Rofecoxib, 25 mg/day, was more effective than rofecoxib, 12.5 mg/day, celecoxib, or acetaminophen in osteoarthritis of the knee

Geba GP, Weaver AL, Polis AB, et al, for the VACT Group. *Efficacy of rofecoxib, celecoxib, and acetaminophen in osteoarthritis of the knee. A randomized trial.* JAMA 2002 Jan 2;287:64–71.

QUESTION: In patients with symptomatic osteoarthritis (OA) of the knee, are rofecoxib, celecoxib, and acetaminophen effective and safe?

Design

Randomised (allocation concealed)*†, blinded (clinicians, patients, data collectors and analysts, and outcome assessors)†, controlled trial with 6 weeks of follow up.

Setting

29 clinical centres in the USA.

Patients

382 patients ≥ 40 years of age (mean age 63 y, 68% women) who had symptomatic OA of the knee for ≥ 6 months (American College of Rheumatology criteria and functional class rating of I, II, or III), used non-steroidal anti-inflammatory drugs (NSAIDs) or high dose acetaminophen for ≥ 30 days before study entry, and met relevant entry criteria based on the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) (a visual analogue scale [VAS] ranging from 0 [best] to 100 mm [worst]) and a global assessment measure. Exclusion criteria included pregnancy, concurrent disease, and abnormal laboratory results of clinical significance. 79% of patients completed the study, and 98% were included in a modified intention-to-treat analysis.

Intervention

Patients discontinued any NSAID or acetaminophen use and were allocated to rofecoxib, 25 mg (n=95) or 12.5 mg (n=96) once daily; celecoxib, 200 mg once daily (n=97); or acetaminophen, 4000 mg/day given as 1000 mg 4 times daily (n=94) for 6 weeks. Matching placebo tablets were used to retain blinding and complete the 4 tablets/day dosing schedule.

Main outcome measures

Walking pain, night pain, rest pain, and morning stiffness assessed by individual WOMAC scores; composite pain, composite stiffness, and composite function assessed by WOMAC subscales; global response assessed by the patient global assessment of response to therapy (PGART) scale (a 5 point scale ranging from 0 [none] to 4 [excellent]); and adverse events.

Main results

Analysis was by a modified intention-to-treat method with the last outcome carried forward for the PGART data. Better global responses were seen with rofecoxib, 25 mg/day, than with acetaminophen or celecoxib, and with rofecoxib, 12.5 mg/day, than with acetaminophen (all p values ≤ 0.05). Rofecoxib, 25 mg/day, led to greater symptom relief than did celecoxib or acetaminophen (table). Groups did not differ for adverse events.

Conclusion

In patients with symptomatic osteoarthritis of the knee, rofecoxib, 25 mg/day, was more effective than rofecoxib, 12.5 mg/day, celecoxib, or acetaminophen at 6 weeks.

*See glossary.

†Information provided by author.

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Rofecoxib, 25 mg/day, v celecoxib or acetaminophen for mean decreases in composite WOMAC VAS scores of symptoms of osteoarthritis of the knee at 6 weeks‡

Comparison	Outcomes	Mean decreases in WOMAC VAS scores (mm)	p Values
Rofecoxib v celecoxib	Pain	35 v 29	≤ 0.05
	Stiffness	35 v 28	≤ 0.05
Rofecoxib v acetaminophen	Pain	35 v 25	< 0.01
	Stiffness	35 v 22	< 0.001
	Function	30 v 20	< 0.01

‡WOMAC VAS scores = Western Ontario and McMaster Universities Osteoarthritis Index visual analogue scale scores.

COMMENTARY

OA is a chronic condition requiring long term treatment; even assessments done at 6 weeks may not predict long term results. The study by Geba *et al* showed that at 6 weeks only the 25 mg daily dose of rofecoxib, which is double the recommended starting dose for OA, was more effective than acetaminophen or celecoxib. Unfortunately, this study does not answer the question of whether the higher daily dose (400 mg) of celecoxib, which is not approved for OA, would be as effective as 25 mg of rofecoxib.

The US Food and Drug Administration has recently labelled rofecoxib as safer for the gastrointestinal tract than naproxen, but some cardiovascular concerns with rofecoxib exist.¹ The cyclooxygenase-2 selective NSAIDs have renal side effects similar to older NSAIDs.²

Are drugs needed at all in the treatment of OA? Studies have shown that sustained improvement in symptoms can be achieved with exercise regimens, even as low as 10 minutes of daily exercise.³ I routinely teach isometric leg lifts to all patients with OA and knee pain.

Although in this study patients reported a better response to NSAIDs, 39% reported a good or excellent response to acetaminophen alone. Given the potential toxicity of all NSAIDs, acetaminophen and quadriceps muscle strengthening remain an effective and safe regimen that should be used as initial treatment for OA of the knee. Further pharmacological treatment needs to be individualised for each patient on the basis of their gastrointestinal, cardiac, and renal risk factors.

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