Review: Topical nonsteroidal anti-inflammatory drugs are effective and safe for pain


Question
On the basis of meta-analysis, are topical nonsteroidal anti-inflammatory drugs (NSAIDs) effective and safe for patients with acute and chronic painful conditions?

Data sources
Studies were identified from MEDLINE (1966 to 1996), EMBASE (1981 to 1996), and the Oxford Pain Relief Database (1950 to 1994) using generic and proprietary drug names combined with the search terms administration, topical; gel; ointment; aerosol; and cream. Bibliographies of relevant papers were reviewed, and 12 U.K. pharmaceutical companies were contacted.

Study selection
Randomized controlled trials (RCTs) were selected if they examined the effect of NSAIDs on pain outcomes in acute (strains, sprains, and sports injuries) and chronic (arthritis and rheumatism) conditions. Trials done in experimental settings and those with no concealment of patient allocation were excluded.

Data extraction
Data were extracted on study design, treatment and control conditions, number of patients randomized and analyzed, observation periods, outcome measures, analgesic outcome, local skin irritation, systemic adverse effects, and study withdrawal because of adverse effects. A clinically relevant successful outcome was defined on the basis of a hierarchy of measures (excellent or good by patient global judgment; no or slight pain on movement; no or slight spontaneous or at-rest pain; and excellent or good by physician global judgment).

Main results
86 studies (10,160 patients) met the inclusion criteria. Only studies with dichotomous outcomes (n = 76) were included in the meta-analyses. 47 placebo-controlled trials involving acute painful conditions were identified. 71% of 1747 patients allocated to treatment had a successful outcome compared with 39% of 1492 patients allocated to placebo (4 patients would need to be treated [number needed to treat (NNT)] with a topical NSAID for 1 additional patient to achieve a successful outcome, 95% CI 4 to 5). Meta-analysis of data on individual drugs (≥ 3 studies for each drug) showed that ketoprofen, felbinac, ibuprofen, and piroxicam were better than placebo, but indomethacin and benzydamine were not.

Data from 12 of 13 placebo-controlled trials involving chronic painful conditions were analyzed. 65% of 547 patients allocated to treatment had a successful outcome compared with 30% of 350 patients allocated to placebo (NNT 4, CI 3 to 4). Effectiveness of individual drugs for chronic painful conditions was not included in the meta-analysis because of an insufficient number of trials. For both acute and chronic painful conditions, the groups did not differ for local or systemic adverse effects or patient withdrawals because of adverse effects.

Conclusion
Topical nonsteroidal anti-inflammatory drugs are effective and safe for acute and chronic painful conditions.

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Commentary
Although the side effects of NSAIDs have been known for a long time, these drugs are still widely used and remain one of the most important causes of serious adverse drug reactions, such as acute gastrointestinal bleeding, ulcer perforation, renal impairment, and congestive heart failure. Most of the drugs in common use are nonselective in that they inhibit 2 isoforms of cyclo-oxygenase, COX-1 and COX-2. Inhibition of COX-1 is assumed to be the cause of most of the major toxicity. Development of selective COX-2 inhibitors may improve the safety of this class of drug. Although they are quite potent anti-inflammatory drugs, nonselective NSAIDs are often used for general pain relief and doubts have been raised about the benefit-to-harm ratio when these drugs are widely used in the community. Topical NSAIDs have not really been taken seriously, and it has been assumed that they are ineffective. The systematic review by Moore and colleagues shows, using a clinically relevant outcome, that topical NSAIDs have a modest effect in the treatment of both acute pain and chronic inflammatory processes.

Other research has shown that the risk for gastrointestinal bleeding with topical NSAIDs is low. The question remains whether the apparent safety of topical NSAIDs is because of the low systemic availability of the products and the resultant low blood levels. If so, a similar benefit-to-harm ratio may be achieved by using lower doses of conventional oral NSAIDs. Nevertheless, topical NSAIDs are reasonably effective and safer than oral NSAIDs in conventional doses. It is hoped that this knowledge will lead to increased use of topical NSAIDs for inflammatory pain of mild-to-moderate severity and will reduce the use of conventional oral NSAIDs.

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Reference