Topical Nonsteroidal Anti-Inflammatory Drugs for Chronic Musculoskeletal Pain in Adults

Helen McVeigh, MA, BSc(Hons), RNT, RGN

Objective

To assess the efficacy and safety of different topical NSAIDs compared with oral NSAIDs and a placebo in the treatment of chronic musculoskeletal pain.

Type of Review

An interventional review of the evidence for the treatment of any chronic pain with a topical NSAID and one of a series of systematic reviews on the use and efficacy of topical analgesics.

Relevance to Nursing

Chronic pain can be debilitating and adversely affect quality of life. Pain management and support for patients living with chronic pain is an essential part of holistic nursing care. Topical NSAIDs increasingly are used for pain relief, with their use as a primary treatment option recommended by the National Collaborating Centre for Chronic Conditions (2008). Osteoarthritis (OA) is the most common type of joint disease and a primary cause of pain and physical disability in older adults. Nurses need to be able to identify medications that are effective in the relief of chronic pain. A wider variety of topical NSAIDs is becoming available, and evidence-based practice must guide choices on efficacy. Therefore, a systematic review was warranted.

Characteristics of the Evidence

This review included 34 randomized double-blind controlled trials involving 7,688 participants. Participants were aged 16 years or older with chronic musculoskeletal pain (chronic not defined), most with a diagnosis of primary OA of the knee or hand confirmed by independent radiologic examination prior to trial commencement. Participants were excluded for pregnancy or lactation, known sensitivity to NSAIDs, coexistent skin disease at site of application, secondary OA, or systemic inflammatory disease.

To be eligible for inclusion, participants had to have been treated with a topical NSAID or comparator for at least two weeks with at least 10 participants per treatment arm. Topical NSAIDs had to be applied at least once per day. Twenty-three of the 34 studies compared topical NSAIDs with a placebo, three studies compared topical NSAIDs with a placebo and oral NSAIDs, three with only an oral NSAID, and two compared topical NSAIDs with a different topical NSAID. One study compared a topical NSAID with a placebo and a non-NSAID topical treatment, and two compared a topical NSAID with a non-NSAID topical treatment. A variety of different topical NSAIDs were used within the studies, including diclofenac, ketoprofen, piroxicam, felbinac, flurbiprofen, piroxicam, nimesulide, flufenamate, indomethacin, and ibuprofen applied as solutions, gels, or patches; 17 studies used diclofenac. Treatment application was defined as application of a set quantity of gel or solution or a patch. Actual dose of the medication was not normally calculated but was defined in terms of number of treatments per day and a specified quantity of agent. Administered oral NSAIDs were all in tablet form. Difficulties in calculation of the topical application dose meant that comparisons between studies were not possible. Outcome analysis of the study data used calculations of relative risk (RR), numbers needed to treat (NNT), or numbers needed to harm.

Methodologic quality of included studies was assessed using a five-point scale that considered randomization, blinding, and study withdrawal and dropouts. A risk of bias tool was used to report on allocation of concealment, sequence generation, blinding, and additional risks such as study size and missing data.

Outcomes of interest were clinical success (defined as a 50% reduction in pain or an equivalent measure), adverse events (local or systemic), and number of withdrawals (whether through lack of efficacy or adverse event). Only patient-reported outcomes were used, although measurement tools for documenting pain were varied.

Summary of Key Evidence

Results were presented according to clinical success, any topical NSAID versus placebo (subdivided according to study duration: 2–3, 4–6, or 8–12 weeks), topical NSAID versus active comparator, and adverse events. The following results were obtained.

- For clinical success comparing topical NSAIDs with placebo, data were insufficient to compare any individual topical NSAID other than diclofenac.
  The NNT for successful treatment with diclofenac in studies of 2–3 weeks duration (n = 4) was 5 (95% confidence interval 3.5–10).
No difference in efficacy was found when topical NSAIDs were compared with oral NSAIDs (n = 5). The proportion of participants experiencing successful treatment was 55% (range = 40%-66%) for topical NSAIDs and 54% (range = 34%-70%) for oral NSAIDs.

Data were insufficient for meta-analysis of studies comparing topical NSAIDs and a different topical treatment.

When topical NSAIDs were compared with placebo, local adverse events were reported in 25 studies. For example, skin irritation, including dry skin, itch or pruritis, and redness or erythema, occurred where the NSAID had been applied. These usually were described as mild or transient. Local adverse events were more likely to occur with topical NSAIDs than with placebo; this was statistically significant for topical diclofenac (n = 13) (RR = 1.8, 95% CI [1.5, 2.2]) and was just short of significant for all other NSAIDs.

Systemic adverse events were reported in 12 of the NSAIDs versus placebo studies. Events usually were described as mild and included diarrhea, headache, drowsiness, and dyspepsia. No significant difference was found in participants experiencing systemic adverse events using topical NSAIDs rather than a placebo for either topical diclofenac or all other topical NSAIDs.

Gastrointestinal (GI) adverse events were reported for six studies in the topical versus oral NSAIDs, the proportion of patients experiencing a GI adverse event was 17% with a topical NSAID and 26% with an oral NSAID (RR = 0.66, 95% CI [0.56, 0.77]).

Four studies reported serious adverse events. Of these, one event (deep vein thrombosis) was recorded as related to topical diclofenac.

Withdrawal because of adverse events showed a statistically significant benefit for topical diclofenac (n = 12) when compared to placebo (RR = 1.55, 95% CI [1.14, 2.11]) but not for other topical NSAIDs (n = 7).

Lack of efficacy was reported in 18 studies. Significantly fewer participants withdrew in studies comparing topical diclofenac to a placebo (RR = 0.59, 95% CI [0.47, 0.75]).

Risk of bias assessment indicated that short study duration and small trial size tended to overestimate treatment effect. More recent studies were more likely to be of longer duration (from 4-12 weeks), larger, and of higher reporting quality.

Best Practice Recommendations

Results from the Cochrane Systematic Review indicate that topical NSAIDs are similarly effective to those of oral NSAIDs. Specifically, the efficacy of topical diclofenac in solution was shown as similar to that of oral diclofenac in the treatment of OA of the hand or knee. Study evidence to support topical NSAIDs in other chronic painful conditions is lacking; therefore, the indications from the review only relate to OA.

Topical NSAIDs are associated with an increase in local adverse events, but these are generally mild in nature. The overall evidence points to a lower incidence of systemic adverse events in topical NSAIDs, particularly GI bleeding, which influences the use of oral NSAIDs. Topical NSAIDs may be the preferred option, particularly for older adults and those at greater risk for GI harm. The evidence from the review supports current guidance for OA from the National Collaborating Centre for Chronic Conditions (2008).

Research Recommendations

A need exists for additional high-quality, longer duration studies for NSAIDs and chronic pain. A substantial amount of data from unpublished studies was unavailable, and access to this may have enhanced the sum of knowledge on this topic.

Reference


Bibliography


For more about the Cochrane Library of systematic reviews, visit www.thecochranelibrary.com.