

Treatments for Acute Pain: A Systematic Review

Evidence Summary



Main Points

- Opioids are probably less effective than nonsteroidal anti-inflammatory drugs (NSAIDs) for surgical dental pain and kidney stone pain and might be similarly effective to NSAIDs for low back pain.
- Opioids might be and NSAIDs are probably more effective than acetaminophen for surgical dental pain, but opioids are probably less effective than acetaminophen for kidney stone pain.
- An opioid might be more effective than gabapentin for acute neuropathic pain.
- Opioids are probably associated with increased risk of short-term adverse events versus nonopioid pharmacologic therapy for acute pain, including any adverse event, study withdrawal due to adverse events, nausea, dizziness, and somnolence, but serious adverse events are uncommon in randomized trials.
- Being prescribed an opioid for acute low back pain or postoperative pain might be associated with increased likelihood of use of opioids at long-term followup versus not being prescribed.
- Heat therapy is probably effective for acute low back pain, spinal manipulation might be effective for acute back pain with radiculopathy, massage might be effective for postoperative pain, and a cervical collar or exercise might be effective for acute neck pain with radiculopathy.
- Research is very limited on the comparative effectiveness of therapies for sickle cell pain, acute neuropathic pain, neck pain, and management of postoperative pain following discharge.



Background and Purpose

The purpose of this review is to evaluate the effectiveness and comparative



effectiveness of opioid, nonopioid pharmacologic, and nonpharmacologic therapy in patients with specific types of acute pain, including effects on pain, function, quality of life, adverse events, and long-term use of opioids.



Methods

Electronic databases (Ovid[®] MEDLINE[®], PsycINFO[®], Embase[®], the Cochrane Central Register of Controlled Trials, and the Cochrane Database of Systematic Reviews) were searched through August 5, 2020 for relevant publications. Searches were supplemented by reviewing reference lists and a Federal Register Notice.

Randomized controlled trials (RCTs) of opioid therapy versus nonopioid pharmacologic or nonpharmacologic therapy, nonopioid therapy versus nonpharmacologic therapy, nonpharmacologic therapy versus inactive controls (placebo, sham therapy, attention control, or a minimal intervention), and head-to-head trials of nonopioid pharmacologic and nonpharmacologic therapy were selected using predefined criteria and dual review. Observational studies on the association between being prescribed opioids for acute pain versus no opioids and on factors influencing opioid prescribing for acute pain conditions were also included. This review focused on eight acute pain conditions: low back pain, neck pain, other musculoskeletal pain, neuropathic pain, postoperative pain (excluding inpatient management of pain after major surgical procedures), dental pain, pain due to kidney stones, and pain due to sickle cell disease. The review focused on outpatient management or therapy initiated shortly before discharge (e.g., after surgery or in emergency department). Outcomes were analyzed at <1 day, 1 day to <1 week, 1 week to <2 weeks, 2 to <4 weeks, and ≥ 4 weeks. Meta-analyses were conducted on pharmacologic therapy for dental pain and kidney stone pain and likelihood of repeat or rescue medication use and adverse events. Otherwise, meta-analyses were not conducted due to small number of studies, methodological limitations and study heterogeneity. The magnitude of effects was classified as small, moderate or large using previously defined criteria, and strength of evidence was assessed.



Results

The review included 183 RCTs on the comparative effectiveness of therapies for acute pain. Most studies had methodological limitations. Evidence did not suggest an increased risk of serious harms for any intervention, though studies were not designed to assess serious harms. Effect sizes were primarily small to moderate for pain, the most commonly evaluated outcome. Evidence on how benefits or harms varied in subgroups was lacking. Main findings (focusing on effects on pain) are summarized by acute pain condition.

Low back pain (38 trials): Evidence indicated that there might be no difference between an opioid versus an NSAID and there might be no difference versus a muscle relaxant. Opioids were associated with increased risk of short-term adverse events (any adverse event, study withdrawal due to adverse events, dizziness and nausea) for both comparisons. Serious adverse events were uncommon, but studies were not designed to assess risk of overdose, opioid use disorder, or long-term harms. Being prescribed

opioids might be associated with increased risk of long-term use versus not being prescribed, based on observational studies. Muscle relaxants might be associated with small to moderate improvement versus benzodiazepines. There might be no difference between an NSAID or muscle relaxant versus manipulation at 1 to <2 weeks, 2 to <4 weeks, or ≥ 4 weeks. Acupuncture might be associated with moderate decrease in pain and improved function at 2 to <4 weeks and at 4 weeks. Exercise might be associated with similar effects compared with usual care and probably associated with similar effects compared with bed rest at 1 week to 52 weeks, but might be associated with fewer sick days compared with bed rest at 3 and 12 weeks. Effects of traditional acupuncture varied depending on the type of sham control evaluated. There might be no difference between a brace versus no brace for acute pain associated with osteoporotic compression fracture at 2 to <4 weeks and at ≥ 4 weeks. Heat therapy was probably associated with moderate decrease in pain versus usual care or placebo at 1 day to <1 week and 2 to <4 weeks. There might be no difference between manipulation versus inactive controls at 1 day to <1 week and ≥ 4 weeks. Manipulation might be associated with increased likelihood of improvement in pain in patients with radiculopathy versus sham at 2 to <4 weeks and ≥ 4 weeks.

Neck pain (5 trials): No trial evaluated pharmacologic therapy for acute neck pain. For neck pain with radiculopathy, a cervical collar or exercise might be associated with moderate to large decreases in pain versus usual activity at 2 to <4 weeks and at ≥ 4 weeks; effects of a collar and exercise were similar. For whiplash neck sprain, there might be no difference between ultrasound versus sham at 1 to <2 weeks, and there might be no difference between a cervical collar versus usual activity or exercise at ≥ 4 weeks. Evidence on other nonpharmacologic therapies for nonradicular neck pain was lacking.

Other musculoskeletal pain (30 trials): Evidence on opioids versus NSAIDs was insufficient. An NSAID and acetaminophen were probably associated with similar effects for acute musculoskeletal injury (sprains, strains, minor trauma) at <1 day, at 1 day to <1 week, at 1 to <2 weeks, and at ≥ 4 weeks. There might be no difference between ultrasound versus sham for ankle sprain. Acupressure might be associated with moderate to large decreases in pain at 1 day to <1 week and with small effects at 4 weeks compared with sham acupressure or usual care. Evidence on other nonpharmacologic therapy was insufficient.

Peripheral neuropathic pain (2 trials): An opioid might be associated with increased likelihood of improvement in pain versus gabapentin for acute herpes zoster at 1 to <2 weeks and at ≥ 4 weeks, and increased likelihood of constipation. Evidence for acute neuropathic pain was otherwise lacking.

Postoperative pain (47 trials): Trials of postoperative pain focused on treatment in the immediate postoperative period, usually prior to discharge. A multidose course of opioids was probably associated with increased likelihood of repeat or rescue medication use versus an NSAID at <1 day. Opioids might be associated with increased risk of study withdrawal due to adverse events versus acetaminophen. Being prescribed an opioid for elective or minor surgery might be associated with increased likelihood of long-term use versus not being prescribed. Legislation mandating the use of prescription drug monitoring data and an opioid risk assessment tool might not decrease opioid prescribing. Auricular acupressure might be associated with decreased pain medication use versus sham at <1 day and 1 day to <1 week. There might be no difference between cold therapy

versus sham in pain at 1 day to <1 week, 2 to <4 weeks or ≥ 4 weeks, though cold therapy was associated with decreased pain medication use at <1 weeks. Massage might be associated with moderate to large decrease in pain intensity at <1 day and decreased pain medication use versus no massage. Single trials suggest that exercise or transcutaneous electrical nerve stimulation (TENS) following specific surgical procedures might reduce pain versus no exercise or sham TENS.

Dental pain (46 trials): A single dose of an opioid plus acetaminophen might be associated with decreased pain and decreased likelihood of rescue or repeat medication use at <1 day versus acetaminophen, and probably is associated with increased risk of adverse events. An opioid plus acetaminophen or NSAID is probably associated with a small to moderate increase in pain intensity versus an NSAID at <1 day and increased likelihood of rescue or repeat medication use (NSAID doses were lower in the opioid arm than the NSAID-only arm in some trials); opioids were probably associated with increased likelihood of adverse events. NSAIDs are probably associated with moderate to large decrease in pain versus acetaminophen at <1 day, decreased likelihood of rescue or repeat medication use, and decreased risk of adverse events. Evidence on nonpharmacologic therapy was insufficient.

Kidney stone pain (12 trials): A single dose of morphine is probably associated with increased likelihood of persistent pain at <1 day, decreased likelihood of pain relief, increased likelihood of rescue medication use, and increased likelihood of adverse events versus an NSAID. Findings were similar for a single dose of meperidine, though this medication is discouraged due to concerns about adverse events. NSAIDs might be associated with decreased likelihood of rescue medication use versus acetaminophen. Acupuncture might be associated with moderately increased pain intensity versus a single dose of an NSAID or acetaminophen at <1 day.

Sickle cell pain (3 trials): Evidence was insufficient from three small trials with methodological limitations.



Limitations

We excluded non-English language articles and did not search for studies published only as abstracts. We did not conduct statistical and graphical methods for assessing for small sample effects (a potential marker for publication bias) due to small numbers of trials and heterogeneity in study design methods, patient populations, and outcomes.

The evidence base had important limitations. First, there was very little evidence for sickle cell pain, acute neuropathic pain, and neck pain. Evidence was also limited for musculoskeletal pain other than low back pain and kidney stone pain. Additionally, trials were not designed to evaluate how benefits and harms varied in subgroups. Patients with a history of substance use disorder, who represent an important clinical challenge, were often excluded from trials, and trials were not designed to evaluate how benefits and harms varied according to opioid dose or amount prescribed. Evidence on the accuracy and effectiveness of risk assessment instruments was unavailable, and evidence on how risk mitigation strategies, patient education, and other factors impact prescribing of opioids was very limited.



Implications and Conclusions

Opioid therapy was associated with decreased or similar effectiveness for pain versus an NSAID for surgical dental pain, kidney stone pain, and low back pain. Opioids and NSAIDs were more effective than acetaminophen for pain for surgical dental pain, but opioids were less effective than acetaminophen for kidney stone pain. Being prescribed an opioid for acute low back pain or postoperative pain was associated with increased likelihood of use of opioids at long-term followup versus not being prescribed, based on observational studies. With regard to nonpharmacological therapies, heat therapy is probably effective for acute low back pain, spinal manipulation is probably effective for acute back pain with radiculopathy, acupuncture might be effective for acute low back pain, massage might be effective for postoperative pain, acupressure might be effective for acute musculoskeletal pain, and a cervical collar or exercise might be effective for acute neck pain with radiculopathy. Research is needed to determine the comparative effectiveness of therapies for sickle cell pain, acute neuropathic pain, neck pain, and management of postoperative pain following discharge; effects of therapies for acute pain on non-pain outcomes; effects of therapies on long-term outcomes; and how benefits and harms of therapies vary in subgroups.

Full Report

Chou R, Wagner J, Ahmed AY, Blazina I, Brodt E, Buckley DI, Cheney TP, Choo E, Dana T, Gordon D, Khandelwal S, Kantner S, McDonagh MS, Sedgley C, Skelly AC. Treatments for Acute Pain: A Systematic Review. Comparative Effectiveness Review No. 240. (Prepared by the Pacific Northwest Evidence-based Practice Center under Contract No. 290-2015-00009-I.) AHRQ Publication No. 20(21)-EHC006. Rockville, MD: Agency for Healthcare Research and Quality; December 2020. DOI: <https://doi.org/10.23970/AHRQEPCCER240>. Posted final reports are located on the Effective Health Care Program [search page](#).

