

Review: non-steroidal anti-inflammatory drugs are slightly better than paracetamol for reducing pain in osteoarthritis

Wegman A, van der Windt D, van Tulder M, *et al.* Nonsteroidal antiinflammatory drugs or acetaminophen for osteoarthritis of the hip or knee? A systematic review of evidence and guidelines. *J Rheumatol* 2004;**31**:344–54.

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

Q In patients with osteoarthritis (OA) of the knee or hip, are non-steroidal anti-inflammatory drugs (NSAIDs) more effective than paracetamol (acetaminophen) for reducing OA related pain or disability?

METHODS

	Data sources: Medline, EMBASE/Excerpta Medica, and the Cochrane Database (all up to December 2001), and bibliographies of relevant articles.
	Study selection and assessment: randomised controlled trials (RCTs) (full reports published in any language) that compared an NSAID with paracetamol in patients with OA of the hip or knee, and measured relevant outcomes. Study quality was assessed using the internal validity criteria of the Amsterdam-Maastricht Consensus List for Quality Assessment with emphasis on adequate procedures for randomisation and sufficient blinding (maximum score 11 points).
	Outcomes: overall change in pain and disability (physician assessment), pain on motion (2 scales), pain at rest or general pain (3 scales), and functional disability (2 scales).

MAIN RESULTS

5 RCTs (655 patients) met the selection criteria. Study quality varied between 5 and 8 points. NSAIDs evaluated included diclofenac (150 mg/d), naproxen (750 mg/d), ibuprofen (2400 or 1200 mg/d), ketoprofen (200 mg/d), and fenoprofen (600 mg/d) (1 RCT each). Dosage of paracetamol varied from 990–6000 mg/day. Meta-analyses were done using a random effects model. Improvement in general pain or pain at rest was greater in the NSAID group than the paracetamol group (small but statistically significant effect) (table). For all other outcomes, differences between groups were smaller and showed borderline significance in favour of NSAIDs (table).

CONCLUSION

In patients with osteoarthritis of the knee or hip, non-steroidal anti-inflammatory drugs are slightly better than paracetamol for reducing osteoarthritis related general pain or pain at rest.

For correspondence: Dr D van der Windt, Institute for Research in Extramural Medicine, Amsterdam, The Netherlands. Dawm.vanderwindt@vumc.nl

Source of funding: Leo Pharma.

Commentary

The well done meta-analysis (summarising a limited number of trials) by Wegman *et al* concluded that NSAIDs are slightly more effective than paracetamol in OA. Even older trials, which had purportedly showed equivalence of paracetamol and NSAIDs, actually showed modestly greater efficacy of NSAIDs in a recent analysis¹; however, the results did not reach statistical significance because of inadequate power. In addition, the largest RCT in the meta-analysis by Wegman *et al* reported clear cut superiority of NSAIDs over paracetamol.²

What do the standardised mean differences reported in this meta-analysis mean to clinicians and patients? Generally, a treatment effect in this range is small. For example, in the largest RCT used in the meta-analysis,² pain scores improved by an average of 39% in the NSAID group compared with 22% in the paracetamol group, a difference of 17 on a scale of 0–100.

So, which medications should be used to treat patients? The largest trial² found that paracetamol initially was as effective as NSAIDs in patients with mild symptoms and in those with knee as opposed to hip OA. However, among patients who had already received an NSAID, paracetamol was far weaker than NSAIDs. Based on data from this trial, paracetamol can be tried as initial therapy, especially in patients with mild symptoms and those with knee, but not hip, OA. For optimal relief of pain in patients who have previously taken NSAIDs or in patients with moderate to severe pain or hip OA, NSAIDs or cyclooxygenase (COX)-2 inhibitors should be considered the treatments of choice, with gastro-protective agents used concomitantly if clinically indicated.¹

Because NSAIDs and COX-2 inhibitors can cause fluid retention and worsen renal insufficiency, patients with renal disease or oedema should be treated with paracetamol, perhaps with the addition of an opiate. The difference in efficacy between NSAIDs and paracetamol is not large; hence patients should not be subjected to unnecessary risks for a possible small treatment benefit.

David Felson, MD, MPH
Boston University School of Medicine
Boston, Massachusetts, USA

1 Felson DT. The verdict favors nonsteroidal antiinflammatory drugs for treatment of osteoarthritis and a plea for more evidence on other treatments [editorial]. *Arthritis Rheum* 2001;**44**:1477–80.

2 Pincus T, Koch GG, Sokka T, *et al.* A randomized, double-blind, crossover clinical trial of diclofenac plus misoprostol versus acetaminophen in patients with osteoarthritis of the hip or knee. *Arthritis Rheum* 2001;**44**:1587–98.

Non-steroidal anti-inflammatory drugs (NSAIDs) v paracetamol in osteoarthritis of the knee or hip at 4–6 weeks*

Outcomes	Number of RCTs (n)	Components of the NSAIDs group	Standardised mean difference (95% CI)
Overall change in pain and disability	2 (405)	Naproxen and diclofenac	0.22 (0.02 to 0.43)†
Pain on motion	2 (362)	Naproxen and ibuprofen (2400 mg/d)	0.24 (0.00 to 0.48)†
		Naproxen and ibuprofen (1200 mg/d)	0.18 (–0.06 to 0.42)
Pain at rest or general pain	3 (589)	Naproxen, ibuprofen (2400 mg/d), and diclofenac	0.33 (0.15 to 0.50)†
		Naproxen, ibuprofen (1200 mg/d), and diclofenac	0.33 (0.15 to 0.51)†
Functional disability	3 (589)	Naproxen, ibuprofen (2400 mg/d), and diclofenac	0.19 (0.01 to 0.37)†
		Naproxen, ibuprofen (1200 mg/d), and diclofenac	0.18 (0.00 to 0.35)†

*RCTs = randomised controlled trials; meta-analyses were done using a random effects model. CI defined in glossary.

†Significant differences favour NSAIDs.