Cochrane for Clinicians

Putting Evidence Into Practice

Oral NSAIDs vs. Other Oral Analgesic Agents for Acute Soft Tissue Injury

Karl T. Clebak, MD, MHA, FAAFP, Penn State Health M. S. Hershey Medical Center, Hershey, Pennsylvania

Lynn K. Weaver, MD, University of Massachusetts-Amherst, Amherst, Massachusetts

Jason R. Croad, DO, Penn State Health M. S. Hershey Medical Center, Hershey, Pennsylvania

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Clinical Question

Are oral nonsteroidal anti-inflammatory drugs (NSAIDs) superior to other oral analgesics for the treatment of pain associated with acute soft tissue injuries?

Evidence-Based Answer

There is no difference in effectiveness between NSAIDs and other pain relievers, including acetaminophen and opioids, for pain reduction in patients younger than 65 years who have acute strains and sprains.[1] (Strength of Recommendation: B, inconsistent or limited-quality patient-oriented evidence.)

Practice Pointers

More than 65 million health care visits for musculoskeletal injuries occur annually in the United States.[2] NSAIDs are commonly recommended to reduce pain and inflammation related to these injuries, but they are associated with gastrointestinal, renal, and cardiovascular adverse effects.[3,4] The authors of this Cochrane review sought to determine whether NSAIDs are superior to other agents for treating pain related to acute soft tissue injuries.

The review included 20 randomized or quasi-randomized controlled trials involving 3,305 participants with acute soft tissue injury, defined as a sprain, strain, or contusion of a joint, ligament, tendon, or muscle occurring within the past 48 hours.[1] Eleven studies (n = 1,853) compared NSAIDs with acetaminophen, six studies (n = 1,212) compared NSAIDs with opioids, and four studies (n = 240) compared NSAIDs with the combination of acetaminophen and an opioid. Seven of the studies included patients with ankle sprains only. Three studies included children only (n = 360; six to 17 years of age), and the remaining studies included predominantly young adults. Although studies may have included participants older than 65 years, only one study reported data in that age group that could be aggregated. The average age of participants across all comparisons was 20 to 35 years. Studies were completed in a variety of locations, including primary care clinics, emergency departments, student health centers, sports medicine clinics, research facilities, orthopedic clinics, urgent care centers, and rheumatology clinics. The primary outcome investigated was pain. Secondary outcomes included swelling, function, and adverse effects.

No significant differences were noted between NSAIDs and acetaminophen in pain measured with a visual analog scale at one to two hours, one to three days, or seven days or more following treatment.

There was no difference in pain response for patients treated with NSAIDs vs. those treated with opioids. NSAIDs did not appear to improve swelling compared with opioids, but this conclusion is based on very limited participant numbers. Participants treated with NSAIDs were more likely than those treated with opioids to return to function in seven to 10 days (relative risk [RR] = 1.13 [95% CI, 1.03 to 1.25]; number needed to treat = 11 [95% CI, 6.2 to 43]; n = 749). The NSAID group was less likely than the opioid group to develop gastrointestinal adverse effects (RR = 0.48 [95% CI, 0.36 to 0.62]; number needed to harm [NNH] = 12 [95% CI, 7.7 to 23]; n = 1,151) or neurologic adverse effects (RR = 0.40 [95% CI, 0.30 to 0.53]; NNH = 10 [95% CI, 7.0 to 17]; n = 1,151). Studies comparing NSAIDs with the combination of acetaminophen and an opioid showed no difference in pain response at day 1, days 1 to 3, or day 7 or later.

These findings are consistent with recent guidelines by the American College of Physicians and the American Academy of Family Physicians, which suggest that patients should use topical or oral NSAIDs or acetaminophen rather than opioids for acute musculoskeletal pain not involving the back.[5]

Editor's Note: The NNHs, number needed to treat, and related CIs reported in this Cochrane for Clinicians were calculated by the authors based on raw data provided in the original Cochrane review.

The practice recommendations in this activity are available at https://www.cochrane.org/CD007789

These are summaries of reviews from the Cochrane Library.

This series is coordinated by Corey D. Fogleman, MD, assistant medical editor.

A collection of Cochrane for Clinicians published in *AFP* is available at https://www.aafp.org/afp/cochrane.

CME This clinical content conforms to AAFP criteria for CME. See CME Quiz on page 15.

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Medical Methods for First-Trimester Abortion

Donna Cohen, MD, MSc, and Lisa Golden, MD

Family and Community Medicine Residency Program, Lancaster, Pennsylvania

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Clinical Question

What are the effectiveness, safety, and adverse effects of different medical methods for first-trimester abortion?

Evidence-Based Answer

There is moderate-quality evidence that a combined regimen of mifepristone and misoprostol is more effective than misoprostol alone for medication abortions before 12 weeks of gestation. (Strength of Recommendation [SOR]: B, inconsistent or limited-quality patient-oriented evidence.) The effectiveness of this regimen is no different with a mifepristone dose of 200 mg compared with 600 mg. (SOR: B, inconsistent or limited-quality patient-oriented evidence.) Vaginal administration of misoprostol is more effective than oral administration. (SOR: B, inconsistent or limited-quality patient-oriented evidence.) Adverse effects are typically self-limited and commonly include nausea, vomiting, and diarrhea. Major complications are rare.[1]

Practice Pointers

In the United States, 20% of pregnancies, excluding miscarriages, end in abortion,[2] and more than one-half of abortions provided by U.S. facilities use medication rather than surgery.[3] Many regimens have been used worldwide for medication abortion, most commonly prostaglandins, mifepristone, or a combination. Within these regimens, widely varying dosages, timing, and routes of administration have been used. The objective of this Cochrane review was to compare the effectiveness and adverse effects of different regimens.

The Cochrane review included 99 randomized trials examining patients 18 years and older undergoing medication abortion in the first trimester. Most studies were conducted in high-income countries where patients had access to medical follow-up. Because of the many combinations of medication regimens, the studies were grouped to evaluate 24 different comparisons via meta-analysis. The main outcome measured was the failure to achieve complete abortion within two weeks of a medication abortion. Overall, there was a low rate of major complications; the need for blood transfusion was the most severe complication and occurred less than 1% of the time.

Combination regimens were more effective than misoprostol alone (relative risk [RR] = 2.39; 95% CI, 1.89 to 3.02), regardless of the route of misoprostol administration. Combination regimens included misoprostol combined with mifepristone, letrozole, estradiol, tamoxifen, or methotrexate. In patients treated with the combined regimen of misoprostol and mifepristone, no significant differences were noted between 600-mg and 200-mg doses of mifepristone (RR = 1.07; 95% CI, 0.87 to 1.33). Significantly lower failure rates occurred in patients who received 800 mcg of misoprostol compared with 400 mcg (RR = 0.63; 95% CI, 0.51 to 0.78) after treatment with mifepristone. Because studies are limited, no definitive conclusions could be drawn regarding alternative regimens, such as those using methotrexate or tamoxifen combined with prostaglandins.

There was variability among trials in the timing of the misoprostol dose after mifepristone administration. In patients treated with misoprostol one day after receiving mifepristone, complete abortion was less likely to fail vs. patients who took misoprostol six hours after mifepristone (RR = 0.65; 95% CI, 0.46 to 0.91). Overall failure rates were similar in all estimated gestational ages when comparing administration of misoprostol one day after mifepristone vs. two days after mifepristone. In pregnancies with an estimated gestational age of more than 49 days, failure rates were higher when misoprostol was administered on day 2 compared with day 1 (RR = 1.57; 95% CI, 1.09 to 2.27).

When comparing routes of administration of misoprostol in combination with mifepristone, the vaginal route was significantly more effective than the oral route (RR = 2.38; 95% CI, 1.46 to 3.87). Sublingual misoprostol was more effective than oral misoprostol (RR = 0.26; 95% CI, 0.10 to 0.68). Patients treated with vaginal medication were less likely to experience gastrointestinal adverse effects than those treated with oral, buccal, and sublingual medication, although this trend was not statistically significant.

Practice guidelines from the American College of Obstetricians and Gynecologists, Society of Family Planning, and National Abortion Federation recommend first-trimester medication abortions as a safe and effective method of ending an undesired pregnancy.[4,5] These guidelines support the

use of 200-mg mifepristone, when available, and mifepristone combined with misoprostol over a regimen of misoprostol alone. The American College of Obstetricians and Gynecologists recommends against oral administration of misoprostol because of possible lower effectiveness.[4] Most trials in the Cochrane review required confirmation of intrauterine pregnancy by ultrasonography, availability of emergency back-up facilities, and close medical follow-up, which may limit the applicability of these findings to resource-poor settings or in patients pursuing self-managed abortions.

Editor's Note: We strive to provide the best available evidence to counsel patients presenting with undesired pregnancy but recognize this is a controversial topic.—Sumi Sexton, MD, Editor-in-Chief

The practice recommendations in this activity are available at https://www.cochrane.org/CD002855.

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