Review: Misoprostol or COX-2–specific or selective NSAIDs reduce gastrointestinal complications and symptomatic ulcers


**Question**

In patients taking nonselective nonsteroidal antiinflammatory drugs (NSAIDs), what are the effects of 5 gastroprotective strategies (NSAIDs plus H₂-receptor antagonists, NSAIDs plus proton-pump inhibitors, NSAIDs plus misoprostol, cyclooxygenase-2 [COX-2]–selective NSAIDs alone, and COX-2–specific NSAIDs alone) for preventing gastrointestinal (GI) toxicity?

**Methods**

Data sources: 5 databases, bibliographies of relevant studies, and contacting authors.

Study selection and assessment: Randomized controlled trials (RCTs) ≥ 21 days in duration comparing 1 of the 5 gastroprotective strategies with nonselective NSAIDs alone on outcomes of GI toxicity. Quality assessment included randomization procedures, allocation concealment, blinding, and follow-up.

Outcomes: Primary outcomes included serious GI complications (e.g., hemorrhage, hemorrhagic erosions, recurrent upper GI bleeding, perforation, and pyloric obstruction) and symptomatic ulcers.

**Main results**

112 RCTs (n = 74 666) met the selection criteria. 15 RCTs (n = 2621) compared H₂-receptor antagonists with placebo, 6 RCTs (n = 1358) compared proton-pump inhibitors with placebo, 23 RCTs (n = 16 945) compared misoprostol with placebo, 51 RCTs (n = 28 178) compared COX-2–selective drugs with nonselective NSAIDs, and 17 RCTs (n = 25 564) compared COX-2–specific drugs with nonselective NSAIDs.

**Conclusions**

In patients taking NSAIDs, misoprostol or COX-2–specific NSAIDs alone reduce serious gastrointestinal complications and symptomatic ulcers more than nonselective NSAIDs alone. Misoprostol, proton-pump inhibitors, and COX-2–selective and COX-2–specific NSAIDs reduce symptomatic ulcers more than NSAIDs alone.

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**Commentary**

Several important conclusions can be drawn from this review by Hooper and colleagues. First, although the investigators found that COX-2–selective NSAIDs reduced the risk for symptomatic ulcers and gastrointestinal symptoms, no reductions were seen in endoscopic ulcers and ulcer complications. This finding raises concerns that COX-2–selective NSAIDs might actually do more harm than good by masking dyspeptic symptoms and should be avoided in high-risk patients. Second, although COX-2–specific NSAIDs, as a class, seem to reduce the risk for ulcer complications, only rofecoxib has been clearly shown to achieve this goal. Third, the strongest evidence for prevention of NSAID-induced ulcer complications was found with misoprostol, but its use is limited by other adverse effects. Although low-dose misoprostol is better tolerated, it fails to prevent ulcer complications (1). Fourth, no evidence exists from randomized, placebo-controlled trials that proton-pump inhibitors prevent ulcer complications as an adjunct to NSAID therapy.

This meta-analysis did not include direct comparisons of some of the treatment options. It is therefore unknown whether proton-pump inhibitors are more effective than double-dose H₂-receptor antagonists or full-dose misoprostol (2). Although celecoxib was comparable to omeprazole and diclofenac for reducing the risk for recurrent ulcer bleeding (3), neither treatment could eliminate the hazard of ulcers in high-risk patients (4).

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**References**