Altman RD, Dreiser R-L, et al. Diclofenac Sodium Gel in Patients with Primary Hand Osteoarthritis: A Randomized, Double-blind, Placebo-controlled trial. J Rheumatol 2009;36:1991-9.

Design; Randomized clinical trial

Population/sample size/setting:

- 385 patients (89 men, 296 women, mean age 64) treated for hand osteoarthritis at centers in the US, France, Switzerland, and Germany
- Inclusion criteria included OA pain in dominant hand for at least 12 months and use of an NSAID for at least 1 episode of pain; a 7 day NSAID washout period was required, during which OA pain in dominant hand had to be (1) at least 40 mm on a VAS scale of 100 mm, (2) at least 20 mm greater than pain in nondominant hand, and (3) at least 15 mm greater during the NSAID washout period than while taking NSAID
- Exclusion criteria were Kellgren-Lawrence grade 4 OA, symptomatic OA requiring treatment in areas other than the hand, laboratory values suggesting rheumatoid arthritis or other inflammatory disease, fibromyalgia, and being ambidextrous

Main outcome measures:

- All received topical gel for treatment, and were randomized to diclofenac (n=198) or placebo gel alone (n=187)
- Gel was applied 4 times daily, 2 g to each hand, for 8 weeks, covering base of thumb and all 5 digits, using gentle massage without rubbing
- Primary efficacy measures were taken at 4 and 6 weeks, and included (1) pain VAS on a 100 mm scale, (2) Australian/Canadian Osteoarthritis Hand Index (AUSCAN), a self-administered questionnaire assessing pain, disability, and stiffness, and (3) a global rating of disease activity; all 3 outcomes were measured on a scale of 0 to 100, with 100 the worst score possible
- Treatment failure was defined as 4 consecutive days of taking at least 2 g of acetaminophen for relief of hand pain, or at least 1 prescription NSAID or COX-2 selective medication
- Diclofenac gel began to show superiority to placebo gel at 1 week, and at 4 weeks, had reduced pain by 42% (compared to 24% reduction for placebo)
- At 6 weeks, both groups had improved on pain, AUSCAN, and global assessment of disease activity, but diclofenac was superior to placebo (reductions of 33.7 mm, 25.9 mm, and 23.1 mm respectively, compared to placebo reductions of 26.7 mm, 18.6 mm, and 16.3 mm)
- Treatment failed in 24 diclofenac and in 25 placebo patients, most commonly for excessive use of acetaminophen for hand pain; these patients were discontinued from the study but their data was used in the analysis
- Use of acetaminophen for hand pain did not differ between the diclofenac and placebo groups; most patients used acetaminophen at least occasionally during the trial, (82% in each group)

- Primary outcome measures were taken at 4 and 6 weeks, but additional measures taken at 8 weeks showed that the difference between diclofenac and placebo had narrowed, due to plateau of diclofenac effectiveness and continued improvement of placebo group
- At the end of the study, 47.7% of diclofenac patients and 36.5% of placebo patients rated treatment as very good or excellent
- At least one adverse event was reported by 52% of diclofenac and 44% of placebo patients; but only 2.5% of diclofenac patients and 2.1% of placebo patients had severe events; no ulcers or GI bleeding were reported
- Most common adverse effect leading to discontinuation was dermatitis; 10 diclofenac patients and 4 placebo patient discontinued treatment for adverse effects

Authors' conclusions:

- Diclofenac gel applied qid for mild to moderate hand OA reduces pain and improves function compared to placebo at 4 and 6 weeks
- The narrowing of the difference between diclofenac and placebo at 8 weeks represents a catch-up effect of placebo, since there is some therapeutic effect of rubbing the gel by itself
- Diclofenac gel should be considered a safe and effective treatment of hand OA

Comments:

- Generally satisfactory methods and analysis were done
- Most of the withdrawals for failure from the study did preserve the intention-to-treat principle, since the worst scores for both groups were carried forward for the analysis, and all randomized patients were analyzed in their groups
- Efficacy assessments were not done at 4 and 6 weeks if the patient had not used study medication on the day of the visit or for the 2 preceding days; the reason for this is not clear, and the number of patients affected by this was not reported in Table 2B
- The number of centers participating in the study is not clear, even though several countries seem to have been involved
- Even though pain and function improved in the diclofenac group more than the placebo group, less than half (47.7%) of them reported very good or excellent success of treatment at the end of the trial
- The inclusion and exclusion criteria were complex (e.g., dominant hand pain at least 20 mm greater than nondominant hand, with 15 mm exacerbation during NSAID washout period); this does not create bias in the group comparisons, but makes it difficult to generalize the results to other patient populations

Assessment: High-quality for an evidence statement that topical diclofenac gel is more effective than placebo gel in improving pain and function in mild to moderate hand OA