as the number of medications in a regimen increases.
% Use adjuvant medications that are specific for a given pain condition.
% If possible, titrate only one drug at a time, while observing the patient for additive effects.
Inappropriate medications should be tapered while initiating an appropriate pharmacologic regimen.

2. What signs may you see in a person with a prescription opioid problem?

The following guidelines were developed in a pain clinic setting. These guidelines may be a useful monitoring tool in managing chronic pain patients in your office setting. A patient may qualify as a prescription opiate abuser by meeting three or more of the criteria listed below. Physicians are encouraged to seek consultations (addictionologist, pain clinic, etc.) if 3 or more of these criteria are met. The patient:

a) Displays an overwhelming focus on opioid issues. For example, discussion of opioids occupies a significant portion of the visit and impedes progress with other issues regarding the patient's pain. This behavior persists beyond the third clinic session.
b) Has a pattern of early refills (3 or more) or escalating drug use in the absence of physician direction to do so.
c) Generates multiple telephone calls or visits to the office to request more opioids, early refills, or problems associated with the opioid prescription. A patient may qualify with fewer visits if he or she creates a disturbance with the office staff.
d) Demonstrates pattern of prescription problems for a variety of reasons that may include lost medications, spilled medications or stolen medications.

e) Has supplemental sources of opioids obtained from multiple providers, emergency rooms or illegal sources.
f) Has illicit drugs on urine screen.

Rating: 7a

Washington State Department of Labor and Industries. Antiepileptic drugs guideline for chronic pain. Provider Bull 2005 Aug;(PB 05-10):1-3.

MAJOR RECOMMENDATIONS
Currently, there is lack of evidence to demonstrate that antiepileptic drugs (AEDs) significantly reduce the level of acute pain, myofascial pain, low back pain, or other sources of somatic pain. The evidence of efficacy and safety on AEDs in the treatment of neuropathic pain varies and depends on the specific agent in this drug class. Neuropathic pain may be defined as pain initiated or caused by a primary lesion or dysfunction in the nervous system, and is characterized by spontaneous pain described as lancinating, paroxysmal, burning, constant, cramping; and evoked pain of dysesthesia, allodynia, hyperalgia, or hyperpathia. Gabapentin, along with older antiepileptic drugs, may be used as a first line therapy in the treatment of chronic neuropathic pain. Because evidence of efficacy with lamotrigine has been inconsistent and there is no evidence of efficacy and safety for levetiracetam, oxcarbazepine, tiagabine, topiramate, and zonisamide, these drugs will not routinely be covered by the department for the treatment of neuropathic pain. In addition, the Food and Drug Administration (FDA) has recently issued an alert strongly discouraging the off-label use of tiagabine due to a paradoxical occurrence of seizures in patients without epilepsy.
Group 1, Neuropathic Pain Conditions
Gabapentin, and older antiepileptic drugs, are most likely to be effective when prescribed for the following neuropathic pain conditions or diseases that are known to cause neuropathy: Diabetic neuropathy, Post herpetic neuralgia, Trigeminal neuralgia, Spinal cord injury, Cauda equina syndrome, Phantom limb pain, Human immunodeficiency virus (HIV) neuropathy, Cancer,
Traumatic nerve injury, Chronic radiculopathy confirmed by pain radiating to the extremity in a dermatomal pattern and either objective examination findings of motor, sensory, or reflex changes, or abnormal imaging; or electromyography/nerve conduction velocity EMG/NCV abnormality.
Group 2, Questionable Neuropathic Pain Conditions
Gabapentin is less likely to be effective for questionable neuropathic pain conditions with no objective finding of nerve injury. Use of gabapentin for questionable neuropathic pain conditions should be authorized only after consultation and recommendation from a physician specializing in pain therapies, rehabilitation and physical medicine, anesthesiology, or neurology. It is recommended that a physician specializing in pain therapies have a subspecialty certification in pain medicine from the American Board of Medical Specialties.
Group 3, Non-Neuropathic Pain Conditions
There is no scientific evidence that antiepileptic drugs are effective in treating acute pain, somatic pain from strains or sprains, or myofascial pain. Gabapentin would not be authorized for non-neuropathic

pain conditions such as: Acute musculoskeletal pain, Primary somatic pain from chronic musculoskeletal strain/sprain, Low back pain without radiculopathy, Tendonitis, Repetitive strain without evidence of entrapment neuropathy

Rating: 7a

Washington State Department of Labor and Industries. Complex regional pain syndrome (CRPS). Olympia (WA): Washington State Department of Labor and Industries; 2002 Aug.

MAJOR RECOMMENDATIONS
I. What is Complex Regional Pain Syndrome (CRPS)?
Complex regional pain syndromes are painful conditions that usually affect the distal part of an upper or lower extremity and are associated with characteristic clinical phenomena (see Table 1 below). There are two subtypes -- CRPS Type I and CRPS Type II. The term "complex regional pain syndrome" was introduced to replace the term "reflex sympathetic dystrophy." CRPS Type I used to be called reflex sympathetic dystrophy. CRPS Type II used to be called causalgia. The terminology was changed because the pathophysiology of CRPS is not known with certainty. It was determined that a descriptive term such as CRPS was preferable to "reflex sympathetic dystrophy" which carries with it the assumption that the sympathetic nervous system is important in the pathophysiology of the painful condition. The terms CRPS Type I and CRPS Type II are meant as descriptors of certain chronic pain syndromes. They do not embody any assumptions about pathophysiology. For the most part the clinical phenomena characteristics of CRPS Type I are the same as seen in CRPS Type II. The central difference between Type I and Type II is that, by definition, Type II occurs following a known peripheral nerve injury, whereas Type I occurs in the absence of any known nerve injury. Pain that can be abolished or greatly reduced by sympathetic blockade (for example, a stellate ganglion block) is called sympathetically maintained pain. Pain that is not affected by sympathetic blockade is called sympathetically independent pain. The pain in some CRPS patients is sympathetically maintained; in others, the pain is sympathetically independent. If a physician believes the CRPS condition is related to an accepted occupational injury, written documentation of the relationship (on a more probable than not basis) to the original condition should be provided. Treatment for CRPS will only be authorized if the relationship to an accepted injury is established.
II. Key Issues in Making a Diagnosis
A. CRPS is a syndrome - patient's symptoms and signs match criteria described in Table 1.
B. CRPS is Uncommon - Most patients with widespread pain in an extremity do NOT have CRPS. Avoid the mistake of diagnosing CRPS primarily because a patient has widespread extremity pain that does not fit an obvious anatomic pattern. In many instances, there is no diagnostic label that adequately describes the patient's clinical findings. It is often more appropriate to describe a patient as having "regional pain of undetermined origin" than to diagnose CRPS.
C. Is CRPS a Disease? - Many clinicians believe that CRPS can best be construed as a "reaction pattern" to injury or to excessive activity restrictions (including immobilization) following injury. From

this perspective, CRPS may be a complication of an injury or be iatrogenically induced, but it is not an independent disease process.

D. Type I CRPS vs. Type II CRPS - In a patient with clinical findings of CRPS, the distinction between Type I and Type II CRPS depends on the physician's assessment of the nature of the injury underlying the CRPS. In many situations, the distinction is obvious - if CRPS onsets following an ankle sprain or a fracture of the hand, it is Type I CRPS. If CRPS onsets following a gunshot wound that severely injures the median nerve, it is Type II CRPS. In ambiguous situations (for example, CRPS in the context of a possible lumbar radiculopathy), the physician should be conservative in diagnosing Type II CRPS. This diagnosis should be made only when there is a known nerve injury with definable loss of sensory and/or motor function.

Table 1. Labor and Industries Criteria Number 13. Chronic Regional Pain Syndrome (CRPS) Conservative Treatment Guideline

Examination Findings And Diagnostic Test Results Conservative Care

At least four of the following must be present in order for a diagnosis of CRPS to be made.

Examination Findings

1. Temperature/color change
2. Edema
3. Trophic skin, hair, nail growth abnormalities
4. Impaired motor function
5. Hyperpathia/allodynia
6. Sudomotor changes

Diagnostic Test Results

7. Three phase bone scan that is abnormal in pattern characteristics for CRPS. This test is not needed if 4 or more of the above examination findings are present. Early aggressive care is encouraged. Emphasis should be on improved functioning of the symptomatic limb.

First Six Weeks Of Care:

- Sympathetic blocks, maximum of five. Each block should be followed immediately by physical/occupational therapy.
- Physical/occupational therapy should be focused on increasing functional level (see Table 2).
- Other treatment (e.g., medication at MD's discretion) as long as it promotes improved function.

After The 1st Six Weeks Of Care:

- Strongly consider psychiatric or psychological consultation if disability has extended beyond 3 months
- Continued physical/occupational therapy based on documented progress towards goals established during first 6 weeks (referenced above).
- Sympathetic blocks only if response to previous blocks has been positive, maximum of 3** every six weeks for a maximum of 12 weeks.

Surgical Interventions (Sympathetectomy) For Treatment Of This Condition Is Not Covered **A maximum of 11 blocks can be delivered over the total 18 week period

Table 2. Protocol for Physical Therapy/Occupational Therapy for CRPS

1. Evaluation should:

A. Include a date of onset of original injury (helpful in determining if early or late stage) and a date of onset of the CRPS symptoms.

B. Establish a baseline for strength and motion.

C. Establish a baseline for weight bearing for lower extremity.

D. If lower extremity, evaluate distance able to walk and need for assistive device.

E. If upper extremity, establish a baseline for grip strength, pinch strength, and shoulder range of motion.

F. If possible, objectify swelling (e.g., do volume displacements).

G. Define functional limitations.

2. Set specific functional goals for treatment related to affected extremity.

3. All treatment programs should include a core of:

A. A progressive active exercise program, including a monitored home exercise program

B. Progressive weight bearing for the lower extremity (if involved)

C. Progressive improvement of grip strength, pinch strength, and shoulder range of motion of the upper extremity (if involved)

D. A desensitization program

4. For specific cases, additional treatment options may be indicated to enhance effectiveness of the above core elements. Documentation should reflect reasons for these additional treatment options.

5. Documentation should include:

A. At least every two weeks, assessment of progress toward goals

B. Response to treatment used in addition to core elements (listed above in section 3)

C. Evidence of motivation and participation in home exercise program (i.e., diary or quota system)

Rating: 7a

Washington State Agency Medical Director's Group. Opioid Dosing Guideline for Chronic Non-Cancer Pain. 2007 Available at: http://www.agencymeddirectors.wa.gov/opioiddosing.asp. Accessed March 2007.

The opioid dosing guideline is part of a year-long educational pilot to improve care and safety when treating chronic non-cancer pain with opioids. It was developed by an Interagency Workgroup on Practice Guidelines in collaboration with actively practicing physicians who specialize in pain management. This guideline does not apply to the treatment of cancer pain or end-of-life (hospice) care. The purpose of Part I of the dosing guideline is to assist the primary care provider who does not specialize in pain medicine in prescribing opioids for adults in a safe and effective manner when:

Instituting or transitioning opioid treatment from acute to chronic non-cancer pain;
Assessing and monitoring opioid treatment for chronic non-cancer pain; and
Weaning opioids if an opioid trial fails to yield improvements in function and pain.

The purpose of Part II of the guideline is to assist primary care providers in treating patients whose morphine equivalent dose (MED) already exceeds 120 mg per day.

Rating: 7a

Dosing threshold for pain consultation
In order to improve the quality of care in the state of Washington, the state agencies, in collaboration with the physician panel, reviewed the available evidence and made the following recommendations:
• In general, the total daily dose of opioid should not exceed 120 mg oral morphine equivalents.
• Rarely, and only after pain management consultation, should the total daily dose of opioid be increased above 120 mg oral morphine equivalents.
• Safety and effectiveness of opioid therapy for chronic non-cancer pain should be routinely evaluated by the prescriber.
• Assessing the effectiveness of opioid treatment should entail tracking and documenting both functional improvement and pain relief.
• A specialty consultation may be considered at any time if there is evidence of frequent adverse effects or lack of response to an opioid trial.
Morphine equivalent dose calculation
For patients taking more than one opioid, the morphine equivalent doses of the different opioids must be added together to determine the cumulative dose
Opioid Dosing Calculator
Opioid (oral or transdermal): mg per day*:
Morphine equivalent factor:
Codeine - 0.15
fentanyl transdermal (in mcg/hr) - 2.4
hydrocodone - 1
hydromorphone - 4
methadone -
up to 20mg per day - 4
21 to 40mg per day - Since doses at or below 40mg per day are below the threshold for pain management consultation no opioid conversion calculations are necessary for this dosing range (assuming no other opioids are being taken).
41 to 60mg per day - 10
>60mg per day - 12
morphine - 1
oxycodone - 1.5
oxymorphone - 3
* Note: All doses expressed in mg per day with exception of fentanyl transdermal, which is expressed in mcg per hour
CAUTION: This calculator should NOT be used to determine doses when converting a patient from one opioid to another. This is especially important for fentanyl and methadone conversions. Equianalgesic

dosing ratios are only approximations and do not account for genetic factors, incomplete cross-tolerance, and pharmacokinetics.

Wasner G, Schattschneider J, Baron R. Skin temperature side differences--a diagnostic tool for CRPS? Pain. 2002 Jul;98(1-2):19-26.

Klinik für Neurologie, Universitätsklinikum Kiel der Christian-Albrechts-Universität, Niemannsweg 147, 24105 Kiel, Germany.

Skin temperature differences in the distal limbs are capable of reliably distinguishing CRPS I from other extremity pain syndromes with high sensitivity and specificity.

PMID: 12098613

Watkins PB, Kaplowitz N, Slattery JT, Colonese CR, Colucci SV, Stewart PW, Harris SC. Aminotransferase elevations in healthy adults receiving 4 grams of acetaminophen daily: a randomized controlled trial. JAMA. 2006 Jul 5;296(1):87-93.

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This was a randomized, single-blind, placebo-controlled, 5-treatment, parallel-group, inpatient, diet-controlled (meals provided), longitudinal study of 145 healthy adults in 2 US inpatient clinical pharmacology units. Each participant received either placebo (n = 39), 1 of 3 acetaminophen/opioid combinations (n = 80), or acetaminophen alone (n = 26). Each active treatment included 4 g of acetaminophen daily, the maximum recommended daily dosage. The intended treatment duration was 14 days. Initiation of recurrent daily intake of 4 g of acetaminophen in healthy adults is associated with alanine aminotransferase elevations and concomitant treatment with opioids does not seem to increase this effect. Should add caution about daily dose of acetaminophen and liver disease if > 4 g/day or in combination with other NSAID.

PMID: 16820551

Rating: 2b

Weaver M, Schnoll S. Abuse liability in opioid therapy for pain treatment in patients with an addiction history. Clin J Pain. 2002 Jul-Aug;18(4 Suppl):S61-9.

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Patients may present to physicians with complaints of acute or chronic pain. Some of these patients will have a history of addiction to drugs or alcohol, and a few will have active addiction. Controlled-substance prescriptions, especially opioid pain medications, can be very beneficial for treatment of pain in patients. There are clear differences between physical dependence on medication, active addiction, addiction in remission, and pseudoaddiction. A search of the medical literature revealed different rates of addiction in patients with chronic pain because different criteria were used to define addiction and the types of chronic pain. It appears that rates of addiction in patient populations with chronic pain are no different than rates of addiction in the general population, according to some recent studies. "Drug-seeking behavior" may be seen with either active addiction or pseudoaddiction. A way to distinguish between these conditions is by giving the patient more pain medication and observing the patient's pattern of behavior. Some patients may be at higher risk to abuse prescription opioids, and some types of drug-seeking behavior may be more predictive of active addiction than pseudoaddiction. General guidelines can improve physicians' comfort level in prescribing opioids for patients with chronic pain, even those with a history of addiction. These include using a medication agreement or contract, setting appropriate goals with the patient, giving appropriate amounts of pain medication, monitoring with drug screens and pill counts, and documenting the case carefully. Even patients with a history of addiction can benefit from opioid pain medications if the patients are monitored appropriately.

PMID: 12479255

Rating: 5b

Webster BS, Verma SK, Gatchel RJ. Relationship between early opioid prescribing for acute occupational low back pain and disability duration, medical costs, subsequent surgery and late opioid use. Spine. 2007 Sep 1;32(19):2127-32.

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STUDY DESIGN: Retrospective cohort study of workers' compensation (WC) claims with acute disabling low back pain (LBP). OBJECTIVE: To examine the association between early opioid use for acute LBP and outcomes: disability duration, medical costs, "late opioid" use (> or = 5 prescriptions from 30 to 730 days), and surgery in a 2-year period following LBP onset. SUMMARY OF BACKGROUND DATA: Opioid analgesics have become more accepted for acute pain management. However, treatment guidelines recommend limited opioid use for acute LBP management. Little is known about the long-term impact on outcomes of opioid use for acute LBP. METHODS: The sample consisted of 8443 claimants from a large WC database with new-onset, disabling LBP that occurred between January 1, 2002 and December 31, 2003. Based on morphine equivalent amount (MEA) in milligrams received in the first 15 days ("early opioids"), claimants were divided into 5 groups (0, 1-140, 141-225, 226-450, 450+). The associations between early opioids and outcomes were evaluated

using multivariate linear and logistic regression models. Covariates included age, gender, job tenure, and low back injury severity. Injury severity was classified using ICD-9 codes. RESULTS: Twenty-one percent of claimants received at least 1 early opioid prescription. After controlling for the covariates, mean disability duration, mean medical costs, and risk of surgery and late opioid use increased monotonically with increasing MEA. Those who received more than 450 mg MEA were, on average, disabled 69 days longer than those who received no early opioids (95% confidence interval [CI], 49.2-88.9). Compared with the lowest MEA group (0 mg opioid), the risk for surgery was 3 times greater (95% CI, 2.4-4.0) and the risk of receiving late opioids was 6 times greater (95% CI, 4.9-7.7) in the highest MEA group. Low back injury severity was a strong predictor of all the outcomes. CONCLUSION: Given the negative association between receipt of early opioids for acute LBP and outcomes, it is suggested that the use of opioids for the management of acute LBP may be counterproductive to recovery.

PMID: 17762815

Rating: 3a

Weiner DK, Perera S, Rudy TE, Glick RM, Shenoy S, Delitto A. Efficacy of percutaneous electrical nerve stimulation and therapeutic exercise for older adults with chronic low back pain: A randomized controlled trial. Pain. 2008 Oct 16. [Epub ahead of print].

Department of Medicine, University of Pittsburgh, PA, USA; Department of Anesthesiology, University of Pittsburgh, PA, USA; Department of Psychiatry, University of Pittsburgh, PA, USA; Geriatric Research Education and Clinical Center, VA Pittsburgh Healthcare System, Pittsburgh, PA, USA.

We conducted a randomized controlled trial in 200 men and women. All four groups experienced significantly reduced pain. Since brief electrical stimulation (i.e., control-PENS) facilitated comparably reduced pain and improved function at 6 months as compared with PENS, the exact dose of electrical stimulation required for analgesia cannot be determined. GCAE was more effective than PENS alone in reducing fear avoidance beliefs, but not in reducing pain or in improving physical function.

PMID: 18930352

Rating: 2b

Wermeling DP. Ziconotide, an intrathecally administered N-type calcium channel antagonist for the treatment of chronic pain. Pharmacotherapy. 2005 Aug;25(8):1084-94.

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Ziconotide is a novel peptide that blocks the entry of calcium into neuronal N-type voltage-sensitive calcium channels, preventing the conduction of nerve signals. N-type calcium channels are present in the superficial laminae of the dorsal horn of the spinal cord. In various animal models of pain, intrathecal administration of ziconotide blocked nerve transmission and nociception. The United States Food and Drug Administration recently approved ziconotide intrathecal infusion for the management of severe chronic pain in patients who require intrathecal therapy and who are intolerant of or refractory to other treatment, such as systemic analgesics, adjunctive therapies, or intrathecal morphine. The drug has a narrow therapeutic window and a lag time for the onset and offset of analgesia and adverse events. In early clinical trials, frequent and severe psychiatric and central nervous system adverse effects were associated with rapid intrathecal infusion (0.4 microg/hr) and frequent up-titration (every 12 hrs). Therefore, patients with psychiatric symptoms are not candidates for this drug. Drug trials of external intrathecal catheters and microinfusion devices demonstrated a 3% risk of meningitis. A low initial infusion rate of 0.1 microg/hour and limiting infusion rate increases to 2-3 times/week are now recommended. Patients responsive to intrathecal ziconotide require an implanted infusion system to receive long-term therapy.

Publication Types:
Review

PMID: 16207099

Rating: 5a

Weschules DJ, Bain KT, Richeimer S. Actual and potential drug interactions associated with methadone. Pain Med. 2008;9:315-44.

excelleRx, Inc., an Omnicare Company, Philadelphia, Pennsylvania, USA. dweschules@excellerx.com

OBJECTIVE: To identify and characterize methadone-related drug interactions, as well as factors accounting for the variability in manifesting these interactions clinically. DESIGN: Systematic review of the primary literature. METHODS: Over 200 articles, reports of clinical trials, and case reports were reviewed. Studies and case reports were included if they revealed either quantitative or qualitative methods to identify, evaluate severity of, or compare methadone-related drug interactions. RESULTS OF DATA SYNTHESIS: The evidence base associated with methadone drug interactions is underdeveloped in general, as the majority of references found were case reports or case series. Most of the studies and reports focused on inpatients receiving methadone maintenance treatment (MMT) that were between 20 and 60 years of age, taking 200 mg/day of methadone or less. Evidence supporting the involvement of lesser known cytochrome P450 enzymes such as 2B6 is emerging, which may partially explain the inconsistencies previously found in studies looking specifically at 3A4 in vitro and in vivo. Genetic variability may play a role in the pharmacokinetics and pharmacodynamics of many medications, including methadone. CONCLUSIONS: Drug interactions associated with methadone and

their clinical significance are still poorly understood in general. Many tertiary drug information references and review articles report interactions associated with methadone in a general sense, much of which is theoretical and not verified by case reports, much less well-designed clinical trials. The majority of drug interaction reports that do exist were performed in the MMT population, which may differ significantly from chronic pain or cancer pain populations.

PMID: 18386306

Rating: 1a

Wheeler AH, Goolkasian P, Gretz SS. A Randomized, Double-Blind, Prospective Pilot Study of Botulinum Toxin Injection for Refractory, Unilateral, Cervicothroacic, Paraspinal, Myofascial Pain Syndrome. Spine 1998;23:1662-7.

Charlotte Spine Center, Suite 210, 2001 Randolph Road, Charlotte, NC 28207, USA

CONCLUSIONS: "Although no statistically significant benefit of botulinum toxin type A over placebo was demonstrated in this study, the high incidence of patients who were asymptomatic after a second injection suggests that further research is needed to determine whether higher dosages and sequential injections in a larger cohort might show a botulinum toxin type A effect."

Note:

First injections of Botox were not significantly different from saline injection, and not clearly better than would be expected from dry needling
Second injection did produce noticeable group difference, with advantage for those who had received Botox at first injection, but difference not significant and meaning unclear

Publication Type: RCT, 32

PMID: 11731062

Rating: 2b

Widerstrom-Noga EG, Duncan R, Felipe-Cuervo E, Turk DC. Assessment of the impact of pain and impairments associated with spinal cord injuries. Arch Physical Medicine Rehabilitation. 2002 Mar;83(3):395-404.

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Abstract:

OBJECTIVES: To determine the adequacy of the Multidimensional Pain Inventory (MPI) for assessing pain impact after spinal cord injury (SCI) and to determine whether the impact of pain can be separated from other consequences of SCI. DESIGN: Postal survey. SETTING: General community. PARTICIPANTS: Of the 159 subjects contacted who experienced chronic pain, 120 (75.5%) participated. INTERVENTIONS: Subjects were mailed the original MPI and a set of additional items specific to SCI. MAIN OUTCOME MEASURE: The MPI. RESULTS: Confirmatory (CFA) and exploratory factor analyses were performed for each section of the MPI. Elimination of several items, including those related to work in section 1 (pain impact), improved the goodness-of-fit index (GFI). A CFA for section 2 (response of significant other) resulted in acceptable GFI after 2 items were deleted. Decrease in activity levels (section 3) because of other consequences of injury was significantly greater after tetraplegia than after paraplegia. In contrast, pain-related reduction in activities was not associated with injury level. Although other consequences of SCI may have greater impact on activities than pain, severe pain is likely to affect activity levels significantly. CONCLUSION: The MPI appears to be appropriate for use in a SCI population when modified to eliminate questions related to work and to supplement the activity scale with items addressing decreased activity levels due to pain.

Publication Type: Case Control Study, 159 cases

PMID: 11887122

Wiffen P, Collins S, McQuay H, Carroll D, Jadad A, Moore A. Anticonvulsant drugs for acute and chronic pain. Cochrane Database Syst Rev. 2005 Jul 20;(3):CD001133.

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BACKGROUND: Anticonvulsant drugs have been used in the management of pain since the 1960s. The clinical impression is that they are useful for chronic neuropathic pain, especially when the pain is lancinating or burning. Readers are referred to reviews of carbamazepine and gabapentin in the Cochrane Library which replace the information on those drugs in this review. Other drugs remain unchanged at present in this review OBJECTIVES: To evaluate the analgesic effectiveness and adverse effects of anticonvulsant drugs for pain management in clinical practice . Migraine and headache studies are excluded in this revision. SEARCH STRATEGY: Randomised trials of anticonvulsants in acute, chronic or cancer pain were identified by MEDLINE (1966-1999), EMBASE (1994-1999), SIGLE (1980-1999) and the Cochrane Controlled Trials Register (CENTRAL/CCTR) (Cochrane Library Issue 3, 1999). In addition, 41 medical journals were hand searched. Additional reports were identified from the reference list of the retrieved papers, and by contacting investigators. Date of most recent search: September 1999. SELECTION CRITERIA: Randomised trials reporting the analgesic effects of anticonvulsant drugs in patients, with subjective pain assessment as either the primary or a secondary

outcome. DATA COLLECTION AND ANALYSIS: Data were extracted by two independent reviewers, and trials were quality scored. Numbers-needed-to-treat (NNTs) were calculated from dichotomous data for effectiveness, adverse effects and drug-related study withdrawal, for individual studies and for pooled data. MAIN RESULTS: Twenty-three trials of six anticonvulsants were considered eligible (1,074 patients).The only placebo-controlled study in acute pain found no analgesic effect of sodium valproate.Three placebo-controlled studies of carbamazepine in trigeminal neuralgia had a combined NNT (95% confidence interval (CI)) for effectiveness of 2.5 (CI 2.0-3.4). A single placebo-controlled trial of gabapentin in post-herpetic neuralgia had an NNT of 3.2 (CI 2.4-5.0). For diabetic neuropathy NNTs for effectiveness were as follows: (one RCT for each drug) carbamazepine 2.3 (CI 1.6-3.8), gabapentin 3.8 (CI 2.4-8.7) and phenytoin 2.1 (CI 1.5-3.6).Numbers-needed-to-harm (NNHs) were calculated where possible by combining studies for each drug entity irrespective of the condition treated. The results were, for minor harm, carbamazepine 3.7 (CI 2.4-7.8), gabapentin 2.5 (CI 2.0-3.2), phenytoin 3.2 (CI 2.1-6.3). NNHs for major harm were not statistically significant for any drug compared with placebo.Phenytoin had no effect in irritable bowel syndrome, and carbamazepine little effect in post-stroke pain. Clonazepam was effective in one study of temporomandibular joint dysfunction. AUTHORS' CONCLUSIONS: Although anticonvulsants are used widely in chronic pain surprisingly few trials show analgesic effectiveness. Only one study considered cancer pain. There is no evidence that anticonvulsants are effective for acute pain. In chronic pain syndromes other than trigeminal neuralgia, anticonvulsants should be withheld until other interventions have been tried. While gabapentin is increasingly being used for neuropathic pain the evidence would suggest that it is not superior to carbamazepine.

Publication Types:
Review

PMID: 16034857

Rating: 1a

Conclusion: Currently, there is lack of evidence to demonstrate that AEDs significantly reduce the level of acute pain, myofascial pain, low back pain, or other sources of somatic pain.(2)
(2) Cochrane Review. Anticonvulsant drugs for acute and chronic pain. The Cochrane Database of Systematic Reviews, 2005; 1.

Wiffen PJ, McQuay HJ, Edwards JE, Moore RA. Gabapentin for acute and chronic pain. Cochrane Database Syst Rev. 2005 Jul 20;(3):CD005452.

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BACKGROUND: Anticonvulsant drugs have been used in the management of pain since the 1960s. The clinical impression is that they are useful for chronic neuropathic pain, especially when the pain is lancinating or burning. OBJECTIVES: To evaluate the analgesic effectiveness and adverse effects of gabapentin for pain management in clinical practice. SEARCH STRATEGY: Randomised trials of gabapentin in acute, chronic or cancer pain were identified by MEDLINE (1966-Nov 2004), EMBASE (1994-Nov 2004), SIGLE (1980-Jan 2004) and the Cochrane Central Register of Controlled Trials (CENTRAL) (Cochrane Library Issue 4, 2004). Additional reports were identified from the reference list of the retrieved papers, and by contacting investigators. Date of most recent search: January 2004. SELECTION CRITERIA: Randomised trials reporting the analgesic effects of gabapentin in patients, with subjective pain assessment as either the primary or a secondary outcome. DATA COLLECTION AND ANALYSIS: Data were extracted by two independent reviewers, and trials were quality scored. Numbers-needed-to-treat (NNTs) were calculated, where possible, from dichotomous data for effectiveness, adverse effects and drug-related study withdrawal. MAIN RESULTS: Fourteen reports describing 15 studies of gabapentin were considered eligible (1468 participants). One was a study of acute pain. The remainder included the following conditions: post-herpetic neuralgia (two studies), diabetic neuropathy (seven studies), a cancer related neuropathic pain (one study) phantom limb pain (one study), Guillain Barre syndrome (one study), spinal chord injury pain (one study) and various neuropathic pains (one study). The study in acute post-operative pain (70 participants) showed no benefit for gabapentin compared to placebo for pain at rest.In chronic pain, the NNT for improvement in all trials with evaluable data is 4.3 (95%CI 3.5-5.7). Forty two percent of participants improved on gabapentin compared to 19% on placebo. The number needed to harm(NNH) for adverse events leading to withdrawal from a trial was not significant. Fourteen percent of participants withdrew from active arms compared to 10% in placebo arms. The NNH for minor harm was 3.7 (95% CI 2.4 to 5.4). The NNT for effective pain relief in diabetic neuropathy was 2.9 (95% CI 2.2 to 4.3) and for post herpetic neuralgia 3.9 (95% CI 3 to 5.7). AUTHORS' CONCLUSIONS: There is evidence to show that gabapentin is effective in neuropathic pain. There is limited evidence to show that gabapentin is ineffective in acute pain.

Publication Types:
Meta-Analysis
Review

PMID: 16034978

Rating: 1a

Wiffen PJ, Rees J. Lamotrigine for acute and chronic pain. Cochrane Database Syst Rev. 2007 Apr 18;(2):CD006044.

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BACKGROUND: Anticonvulsant medicines have a place in the treatment of neuropathic pain (pain due to nerve damage). This review looks at the evidence for the pain relieving properties of lamotrigine. OBJECTIVES: To assess the analgesic efficacy and adverse effects of the anticonvulsant lamotrigine for acute and chronic pain. SEARCH STRATEGY: Randomised Controlled Trials (RCTs) of lamotrigine (and key brand names Lamictal, Lamictin, Neurium) in acute, chronic or cancer pain were identified from MEDLINE (1966 to August 2006), EMBASE 1994 to August 2006 and the CENTRAL register on The Cochrane Library (Issue 3, 2006). Additional reports were sought from the reference list of the retrieved papers. SELECTION CRITERIA: RCTs investigating the use of lamotrigine (any dose and by any route) for treatment of acute or chronic pain. Assessment of pain intensity or pain relief, or both, using validated scales. Participants were adults aged 18 and over. Only full journal publication articles were included. DATA COLLECTION AND ANALYSIS: Dichotomous data were used to calculate relative risk with 95% confidence intervals using a fixed effects model unless significant statistical heterogeneity was found. Continuous data was also reported where available. Meta-analysis was undertaken using a fixed effect model unless significant heterogeneity was present (I(2) >50%) in which case a random effects model was used. Numbers-needed-to-treat (NNTs) were calculated as the reciprocal of the absolute risk reduction. For unwanted effects, the NNT becomes the number-needed-to-harm (NNH) and was calculated. MAIN RESULTS: Sixteen studies were identified. Nine studies were excluded. No studies for acute pain were identified. The seven included studies involved 502 participants, all for neuropathic pain. The studies covered the following conditions: central post stroke pain (1), diabetic neuropathy (1), HIV related neuropathy (2), intractable neuropathic pain (1), spinal cord injury related pain (1) and trigeminal neuralgia (1). The studies included participants in the age range of 26 to 77 years. Only one study for HIV related neuropathy had a statistically significant result for a sub group of patients on anti-retroviral therapy; this result is unlikely to be clinically significant NNT 4.3 (95% CI 2.3 to 37). Approximately 7% of participants taking lamotrigine reported a skin rash. AUTHORS' CONCLUSIONS: Given the availability of more effective treatments including anticonvulsants and antidepressant medicines, lamotrigine does not have a significant place in therapy at present. The limited evidence currently available suggests that lamotrigine is unlikely to be of benefit for the treatment of neuropathic pain.

PMID: 17443611

Rating: 1b

Wilsey B, Marcotte T, Tsodikov A, Millman J, Bentley H, Gouaux B, Fishman S. A randomized, placebo-controlled, crossover trial of cannabis cigarettes in neuropathic pain. J Pain. 2008 Jun;9(6):506-21. Epub 2008 Apr 10.

VA Northern California Health Care System, Department of Anesthesiology and Pain Medicine, University of California, Davis Medical Center, Davis, California.

The Food and Drug Administration (FDA), Substance Abuse and Mental Health Services Administration (SAMHSA), and the National Institute for Drug Abuse (NIDA) report that no sound scientific studies support the medicinal use of cannabis. Despite this lack of scientific validation, many patients routinely use "medical marijuana," and in many cases this use is for pain related to nerve injury. We conducted a double-blinded, placebo-controlled, crossover study evaluating the analgesic efficacy of smoking cannabis for neuropathic pain. Thirty-eight patients with central and peripheral neuropathic pain underwent a standardized procedure for smoking either high-dose (7%), low-dose (3.5%), or placebo cannabis. In addition to the primary outcome of pain intensity, secondary outcome measures included evoked pain using heat-pain threshold, sensitivity to light touch, psychoactive side effects, and neuropsychological performance. A mixed linear model demonstrated an analgesic response to smoking cannabis. No effect on evoked pain was seen. Psychoactive effects were minimal and well-tolerated, with some acute cognitive effects, particularly with memory, at higher doses. PERSPECTIVE: This study adds to a growing body of evidence that cannabis may be effective at ameliorating neuropathic pain, and may be an alternative for patients who do not respond to, or cannot tolerate, other drugs. However, the use of marijuana as medicine may be limited by its method of administration (smoking) and modest acute cognitive effects, particularly at higher doses.

PMID: 18403272

Rating: 2c

Wilson KG, Eriksson MY, D'Eon JL, Mikail SF, Emery PC. Major depression and insomnia in chronic pain. Clinical Journal of Pain. 2002 Mar-Apr;18(2):77-83.

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This study concluded, "patients with chronic pain and concurrent major depression and insomnia report the highest levels of pain-related impairment, but insomnia in the absence of major depression is also associated with increased pain and distress."

Publication Type: Case Control Study, 143 cases

PMID: 11882770

Winkelmuller M, Winkelmuller W. Long-term effects of continuous intrathecal opioid treatment in chronic pain of nonmalignant etiology. J Neurosurg. 1996 Sep;85(3):458-67.

Department of Neurosurgery, Stadtisches Klinikum Braunschweig, Germany.

In the present retrospective investigation, the long-term effects of continuous intrathecal opioid therapy via implantable infusion pump systems were examined in 120 patients with chronic, nonmalignant pain syndromes. The follow-up period was 6 months to 5.7 years (mean 3.4 years +/- 1.3 standard error of the mean). Deafferentation pain and neuropathic pain showed the best long-term results, with 68% and 62% pain reduction (visual analog scale), respectively. The mean morphine dosage initially administered was 2.7 mg/day (range 0.3-12 mg/day); after an average of 3.4 years, it was 4.7 mg/day (range 0.3-12 mg/day). In a long-term observation of 28 patients who received intrathecal morphine for longer than 4 years. 18 patients (64.3%) had a constant dosage history and 10 patients (35.7%) showed an increase in morphine dosage to more than 6 mg/day 1 year after dosage determination. In seven cases, a tolerance developed: in four patients the tolerance was controlled by means of "drug holidays"; but in three patients it was necessary to remove the pump systems. Explantation of the pump system occurred in 22 additional cases for other reasons. Throughout the follow-up period, 74.2% of the patients profited from the intrathecal opiate therapy: the average pain reduction after 6 months was 67.4% and, as of the last follow-up examination, it was 58.1%. Ninety-two percent of the patients were satisfied with the therapy and 81% reported an improvement in their quality of life. The authors' 6-year experience with administration of intrathecal opioid medications for nonmalignant pain should encourage the use of this method in carefully selected patients.

Publication Type:
Cohort Study

PMID: 8751633

Rating: 3b

Wisconsin Medical Society Task Force on Pain Management. Guidelines for the assessment and management of chronic pain. WMJ. 2004;103(3):13-42.

Publication Types:
Guideline
Practice Guideline

PMID: 15217111

Rating: 7b

Treatment Plan: If chronic opiate use is indicated (daily opiates for greater than 60 days) a treatment plan is ideally documented in the medical record. In formulation of the treatment plan, consideration should be given to both pharmacologic and non-pharmacologic modalities, including behavioral strategies, psychotherapy, coping skills training, relaxation techniques, non-invasive somatic

interventions, and involvement with a formal pain rehabilitation program. It is no longer considered a standard of medical practice to categorically avoid the use of opioids for chronic non-malignant conditions. However, the potential benefits and risks must be clearly evaluated and explained to the patient. Whenever a trial of opioids is selected, the patient or the patient's guardian should be informed of potential risks, such as sedation, tolerance with chronic use, and withdrawal with abrupt discontinuation after chronic use. With the patient's consent, his/her family or significant other may be similarly informed. Realistic risks about the potential for development of addiction should be reviewed, including education about the differences between physical dependence (the normal, predictable development of tolerance, possible needs for dosage escalation, and withdrawal) and the condition of addiction (loss of control over amounts prescribed, preoccupation, drug hunger, inappropriate medication seeking, or functional impairment due to substance use). The use of a treatment contract, signed by the patient and possibly by the significant other as well, may be considered. Such a contract reviews the conditions under which opioids will be prescribed (e.g., a single prescriber, a single dispensing pharmacy, prohibitions against sharing of the patient's medication with others or the patient's use of another party's medications, responses to misplaced medication supplies, etc.). Patient and family education should emphasize how opioids have a wide margin of safety and efficacy, and should not be irrationally avoided in a treatment plan even though prudent precautions regarding chronic administration are appropriate. Particular challenges are present when a candidate for opioid therapy has an addictive disorder. Patients with opiate dependency are at special risk for experiencing euphoria when opiates are administered in usual dosages, and of developing drug-liking, preoccupation, and a rekindling of psychological dependence. Loss of control is a distinct risk with chemically dependent patients. Even patients with alcohol or other non-opioid addiction are at special risk of relapse when opioids are administered. These factors do not constitute an absolute contraindication to the use of opioids when thorough evaluation finds them indicated for such patients; however, consultation with an addiction medicine specialist or certified addiction counselor is essential when anything more than the briefest course of opioid therapy is planned for a patient with a substance dependence disorder. A positive family history of addictive disorder, or a personal history of addiction on long-term stable remission, still are relative indications for consultation with an addiction specialist.

Wolfe F, Smythe HA, Yunus MB, Bennett RM, Bombardier C, Goldenberg DL, et al. The American College of Rheumatology 1990 criteria for the classification of fibromyalgia: report of the multicenter criteria committee. Arthritis Rheum 1990;33:160---72.

American College of Rheumatology
1990 criteria for the classification of Fibromyalgia

1. History of widespread pain.
Definition. Pain is considered widespread when all of the following are present: pain in the left side of the body, pain in the right side of the body, pain above the waist, and pain below the waist. In addition, axial skeletal pain (cervical spine or anterior chest or thoracic spine or low back) must be present. In this

definition, shoulder and buttock pain is considered as pain for each involved side. "Low back" pain is considered lower segment pain.

2. Pain in 11 of 18 tender point sites on digital palpation.
Definition. Pain, on digital palpation, must be present in at least 11 of the following 18 sites:
Occiput: Bilateral, at the suboccipital muscle insertions.
Low cervical: bilateral, at the anterior aspects of the intertransverse spaces at C5-C7.
Trapezius: bilateral, at the midpoint of the upper border.
Supraspinatus: bilateral, at origins, above the scapula spine near the medial border.
Second rib: bilateral, at he second costochondral junctions, just lateral to the junctions on upper surfaces.
Lateral epicondyle: bilateral, 2 cm distal to the epicondyles.
Gluteal: bilateral, in upper outer quadrants of buttocks in anterior fold of muscle.
Greater trochanter: bilateral, posterior to the trochanteric prominence.
Knee: bilateral, at the medial fat pad proximal to the joint line.

Digital palpation should be performed with an approximate force of 4 kg.
For a tender point to be considered "positive" the subject must state that the palpation was painful. "Tender is not to be considered "painful."

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* For classification purposes, patients will be said to have fibromyalgia if both criteria are satisfied. Widespread pain must have been present for at least 3 months. The presence of a second clinical disorder does not exclude the diagnosis of fibromyalgia.

Rating: 6b

Wolfe GI, Trivedi JR. Painful peripheral neuropathy and its nonsurgical treatment. Muscle Nerve. 2004;30:3-19.

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Treatment of neuropathic pain is the primary focus of management for many patients with painful peripheral neuropathy. Antidepressants and anticonvulsants are the two pharmacological classes most widely studied and represent first-line agents in the management of neuropathic pain. The number of pharmacological agents that have demonstrated effectiveness for neuropathic pain continues to expand. In the current review, we summarize data from randomized, controlled pharmacological trials in painful peripheral neuropathies. Although neuropathic pain management remains challenging because the response to therapy varies considerably between patients, and pain relief is rarely complete, a majority

of patients can benefit from monotherapy using a well-chosen agent or polypharmacy that combines medications with different mechanisms of action.

PMID: 15221874

Rating: 5b

Wong MC, Chung JW, Wong TK. Effects of treatments for symptoms of painful diabetic neuropathy: systematic review. BMJ. 2007;335:87. Epub 2007 Jun 11.

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OBJECTIVE: To evaluate the effects of treatments for the symptoms of painful diabetic neuropathy. DESIGN: Systematic review. DATA SOURCES: Articles (English and full text) on double blind randomised trials found by searching with the key words anticonvulsant, antidepressant, non-steroidal anti-inflammatory drugs, tramadol, opioid, ion channel blocker, diabetic neuropathy, diabetic peripheral neuropathy, peripheral neuropathy, and neuropathy. The search included Medline, Embase, EMB reviews-AP Journal club, and the Cochrane central register of controlled trials. STUDY SELECTION: Randomised controlled trials comparing topically applied and orally administered drugs with a placebo in adults with painful diabetic neuropathy. DATA EXTRACTION: Data were extracted to examine quality of methods, characteristics of studies and patients, efficacy, and side effects. The primary outcome was dichotomous information for 50% or moderate reduction of pain. Secondary outcomes were 30% reduction of pain and withdrawals related to adverse events. RESULTS: Odds ratios were calculated for achievement of 30%, 50%, or moderate pain relief and for withdrawals related to adverse effects. Twenty five reports were included and seven were excluded. The 25 included reports compared anticonvulsants (n=1270), antidepressants (94), opioids (329), ion channel blockers (173), N-methyl-D-aspartate antagonist (14), duloxetine (805), capsaicin (277), and isosorbide dinitrate spray (22) with placebo. The odds ratios in terms of 50% pain relief were 5.33 (95% confidence interval 1.77 to 16.02) for traditional anticonvulsants, 3.25 (2.27 to 4.66) for newer generation anticonvulsants, and 22.24 (5.83 to 84.75) for tricylic antidepressants. The odds ratios in terms of withdrawals related to adverse events were 1.51 (0.33 to 6.96) for traditional anticonvulsants, 2.98 (1.75 to 5.07) for newer generation anticonvulsants, and 2.32 (0.59 to 9.69) for tricylic antidepressants. Insufficient dichotomous data were available to calculate the odds ratios for ion channel blockers. CONCLUSION: Anticonvulsants and antidepressants are still the most commonly used options to manage diabetic neuropathy. Oral tricyclic antidepressants and traditional anticonvulsants are better for short term pain relief than newer generation anticonvulsants. Evidence of the long term effects of oral antidepressants and anticonvulsants is still lacking. Further studies are needed on opioids, N-methyl-D-aspartate antagonists, and ion channel blockers.

PMID: 17562735

Rating: 1b

Wootton J, Sparber A. Surveys of Complementary and Alternative Medicine: Part I. General Trends and Demographic Groups. Journal of Alternative and Complementary Medicine 2001;7(2):195-208.

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Abstract:
Surveys of general complementary and alternative medicine (CAM) use have suggested an association with high levels of depression and anxiety. This raises the question of whether anxious or depressed people seek CAM, or whether there are underlying factors associated with long-term chronic illness. There is no clear indication from four surveys of psychiatric patients. These are summarized and presented. A separate table summarizes three studies of patients with neurologic diseases, two of patients with multiple sclerosis, and one of a mixed patient population. More studies are amassing in specific disease areas, although it is difficult to detect clear trends because of methodological and terminological incompatibilities.

PMID: 11890442

Wu CL, Raja SN. An update on the treatment of postherpetic neuralgia. J Pain. 2008;9:S19-30.

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Like other types of neuropathic pain, postherpetic neuralgia (PHN) can be resistant to many types of pharmacologic and interventional therapies. Although many analgesic agents have been used for the treatment of other types of neuropathic pain, tricyclic antidepressants, antiepileptic drugs, opioids, and lidocaine patch appear to demonstrate relative analgesic efficacy for the treatment of pain from PHN. There are fewer studies on the use of interventional options for the treatment of pain from PHN. The majority of interventional therapies show equivocal analgesic efficacy although some data indicate that intrathecal methylprednisolone may be effective. Further randomized, controlled trials will be needed to confirm the analgesic efficacy of analgesic and interventional therapies to determine their role in the overall treatment of patients with PHN. PERSPECTIVE: This article reviews the analgesic options for the treatment of PHN and suggests that tricyclic antidepressants, membrane stabilizers, opioids, and lidocaine patch may demonstrate analgesic efficacy in this group of patients. These data may potentially help clinicians who attempt to provide analgesia in patients with PHN.

PMID: 18166462

Rating: 5a

Yokoyama M, Sun X, Oku S, Taga N, Sato K, Mizobuchi S, Takahashi T, Morita K. Comparison of percutaneous electrical nerve stimulation with transcutaneous electrical nerve stimulation for long-term pain relief in patients with chronic low back pain. Anesth Analg. 2004 Jun;98(6):1552-6, table of contents.

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The long-term effect of percutaneous electrical nerve stimulation (PENS) on chronic low back pain (LBP) is unclear. We evaluated the number of sessions for which PENS should be performed to alleviate chronic LBP and how long analgesia is sustained. Patients underwent treatment on a twice-weekly schedule for 8 wk. Group A (n = 18) received PENS for 8 wk, group B (n = 17) received PENS for the first 4 wk and transcutaneous electrical nerve stimulation (TENS) for the second 4 wk, and group C (n = 18) received TENS for 8 wk. Pain level, degree of physical impairment, and the daily intake of nonsteroidal antiinflammatory drugs (NSAIDs) were assessed before the first treatment, 3 days after Week 2, Week 4, and Week 8 treatments, and at 1 and 2 mo after the sessions. During PENS therapy, the pain level decreased significantly from Week 2 in Groups A and B ($P < 0.05$ or 0.01), and physical impairment and required NSAIDs decreased significantly from Week 4 ($P < 0.05$ or 0.01) in Group A but only at Week 4 in Group B ($P < 0.05$ or 0.01). These effects were sustained until 1-mo follow-up ($P < 0.01$) in Group A but not in Group B; these effects were not observed at 2-mo follow-up even in Group A. In Group C, pain level decreased significantly only at Week 8 ($P < 0.05$). Our results indicate that repeated PENS is more effective than TENS for chronic LBP but must be continued to sustain the analgesic effect. IMPLICATIONS: A cumulative analgesic effect was observed in patients with chronic low back pain (LBP) after repeated percutaneous electrical nerve stimulation (PENS), but this effect gradually faded after the treatment was terminated. Results indicate that although PENS is effective for chronic LBP, treatments need to be continued to sustain analgesia.

Publication Types:
- Clinical Trial
- Randomized Controlled Trial

PMID: 15155304

Rating: 2b

Note: Not a "curative" treatment.

Yoshida GM, Nelson RW, Capen DA, Nagelberg S, Thomas JC, Rimoldi RL, Haye W. Evaluation of continuous intraspinal narcotic analgesia for chronic pain from benign causes. Am J Orthop. 1996 Oct;25(10):693-4.

Complex Spine Clinic, Rancho Los Amigos Medical Center, Downey, California, USA.

Intraspinal narcotic analgesia (INA) has been used for chronic pain from nonmalignant causes with moderate success. To ascertain the efficacy of the morphine pump, we reviewed the 2-year results of continuous INA in 18 patients with failed back syndrome or arachnoiditis and intractable, debilitating pain that was unrelieved by conventional means. All patients underwent a trial screening of single-dose intrathecal narcotics with good pain relief. After 2 years, 8 pumps were still functioning, 8 patients had the pump removed or turned off, and 2 patients were lost to follow-up. Our patients averaged 1.4 additional procedures or hospitalizations after initial pump insertion. Overall, only 4 patients had objective evidence of benefit from INA, for a success rate of 25%. Results of this review suggest INA should not be used for the long-term management of chronic pain from nonmalignant causes.

PMID: 8922167

Rating: 4b

Yousefi-Nooraie R, Schonstein E, Heidari K, Rashidian A, Akbari-Kamrani M, Irani S, Shakiba B, Mortaz Hejri S, Mortaz Hejri S, Jonaidi A. Low level laser therapy for nonspecific low-back pain. Cochrane Database Syst Rev. 2007 Apr 18;(2):CD005107.

BACKGROUND: Low-back pain (LBP) and related disabilities are major public health problems and a major cause of medical expenses, absenteeism and disablement. Low level laser therapy (LLLT) can be used as a therapeutic intervention for musculoskeletal disorders such as back pain. OBJECTIVES: To assess the effects of LLLT in patients with non-specific low-back pain and to explore the most effective method of administering LLLT for this disorder. SELECTION CRITERIA: Only randomised controlled clinical trials (RCTs) investigating low level laser therapy as a light source treatment for non-specific low-back pain were included. MAIN RESULTS: Six RCTs with reasonable quality were included in the review. All of them were published in English. There is some evidence of pain relief with LLLT, compared to sham therapy for subacute and chronic low-back pain. These effects were only observed at short-term and intermediate-term follow-ups. Long-term follow-ups were not reported. There was no difference between LLLT and comparison groups for pain-related disability. There is insufficient evidence to determine the effectiveness of LLLT on antero-posterior lumbar range of motion compared to control group in short-term follow-up. The relapse rate in the LLLT group was significantly lower than in the control group at six months follow-up period according to the findings of two trials. AUTHORS' CONCLUSIONS: No side effects were reported. However, we conclude that there are insufficient data to draw firm conclusions. There is a need for further methodologically rigorous RCTs to evaluate the effects of LLLT compared to other treatments, different lengths of treatment, different wavelengths and different dosages. Comparison of different LLLT treatments will be more reasonable if dose calculation methods are harmonized.

PMID: 17443572

Rating: 1b

Yung Chung O, Bruehl SP. Complex Regional Pain Syndrome. Curr Treat Options Neurol. 2003 Nov;5(6):499-511.

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Complex regional pain syndrome (CRPS) is a heterogeneous disorder that falls in the spectrum of neuropathic pain disorders. It is maintained by abnormalities throughout the neuraxis (the peripheral, autonomic, and central nervous systems). The pathophysiology of CRPS is not fully known. There are no scientifically well-established treatments. The diagnostic criteria for CRPS at this time are purely clinical, and the use of diagnostic tests has not been demonstrated. The most appropriate management of CRPS uses a multidisciplinary approach, with the inclusion of medical and psychologic intervention, and physical and occupational therapy. The key is gradual, persistent, functional improvement. The rational use of pain therapies must be grounded in a thorough knowledge of the neurobiology of pain, its endogenous modulation, and the clinical presentation. Potential peripheral pathophysiologic targets (and possible treatments) include increased spontaneous firing and responsiveness of peripheral afferent fibers mediated by inflammatory and other algogenic substances (somatosensory blocks, corticosteroids), altered levels of expression and functioning of multiple ion channels (local anesthetics, calcium channel blockers, anticonvulsants), abnormal interneuronal communication, and increased peripheral expression of adrenergic receptors and sympathetic excitation (sympathetic blocks, alpha-adrenergic antagonists, alpha-2 agonists). CRPS is also perpetuated by central mechanisms, with pathophysiologic targets (and possible treatments) including reorientation of dorsal horn terminals (desensitization techniques), functional reduction in inhibitory interneuron activity (tricyclic antidepressants, gabapentin, opioids), central sensitization and increased central excitability (gabapentin, topiramate, spinal cord stimulation, somatosensory blocks), impaired descending nociceptive inhibition (tricyclic antidepressants, opioids), and adaptive changes in the cortical centers underlying the sensory-discriminative and affective-motivational dimensions of pain (psychologic, physical, and occupational therapies). The treatment choices should be aimed at remodulating, normalizing, disrupting, or preventing the progression of abnormalities in pain processing. Sympathetic nerve blocks should be performed at least once to assess if sympathetically maintained pain is present. To the extent that peripheral somatosensory nerve blocks can diminish nociceptive input to the central nervous system, these techniques may help reduce the nociceptive sensitization of spinal neurons. Pain relief, however it is achieved and however temporary it is, is intended to facilitate participation in functional therapies to normalize use and to improve motion, strength, and dexterity. Psychologic therapies, such as biofeedback and cognitive-behavioral techniques targeting pain, stress, and mood disorders, are valuable adjunctive treatments for pain control and can facilitate functional improvement.

PMID: 14516527

Rating: 5a

Zambito A, Bianchini D, Gatti D, Viapiana O, Rossini M, Adami S. Interferential and horizontal therapies in chronic low back pain: a randomized, double blind, clinical study. Clin Exp Rheumatol. 2006 Sep-Oct;24(5):534-9.

Rheumatologic Rehabilitation, University of Verona, Italy.

OBJECTIVE: Chronic Low Back Pain (CLBP) is one of the most frequent medical problems. Electrical nerve stimulation is frequently used but its efficacy remains controversial. METHODS: Twenty-six men and 94 women with CLBP associated with either degenerative disk disease or previous multiple vertebral osteoporotic fractures were randomly assigned to either interferential currents (IFT), horizontal therapy (HT) or sham HT administered for 10, 40 and 40 minutes, respectively, daily for 5 days per week for two weeks together with a standard flexion-extension stretching exercise program, Blind efficacy assessment were obtained at baseline and at week 2, 6 and 14 and included a functional questionnaire (Backill), the standard visual analog scale (VAS) and the mean analgesic consumption. RESULTS: At week 2 a significant and similar improvement in both the VAS and Backill score was observed in all three groups. The Backill score continued to improve only in the two active groups with changes significantly greater than those observed in control patients at week 14. The pain VAS score returned to baseline values at week 6 and 14 in the control group while in the IFT and HT groups it continued to improve ($p < 0.01$ vs controls). The use of analgesic medications significantly improved at week 14 versus pretreatment assessment and over control patients only in the HT group. CONCLUSION: This randomized double-blind controlled study provides the first evidence that IFT and HT therapy are significantly effective in alleviating both pain and disability in patients with CLBP. The placebo effect is remarkable at the beginning of the treatment but it tends to vanish within a couple of weeks.

PMID: 17181922

Rating: 2b

Zambito A, Bianchini D, Gatti D, Rossini M, Adami S, Viapiana O. Interferential and horizontal therapies in chronic low back pain due to multiple vertebral fractures: a randomized, double blind, clinical study. Osteoporos Int. 2007 Nov;18(11):1541-5. Epub 2007 Jul 4.

Rheumatologic Rehabilitation, University of Verona, Verona, Italy.

SUMMARY: Chronic low back pain due to multiple vertebral fractures is of difficult management. Electrical nerve stimulation is frequently used, but its efficacy has never been properly evaluated. In a randomized placebo-controlled clinical trial, we have shown that both interferential currents and horizontal therapy are more effective than placebo for functional. INTRODUCTION: Multiple vertebral fractures almost invariably ensue in chronic low back pain that remains of difficult management. Electrical nerve stimulation is frequently used but its efficacy has never been properly evaluated. METHODS: One hundred and fifteen women with chronic back pain due to previous multiple vertebral osteoporotic fractures (CBPMF) were randomly assigned to either interferential currents (IFT), horizontal therapy (HT) or sham HT administered for 30 minutes daily for 5 days per week for two weeks together with a standard exercise program. Efficacy assessment was obtained at baseline and at week 2, 6 and 14 and included a functional questionnaire (Backill), the standard visual analog scale (VAS) and the mean analgesic consumption. RESULTS: At week 2 a significant and similar improvement in both the VAS and Backill score was observed in the three groups. The two scores continued to improve in the two active groups with changes significantly ($p < 0.001$) greater than those observed in control patients at week 6 and 14. The use of analgesic medications improved only in the HT group. CONCLUSION: This randomized double-blind controlled study provides the first evidence that IFT and HT therapy are significantly effective in alleviating both pain and disability in patients with CBPMF.

PMID: 17609842

Rating: 2b

Zammit G, Erman M, Wang-Weigand S, Sainati S, Zhang J, Roth T. Evaluation of the efficacy and safety of ramelteon in subjects with chronic insomnia. J Clin Sleep Med. 2007;3:495-504.

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OBJECTIVE: To evaluate efficacy and safety of ramelteon (MT1/MT2-receptor [corrected] agonist) in subjects with chronic primary insomnia. METHODS: Randomized, multicenter, double-blind, placebo-controlled trial of nightly ramelteon treatment (8 mg or 16 mg) in adults (N=405) with primary chronic insomnia (DSM-IV-TR). Latency to persistent sleep (LPS), TST, sleep efficiency, wake time after sleep onset, and number of awakenings were measured by polysomnography. Subject-reported measures were also assessed. RESULTS: LPS at Week 1 (primary measure) was significantly shorter with ramelteon 8 mg (32.2 min) or 16 mg (28.9 min) vs placebo (47.9 min; $p <0.001$). Significant improvements in LPS were maintained at Weeks 3 and 5. TST was significantly longer with both doses of ramelteon at Week 1 ($p <0.001$) vs placebo. Subject-reported sleep latency was significantly shorter with ramelteon 8 mg at Weeks 1, 3, and 5 ($p <0.001$) and ramelteon 16 mg at Weeks 1 and 3 ($p <$ or $=0.050$) vs placebo. Wake time after sleep onset and number of awakenings were not significantly different with ramelteon 8 mg or 16 mg treatment vs placebo. Subjective TST was significantly longer with ramelteon 8 mg at Weeks 1, 3, and 5 ($p <$ or $=0.050$) and ramelteon 16 mg at Week 1 ($p = 0.003$) vs placebo. Ramelteon had no

clinically meaningful effect on sleep architecture, next-morning psychomotor tasks, alertness, or ability to concentrate. No withdrawal or rebound effects were observed. CONCLUSIONS: Ramelteon reduced LPS over 5 weeks of treatment in subjects with chronic insomnia, with no clinically meaningful sleep architecture alterations, next-morning residual pharmacologic effects, and no evidence of rebound insomnia or withdrawal. No numerical differences were observed between the 2 doses of ramelteon.

Rating: 2c

Zaremba PD, Białek M, Błaszczyk B, Cioczek P, Czuczwar SJ. Non-epilepsy uses of antiepilepsy drugs. Pharmacol Rep. 2006;58:1-12.

Department of Pathophysiology, Skubiszewski Medical University of Lublin, Jaczewskiego 8, PL 20-090 Lublin, Poland.

Antiepileptic drugs (AEDs) affect various neurotransmitters (i.e. GABA, glutamate), receptors (i.e. GABAergic, glutamatergic), and ion channels (i.e. for sodium or calcium) which is responsible for their anticonvulsant activity. However, this broad spectrum of action may be also utilized in other pathological conditions. For example, both conventional and newer AEDs may be used in patients suffering from neuropathic pain, migraine, essential tremor, spasticity, restless legs syndrome and a number of psychiatric disorders (f.e. bipolar disease or schizophrenia). Also, isolated data point to their potential use in Parkinson's or Alzheimer's disease. There is experimental background indicating a potent neuroprotective efficacy of AEDs in numerous models of brain ischemia. However, the clinical data are very limited and this problem requires careful assessment.

PMID: 16531624

Review: 5b

Zhang W, Moskowitz RW, Nuki G, Abramson S, Altman RD, Arden N, Bierma-Zeinstra S, Brandt KD, Croft P, Doherty M, Dougados M, Hochberg M, Hunter DJ, Kwoh K, Lohmander LS, Tugwell P. OARSI recommendations for the management of hip and knee osteoarthritis, Part II: OARSI evidence-based, expert consensus guidelines. Osteoarthritis Cartilage. 2008;16:137-62.

University of Edinburgh, Osteoarticular Research Group, The Queen's Medical Research Institute, 47 Little France Crescent, Edinburgh EH16 4TJ, United Kingdom.

CONCLUSION: Twenty-five carefully worded recommendations have been generated based on a critical appraisal of existing guidelines, a systematic review of research evidence and the consensus opinions of an international, multidisciplinary group of experts.

PMID: 18279766

Rating: 6a

Zhang W, Doherty M, Leeb BF, Alekseeva L, Arden NK, Bijlsma JW, Dinçer F, Dziedzic K, Häuselmann HJ, Herrero-Beaumont G, Kaklamanis P, Lohmander S, Maheu E, Martín-Mola E, Pavelka K, Punzi L, Reiter S, Sautner J, Smolen J, Verbruggen G, Zimmermann-Górska I. EULAR evidence based recommendations for the management of hand osteoarthritis: report of a Task Force of the EULAR Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT). Ann Rheum Dis. 2007;66:377-88.

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CONCLUSION: Eleven key recommendations for treatment of hand OA were developed.

PMID: 17046965

Rating: 6a

Zwanzger P, Diemer J, Jabs B. Comparison of combined psycho- and pharmacotherapy with monotherapy in anxiety disorders: controversial viewpoints and clinical perspectives. J Neural Transm. 2008 Sep 23. [Epub ahead of print]

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Anxiety disorders are among the most frequent psychiatric disorders. Experimental evidence supports both psychotherapy as well as pharmacotherapy as effective treatments. There is, however, a controversy concerning the efficacy of a combination of both approaches. While some studies suggest that combined treatment enhances efficacy, others report conflicting results. This article traces the positions in this debate. We present the results from two recent meta-analyses and discuss implications for clinical practice and further research. We suggest that a research strategy that strives to establish differential indications based on patient characteristics should be preferred over attempts to reach a global judgement of the question, which appears too simplistic given the complexity of the issue.

PMID: 18810307

Rating: 5a