

Helicobacter pylori and Nonsteroidal Anti-Inflammatory Drugs: Synergy or Null Effect?

Summary

Both *Helicobacter pylori* infection and nonselective, nonsteroidal anti-inflammatory drugs (NSAIDs) contribute to a greater risk of gastric and duodenal ulcers, ulcer complications, and gastrointestinal bleeding. Prospective investigations are needed to learn what is the net effect of the combination of *H pylori* and NSAIDs.

Helicobacter *pylori* infection and nonselective, nonsteroidal anti-inflammatory drugs (NSAIDs) independently increase the risk for gastric and duodenal ulcers, ulcer complications, and gastrointestinal (GI) tract bleeding. NSAIDs can cause ulceration by both topical and systemic effects through the inhibition of cyclooxygenase-1.

It is not clear from either individual studies or meta-analyses what is the net effect of the combination of *H pylori* infection and NSAID therapy. Some results have suggested that *H pylori* infection protects against NSAID-associated ulcers by stimulating prostaglandin synthesis, accelerating peptic ulcer healing, and reducing recurrence in a patient taking antisecretory drugs. Other data indicated that patients taking NSAIDs have an increased risk of ulcers and complications that cannot be attributed to infection with *H pylori*. A third group of results have suggested that infection with *H pylori* and NSAIDs are synergistic risks for ulcers and GI bleeding.

On one side of the debate, researchers point out that if *H pylori* infection increases the risk for GI complications in NSAID users but not to the same extent that it increases the risk in non-NSAID users, then there is the implication that the adverse effects of *H pylori* infection are counterbalanced by a protective effect.

Results from the Vioxx Gastrointestinal Outcomes Research trial,¹ a prospective study that examined the incidence of upper GI complications among NSAID users (rofecoxib, a COX-2-selective inhibitor, and naproxen), suggested that the interaction between a COX-2-selective NSAID and *H pylori* is neither additive nor synergistic. According to Bombardier et al,¹ *H pylori*-positive status did not increase the incidence of GI complications among rofecoxib users. This was not true for the naproxen group.

Two studies have reported that ulcer healing was significantly more likely to occur in NSAID users who were *H pylori* positive than *H pylori* negative.^{2,3} Results from these studies also suggested that there may be a reduced recurrence of ulcers in patients who are infected with *H pylori* and taking antisecretory therapy, with the exception of those patients also taking misoprostol. Hawkey et al³ offer the following as possible explanations of this protective effect: 1) *H pylori*-stimulated mucosal synthesis of prostaglandins in NSAID users could accelerate healing and reduce relapse; 2) concomitant therapy with the proton pump inhibitor omeprazole results in higher intragastric pH in *H*

pylori-positive patients than in *H pylori*-negative patients; and 3) NSAID-associated ulcers might be of 2 types, primary ulcers and *H pylori*-associated ulcers that are aggravated by NSAID use. However, it should be noted that there were methodological issues with these findings as they did not originate from an *a priori* question in either study. A randomized prospective study may be necessary to confirm that *H pylori* infection is beneficial to NSAID users.

Does *H pylori* eradication protect existing NSAID users? This is an important patient management question facing clinicians. Chan et al⁴ demonstrated that eradication of *H pylori* before NSAID therapy reduces the occurrence of NSAID-induced peptic ulcer. According to the study's findings, NSAID-induced ulcers developed significantly more often in NSAID-naïve patients who had untreated *H pylori* infection than in those patients who received triple therapy to eradicate *H pylori* infection prior to taking NSAID. In contrast, the *Helicobacter* Eradication for Lesion Prevention study did not find a statistically significant ulcer prevention benefit from eradication of *H pylori* in current NSAID users.⁵

Summary

Meta-analyses have been performed to examine the lack of consistency in the *H pylori* treatment study outcomes. Unfortunately, many studies that were included in the meta-analyses lacked the ideal control group needed for com-

parison: *H pylori*-negative non-NSAID users. Presumably, gastric and duodenal ulcers would be rare in this group and the interaction between the 2 risk factors in *H pylori*-positive NSAID users could be assessed.

There continues to be disagreement over whether *H pylori* infection increases the risks associated with NSAIDs. Prospective studies are needed that examine specific parameters in relation to *H pylori* infection to resolve this issue and guide patient management.

... REFERENCES ...

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