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Q / Does topical diclofenac relieve osteoarthritis pain?

EVIDENCE-BASED ANSWER

A / YES, at least in the short term. Topical diclofenac, with and without dimethyl sulfoxide (DMSO), modestly improves pain and function scores (by 4%-8%) for as long as 12 weeks in patients with osteoarthritis (OA) of the knee (strength of recommendation [SOR]: **A**, meta-analyses of multiple randomized controlled trials [RCTs]).

Topical diclofenac modestly decreases pain scores in patients with OA of the

hand in the short term (by 9% at 6 weeks) but no more than placebo at 8 weeks (SOR: **B**, RCT).

Both topical diclofenac with DMSO and oral diclofenac produce similar pain and function scores in patients with OA of the knee. In addition to minor skin dryness, topical diclofenac causes gastrointestinal (GI) adverse effects in about a third of patients (SOR: **B**, RCT).

Evidence summary

Diclofenac gel (\$260-\$330 per 150-mL bottle) and diclofenac with DMSO solution are the only topical nonsteroidal anti-inflammatory drugs (NSAIDs) available in the United States.

Topical diclofenac with DMSO beats placebo

In a meta-analysis of 3 RCTs (697 patients, mean age 63.2, 37% male) with knee OA, topical diclofenac solution with DMSO (Pennsaid, 40 drops applied 4 times daily) demonstrated superiority to vehicle-controlled placebo at 4 to 12 weeks (mean 8.5 weeks) using the Western Ontario and McMaster Universities (WOMAC) Osteoarthritis Index.¹ The WOMAC is a standardized patient questionnaire measuring 5 items for pain (score range 0-20), 2 for stiffness (score range 0-8), and 17 for functional limitation (score range 0-68).

Compared with placebo, topical diclofenac with DMSO resulted in 1.6 units greater reduction in pain (8% difference), 0.6 units greater reduction in stiffness (7.5% difference), and 5.5 units greater improvement in

physical function (8% difference). Patients using diclofenac reported more minor skin dryness than patients using placebo (number needed to harm [NNH]=6).

Diclofenac gel is also effective, but may cause dermatitis

A pooled analysis of 3 12-week randomized, double-blind, parallel-group, multicenter trials of 1426 patients with OA of the knee compared topical diclofenac gel (4 g applied 4 times a day) with vehicle placebo for patients older than 25 years and patients older than 65 years.² Investigators evaluated 972 patients who suffered a symptom flare at 1, 4, 8, and 12 weeks after a one-week washout period.

Diclofenac demonstrated statistical superiority across all age groups when compared with placebo, based on pain and physical function measured on the WOMAC Index. Its effects were modest, however.

At 12 weeks, patients younger than 65 years showed pain improvement of -5.8 vs -4.7 for placebo (a 5.5% improvement on the 20-point scale) and improvement in physical

function of -17.9 vs -14.2 (a 5.4% improvement on the 68-point scale). Patients older than 65 years demonstrated pain improvement of -5.3 vs -4.1 for placebo (6% improvement on the 20-point scale) and physical function improvement of -15.5 vs -11.0 for placebo (6.6% improvement on the 68-point scale).

Dermatitis was more common in the diclofenac groups, with a NNH of 30 in patients younger than 65 years and 19 in patients older than 65 years.

Diclofenac gel effectively treated hand OA for as long as 6 weeks in a randomized, double-blind, placebo-controlled trial of 809 men and women older than 39 years. Pain scores on a 100-point visual analog scale improved when compared with placebo alone.³ At 6 weeks, topical diclofenac reduced pain scores by 45% compared with 36% for placebo ($P=.023$). Pain reductions also were greater in the diclofenac group at 8 weeks, although not statistically different.

Oral diclofenac works well, too, but has more GI adverse effects

An RCT of 622 patients (40-85 years of age) with symptomatic and radiographically di-

agnosed OA of the knee compared topical diclofenac solution (75 mg/d) with oral diclofenac (50 mg 3 times a day) and found similar efficacy at 12 weeks, with no significant difference between oral and topical preparations for pain, physical function, and stiffness measured with the WOMAC Index ($P=.23, .06, .24$, respectively).⁴ Oral diclofenac produced more adverse GI side effects than the topical solution (48% vs 35%; $P=.0006$).

Recommendations

The Agency for Healthcare Research and Quality states that topical and oral NSAIDs reduce knee OA pain equally.⁵

The Guidelines of the American Academy of Orthopaedic Surgeons, American College of Rheumatology, European League Against Rheumatism, Osteoarthritis Research Society International, and National Institute for Health and Care Excellence all state that clinicians may consider topical NSAIDs for patients with mild to moderate OA of the knee or hand, particularly in patients with few affected joints or a history of sensitivity to oral NSAIDs.⁶

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Topical diclofenac, with and without dimethyl sulfoxide, modestly improves pain and function scores for as long as 12 weeks in patients with knee OA.

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