Systematic review with meta-analysis

Topical NSAIDS provide effective pain relief for patients with hand or knee osteoarthritis with similar efficacy, and fewer side effects, than oral NSAIDS

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Context
Topical non-steroidal anti-inflammatory drugs (NSAIDS) are readily available from chemists and supermarkets worldwide and are commonly used in the treatment of a number of painful conditions. Their overall efficacy in the long term, particularly in relation to chronic painful conditions such as osteoarthritis, has not been fully established.

Methods
Derry and colleagues have conducted a thorough and comprehensive review of the area including data from The Cochrane Library, MEDLINE, EMBASE and www.clinicaltrials.gov, as well as their in-house clinical trials registers from 2004 to June 2012. The selection criteria were clearly defined and the methodological quality of each study was appropriately assessed using the Oxford Quality Scale. The studies consisted of randomised double blind studies lasting ≥2 weeks comparing topical NSAID with placebo or an active comparator in ongoing chronic painful conditions. All topical formulations were scrutinised including creams, gels, patches and solutions. The primary outcome of the review was ‘clinical success’, defined as a 50% reduction in pain, or equivalent measure such as a ‘very good’ or ‘excellent’ global assessment of treatment, or ‘none’ or ‘slight’ pain on rest or movement, measured on a categorical scale. Secondary outcomes included the number of participants with adverse events, both local and systemic, with particular emphasis on serious gastrointestinal (GI) complications and treatment withdrawals.

Findings
Results from 7688 participants in 34 studies from 32 publications were analysed and of these, 23 studies directly compared a topical NSAID formulation with placebo. Topical NSAIDS were found to be significantly better than placebo at reducing pain in hand and knee osteoarthritis, but not in other painful conditions. The strongest data was for topical diclofenac–in osteoarthritis of the knee and hand the number needed to treat (NNT) for at least 50% pain relief over 8–12 weeks was 6.4 (4.6–10) for NSAID solution and 11 (7.7–17) for NSAID gel. Analysis of all the studies comparing topical with oral NSAID revealed that the proportion of patients experiencing successful treatment with a topical NSAID was 55% (479/877, range 40–66%) compared with 54% with oral NSAIDS (462/858, range 34–70%) indicating no difference in efficacy. An increase in local adverse events was seen with topical NSAIDs most commonly mild skin reactions such as dry skin, erythema and pruritus. There was no increase in serious adverse events compared with control.

Commentary
Topical NSAIDs were first licensed in the USA by the Food and Drug Administration in 2007, and were recommended as a first line treatment for osteoarthritis by the National Institute of Clinical Excellence (NICE) in 2008. Multiple systematic reviews have examined topical NSAID use in hand and knee osteoarthritis and have in general found their use favourable. Two negative meta-analyses appear to have been a result of the limited availability of studies of adequate duration at the time of writing, and the inclusion of agents such as topical felbinac which failed to show any therapeutic benefit. This current review has established that topical NSAIDS are an effective treatment for hand and knee osteoarthitis after having examined high quality, larger, longer duration studies (up to 12 weeks). It appears that the formulation is important with NSAID solution (NNT 6.4) being more efficacious than NSAID gel (NNT 11), this came close to statistical significance despite the relatively small number of events. Although minor skin reactions were more frequent, there was no increase in serious adverse events including GI bleeding, a well-recognised and potentially life-threatening complication of oral NSAIDs. No evidence of benefit, however, was found for their use in other painful conditions including ‘soft tissue rheumatism’, ‘cervical and lumbar back pain’ and ‘musculoskeletal pain’. This may be due to less precise descriptions of the underlying diagnoses. Currently, topical NSAIDS can be endorsed from the evidence as effective for hand and knee osteoarthritis. This review supports the decision by NICE to recommend topical NSAIDS as the first-line therapy for osteoarthitis. They should be considered in preference to oral NSAIDs due to their equivalent efficacy and improved safety profile. Future studies are required to further evaluate the role of topical NSAIDs in the treatment of other musculoskeletal conditions, NSAIDs other than diclofenac and to determine whether their chronic use results in side effects such as GI bleeding, ischaemic heart disease and renal failure.

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Competing interests
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References