

THERAPEUTICS

Celecoxib was noninferior to diclofenac plus omeprazole for preventing gastroduodenal ulcer recurrence in high-risk patients with arthritis

Chan FK, Hung LC, Suen BY, et al. Celecoxib versus diclofenac plus omeprazole in high-risk arthritis patients: results of a randomized double-blind trial. *Gastroenterology*. 2004;127:1038-43.

QUESTION

In patients with arthritis and previous bleeding ulcer associated with nonsteroidal anti-inflammatory drugs (NSAIDs), is celecoxib noninferior to diclofenac plus omeprazole for preventing gastroduodenal ulcer recurrence?

METHODS

Design: Randomized controlled trial.

Allocation: {Concealed}†.*

Blinding: Blinded {clinicians, patients, data collectors, outcome assessors, monitoring committee, and statisticians}†.*

Follow-up period: Median 6 months.

Setting: A university hospital in Hong Kong.

Patients: 287 patients {mean age 68 y, 44% men}† with arthritis and prior bleeding ulcer while on NSAIDs, who had endoscopy-confirmed ulcer healing and were currently negative for *Helicobacter pylori* infection, and who had anticipated regular use of NSAIDs. Exclusion criteria were concomitant use of anticoagulants or corticosteroids, history of gastric or duodenal surgery, erosive esophagitis, gastric outlet obstruction, renal failure, terminal illness, or cancer.

Intervention: Celecoxib, 200 mg twice daily, plus placebo, once daily {*n* = 144}†, or diclofenac, 75 mg twice daily, plus omeprazole, 20 mg once daily {*n* = 143}†.

Outcome: Combined endpoint of recurrent bleeding and endoscopic gastroduodenal ulcers.

Patient follow-up: 86% (intention-to-treat analysis).

MAIN RESULTS

The celecoxib group did not differ from the diclofenac plus omeprazole group for the combined endpoint of recurrent bleeding ulcers and endoscopic ulcers (Table).

CONCLUSION

In patients with arthritis and previous nonsteroidal anti-inflammatory drug-associated ulcer bleeding, celecoxib was noninferior to diclofenac plus omeprazole, but ulcer recurrence was common with both regimens.

Source of funding: Health Services Research Committee of Hong Kong.

For correspondence: Dr. F.K. Chan, Chinese University of Hong Kong, Shatin, Hong Kong SAR. E-mail fkchan@cuhk.edu.hk.

*See Glossary.

†Information provided by author.

Celecoxib vs diclofenac plus omeprazole in patients with arthritis and previous nonsteroidal antiinflammatory drug-associated ulcer bleeding†

Outcome at median 6 months	Celecoxib	Diclofenac plus omeprazole	Difference (95% CI)
Recurrent bleeding ulcers and endoscopic ulcers	24%	32%	-8.2% (-20 to 2.9) [§]

†CI defined in Glossary.

[§]Criteria for noninferiority were met because the upper limit of this CI is < 6% (the clinically important difference).

COMMENTARY

The study by Chan and colleagues adds to the timely reappraisal of the earlier perception that cyclo-oxygenase (COX)-2 inhibitors reduce the incidence of gastroduodenal ulceration and bleeding compared with COX-1 inhibitors (1, 2). This carefully designed and executed prospective blinded study compared the incidence of these complications in patients with arthritis receiving either the COX-2 inhibitor, celecoxib, or the COX-1 inhibitor, diclofenac, in combination with the proton-pump inhibitor and gastroprotective drug omeprazole.

The study included older patients (mean age > 65 y) who had previous hemorrhage from endoscopy-confirmed ulcers while taking NSAIDs. Thus, they were at high risk for recurrent ulcers and bleeding during the trial. Patients with suspected recurrent gastrointestinal bleeding received endoscopy during the trial period of 6 months, as did most of the asymptomatic patients at the end of the trial. A high incidence of recurrent ulcer bleeding was seen (24 of 287 patients) and of recurrent ulceration detected by endoscopy at the end of the trial (46 of the 226 patients examined) with no significant difference between the 2 treatment groups.

The risk for ulceration in this study was higher in patients with common comorbid conditions, but the correlation may have been coincidental in this age group. The study also showed that dyspepsia is a strong warning signal for gastroduodenal harm in these patients.

These results confirm the need for vigilance in prescribing NSAIDs in any form and for subsequent monitoring. Furthermore, the results reinforce established advice that previous gastroduodenal ulceration contraindicates the use of NSAIDs. The results should particularly encourage physicians to seek alternative means of pain relief in older patients with osteoarthritis.

A. Michael Denman, MD
Imperial College School of Medicine
London, England, UK

References

1. Maetzel A. Motion—Cyclo-oxygenase-2 selective nonsteroidal anti-inflammatory drugs are as safe as placebo for the stomach: arguments against the motion. *Can J Gastroenterol*. 2003;17:335-8.
2. Sturkenboom MC, Burke TA, Dieleman JP, et al. Underutilization of preventive strategies in patients receiving NSAIDs. *Rheumatology (Oxford)*. 2003;42 Suppl 3:iii23-31.