Omeprazole was better than *H. pylori* eradication for preventing recurrent GI bleeding in patients receiving naproxen

Chan FK, Chung S, Suen BY, et al. **Preventing recurrent upper gastrointestinal bleeding in patients with *Helicobacter pylori* infection who are taking low-dose aspirin or naproxen.** N Engl J Med. 2001 Mar 29;344:967-73.

QUESTION

In patients with upper gastrointestinal (GI) bleeding and *Helicobacter pylori* infection who are taking low-dose aspirin or other nonsteroidal anti-inflammatory drugs (NSAIDs), is eradication of *H. pylori* equivalent to maintenance therapy with omeprazole for preventing recurrent upper GI bleeding?

DESIGN

Randomized (allocation concealed*), blinded (outcome assessors),* controlled trial with median follow-up of 6 months.

SETTING

Prince of Wales Hospital, Hong Kong.

PATIENTS

400 patients (mean age 68 y, 62% men) with a history of confirmed upper GI bleeding (ulcers or erosions) who had *H. pylori* infection with an ongoing need for aspirin (≤ 325 mg/d) (n = 250) or other NSAIDs (n = 150). Exclusion criteria included use of nonaspirin NSAIDs plus low-dose aspirin, corticosteroids, or anticoagulants and previous gastric surgery. 95% of patients completed the study.

INTERVENTION

After having ulcers healed while receiving omeprazole, 20 mg/d for ≥ 8 weeks, those patients previously taking aspirin were given aspirin, 80 mg/d, and those previously taking other NSAIDs were given naproxen, 500 mg twice daily, for 6 months. All patients were also separately assigned to omeprazole, 20 mg/d for 6 months, or to eradication therapy for 1 week (bismuth subcitrate, 120 mg; tetracycline, 500 mg; and metronidazole, 400 mg, all 4 times/d) followed by placebo for 6 months. 125 patients in the aspirin group and 75 in the other NSAIDs group were allocated to omeprazole, and 125 patients in the aspirin group and 75 in the other NSAIDs group were allocated to *H. pylori* eradication.

MAIN OUTCOME MEASURE

Recurrent upper GI bleeding.

MAIN RESULTS

Among patients taking NSAIDs, those in the omeprazole group had a lower rate of recurrent upper GI bleeding (P = 0.005) (Table). Among patients taking aspirin, the groups did not differ for recurrent upper GI bleeding (Table).

CONCLUSIONS

In patients with a history of upper gastrointestinal bleeding and *Helicobacter pylori* infection who were taking low-dose aspirin, *H. pylori* eradication was comparable to omeprazole in preventing recurrent bleeding. In contrast, omeprazole was superior to *H. pylori* eradication in preventing recurrent bleeding in patients who were taking other NSAIDs.

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*See Glossary.

Omeprazole vs eradication of *H. pylori* in recurrent upper gastrointestinal bleeding at 6 months in patients who were receiving aspirin or naproxen†

Group	Omeprazole	Eradication	RRR (95% CI)	NNT (CI)
Aspirin	0.9%	1.9%	52% (–145 to 250)	Not significant
Naproxen	4.4%	18.8%	77% (35 to 118)	7 (5 to 23)

†Abbreviations defined in Glossary; RRR, NNT, and CI calculated from data in article.

COMMENTARY

H. pylori infection and NSAID use are independent risk factors for ulcer disease, but whether *H. pylori* infection potentiates the development of NSAID-induced ulcers is controversial. Most trials find that *H. pylori* does not significantly increase the risk for ulcers in NSAID users (1). However, NSAID-naive patients who were given *H. pylori* therapy before beginning an 8-week course of naproxen developed ulcers less often than patients not given *H. pylori* therapy (2). In contrast, a larger double-blind trial subsequently found that *H. pylori* therapy decreased healing of gastric ulcers and had no effect on ulcer recurrence at 6 months in NSAID users (3).

The current study by Chan and colleagues used complicated ulcers, one of the most clinically important adverse effects of NSAIDs, as an inclusion criterion and end point. Rebleeding remained unacceptably high after *H. pylori* therapy in NSAID users (19% at 6 mo). The lack of a placebo group, although ethically understandable, prevents us from determining whether *H. pylori* therapy may provide some benefit. In contrast, recurrent bleeding was uncommon among low-dose aspirin users after *H. pylori* therapy. Again, the relative benefit of *H. pylori* therapy compared with no therapy is uncertain because of the lack of a placebo group.

How should these data be applied in clinical practice? NSAID or aspirin users without past or present ulcer disease need not be tested for *H. pylori*. In individual patients with an ulcer, one cannot be certain whether *H. pylori* or NSAIDs or aspirin is responsible, and each risk should be removed. If low-dose aspirin must be continued, I would add a proton-pump inhibitor, even after *H. pylori* therapy. If NSAIDs must be continued, I would switch to a specific cyclooxygenase 2 inhibitor or add cotherapy, or both.

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References

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