

# Topical diclofenac improved pain and physical function with no systemic side effects in primary osteoarthritis of the knee

Bookman AA, Williams KS, Shainhouse JZ. Effect of a topical diclofenac solution for relieving symptoms of primary osteoarthritis of the knee: a randomized controlled trial. *CMAJ* 2004;**171**:333–8.

Clinical impact ratings GP/FP/Primary care ★★★★★☆ Rheumatology ★★★★★☆ Internal Medicine ★★★★★★

**Q** In patients with primary osteoarthritis (OA) of the knee, is a topical diclofenac (TD) solution more effective than topical vehicle control (VC) or placebo for providing symptom relief?

## METHODS

-  **Design:** randomised vehicle and placebo controlled trial.
-  **Allocation:** concealed.\*
-  **Blinding:** blinded (patients, healthcare providers, data collectors, and outcome assessors).\*
-  **Follow up period:** 28 days.
-  **Setting:** 7 medical centres in Ontario, Canada.
-  **Patients:** 248 patients who were 18–80 years of age (63% women, mean age 62 y) and had primary OA in ≥1 knee (verified radiologically within the previous 6 mo) and at least moderate pain (identified with the Western Ontario and McMaster Universities [WOMAC] LK3.0 OA Index pain subscale). Exclusion criteria included secondary arthritis related to syphilitic neuropathy; ochronosis; metabolic bone disease or acute trauma; sensitivity to intervention ingredients; and active renal, hepatic, or peptic ulcer disease.
-  **Intervention:** patients were allocated to TD (1.5% wt/wt diclofenac sodium solution in a vehicle containing DMSO [45.5% wt/wt], propylene glycol, glycerin, ethanol, and water) (n = 84); VC (vehicle with DMSO but no diclofenac) (n = 80); or placebo (n = 84). Patients applied solution (1.3 ml) 4 times daily.
-  **Outcomes:** change from baseline to final assessment in the WOMAC subscale score for pain, stiffness and physical function, and patient global assessment (PGA); and adverse events at 28 days.
-  **Patient follow up:** 99% (intention to treat analysis).

\*See glossary.

Topical diclofenac (TD) v vehicle control (VC) or placebo solution for osteoarthritis (OA) of the knee at 28 days\*

Outcomes†	Mean change from baseline			Difference in mean change from baseline (95% CI)
	TD	VC	Placebo	
Pain	-3.9	-2.5		1.4 (1.2 to 1.5)
	-3.9		-2.5	1.4 (1.2 to 1.5)
Physical function	-11.6	-5.7		5.9 (5.2 to 6.4)
	-11.6		-7.1	4.5 (4.0 to 5.4)
Stiffness	-1.5	-0.7		0.8 (0.7 to 0.8)
	-1.5		-0.6	0.9 (0.9 to 0.9)
Pain in walking	-0.8	-0.4		0.4 (0.4 to 0.5)
	-0.8		-0.6	0.2 (0.2 to 0.3)

\*CI defined in glossary. Difference in mean change from baseline calculated from data in article.  
†Measured by the Western Ontario and McMaster Universities OA index pain subscale.

## MAIN RESULTS

TD led to more improvement in pain, stiffness, pain in walking, physical function WOMAC scores, and PGA than did VC or placebo (table). Minor skin dryness or flakiness at the application site occurred more in the TD group (36%) than in the VC (14%) or placebo (1%) groups (p = 0.001 and p = 0.0001, respectively). Groups did not differ for systemic adverse events.

## CONCLUSIONS

In patients with osteoarthritis of the knee, topical diclofenac improved pain, stiffness, physical function scores, and patient global assessment more than a vehicle control or placebo at 28 days. The diclofenac treatment resulted in local skin dryness but no systemic adverse events.

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### Commentary

Topical NSAIDs can be used to reduce the pain of OA. Moreover, they may now be more appealing than oral NSAIDs, given the emerging evidence that cyclooxygenase 2 selective drugs are likely associated with an increased risk of cardiovascular events.<sup>1,2</sup>

Previous randomised trials comparing topical NSAIDs with placebo or oral NSAIDs have been of short duration and variable methodological quality, so there has been no evidence to support their longer term use.<sup>3</sup> The 4 week blinded RCT by Bookman *et al* in patients with primary OA of the knee found that topical diclofenac was significantly better than both vehicle controlled and placebo solutions in reducing WOMAC pain, physical dysfunction, and stiffness. Bias was minimised through proper randomisation and blinding. While missing WOMAC data were dealt with by carrying the last observation forward, the percentage missing (other than baseline) was not reported. It is notable that this trial was not a direct equivalence study, so it is not possible to comment informatively on the relative efficacy of topical diclofenac compared with the oral preparation. However, a recent high quality 12 week randomised equivalence trial has, in fact, shown that topical diclofenac has similar efficacy and fewer systemic side effects than oral diclofenac (at doses of 150 mg daily) in the treatment of knee OA.<sup>4</sup> Additional research on long term safety, efficacy, and the precise mechanism of action will help to further clarify the role of topical NSAIDs in the treatment of OA.

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