

# Systematic Review Snapshot

## *Clinical Synopsis*

### TAKE-HOME MESSAGE

Topical nonsteroidal anti-inflammatory drugs effectively reduce pain associated with musculoskeletal conditions compared with placebo, with fewer adverse events compared with oral nonsteroidal anti-inflammatory drugs.

## METHODS

### DATA SOURCES

The authors searched the Cochrane Central Register of Controlled Trials (CENTRAL) (*Cochrane Library*, 2009, issue 4), MEDLINE (to December 2009), EMBASE (to December 2009), Oxford Pain Relief Database, and the authors' in-house database. Unpublished studies were sought by searching online clinical trial registers and manufacturers' Web sites.

### STUDY SELECTION

Randomized placebo-controlled trials including adults (>16 years of age) with acute musculoskeletal injuries (sprains, strains, overuse injuries) were analyzed. The primary outcome was a 50% reduction in pain measured on a categorical scale. Studies describing topical salicylates were not included in this review because they are no longer classified as topical nonsteroidal anti-inflammatory drugs. Only patient-reported outcomes were included in this review and investigator-reported outcomes were not used.

### DATA EXTRACTION AND SYNTHESIS

Quality of study methodology was assessed independently by 2 investigators. Data comparing topical nonsteroidal anti-inflammatory drugs with placebo were analyzed with a fixed-effects model and were expressed as a relative risk (RR) with 95% confidence intervals.

## Should Topical Nonsteroidal Anti-inflammatory Drugs Be Used to Treat Acute Musculoskeletal Conditions?

### EBEM Commentators

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### Results

Performance of topical nonsteroidal anti-inflammatory drugs versus placebo in acute musculoskeletal injuries.

	Studies (Total No. of Patients)	Treatment Benefit,* RR (95% CI)	Adverse Event, <sup>†</sup> RR (95% CI)	P, %
Topical NSAID vs placebo	31 (3,462)	1.5 (1.4–1.6)	1.1 (0.88–1.4)	74

RR, Relative risk; CI, confidence interval; NSAID, nonsteroidal anti-inflammatory drug.

\*Defined as a reduction in pain by at least 50%.

<sup>†</sup>Included local (eg, skin irritation) and systemic events.

### Commentary

Patients with acute musculoskeletal and overuse injuries commonly present to the emergency department. Although oral nonsteroidal anti-inflammatory drugs effectively treat pain from acute injury, they can be associated with severe adverse drug effects such as gastrointestinal hemorrhage and renal impairment. Several clinical trials have demonstrated that topical nonsteroidal anti-inflammatory drugs effectively inhibit cyclooxygenase-2 at the tissue and joint level while reducing pain and adverse events compared with oral nonsteroidal anti-inflammatory drugs.<sup>1-4</sup> Despite these observations, the routine use of topical nonsteroidal anti-inflammatory drugs remains controversial.

Although topical nonsteroidal anti-inflammatory drugs are relatively unknown in the United States, having gained approval by the Food and Drug Administration only in 2007, they are popular in western Europe, as evidenced by 3.8 million prescriptions in 2009.<sup>5</sup> In England, topical nonsteroidal anti-inflammatory drugs are recommended as the first-line therapy for osteoarthritis.<sup>6</sup> According to the Food and Drug Administration, topical diclofenac is the only available topical nonsteroidal anti-inflammatory drug in the United States from the list of those included in this review.<sup>7</sup> This Cochrane review demonstrated that topical nonsteroidal anti-inflammatory drugs, compared with placebo, provide adequate

pain relief in acute musculoskeletal injuries, have no increased risk of local skin reactions, and do not cause the systemic problems commonly observed with oral nonsteroidal anti-inflammatory drugs.

With an estimated number needed to treat of 5 when compared with placebo, topical nonsteroidal anti-inflammatory drugs can be a useful adjunct in the treatment of acute musculoskeletal injuries, especially in patients at risk for systemic adverse events or intolerance to oral nonsteroidal anti-inflammatory drugs.

The search identified 72 potential studies and 47 trials met inclusion criteria. Of the 47 studies (all randomized placebo-controlled trials), 31 compared a topical nonsteroidal anti-inflammatory drug with placebo, 12 compared a topical nonsteroidal anti-inflammatory drug with an active comparator (different topical nonsteroidal anti-inflammatory drug, an oral nonsteroidal anti-inflammatory drug, or the same topical nonsteroidal anti-inflammatory drug in a different formulation), and 4 had both placebo and active compar-

tors. The topical nonsteroidal anti-inflammatory drugs included in this review were piroxicam, indomethacin, diclofenac, ketoprofen, ibuprofen, benzydamine, etofenamate and ketorolac. Study participants were treated for at least 6 days and up to 3 weeks, with the majority of studies lasting 7 to 14 days. There were insufficient data for meta-analysis of studies comparing a topical nonsteroidal anti-inflammatory drug with an active comparator. In 2 of the 3 studies directly comparing a topical nonsteroidal anti-inflammatory drug with an oral nonsteroidal anti-inflammatory drug, the oral nonsteroidal anti-inflammatory drug demonstrated superior pain relief. Ten studies were deemed to be adequately concealed, whereas concealment was unclear in the remaining 37. No studies were identified as being at high risk of methodological bias.

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*Cochrane Database Syst Rev.* 2010;(6):CD007402.

4. Simon LS. Do topical NSAIDs work? *Nat Clin Pract Rheumatol.* 2008;4:458-459.
5. The NHS Information Centre, Prescribing Support Unit. *Prescription Cost Analysis, England 2009.* Leeds, UK: NHS Information Centre; 2009.
6. The care and management of osteoarthritis in adults 2008. Available at: <http://www.nice.org.uk/CG059fullguideline>. Accessed May 1, 2011.
7. FDA approved medications in the United States. Available at: <http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm>. Accessed May 1, 2011.

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