Role of *H. pylori* Eradication in Patients Starting NSAID Therapy

Chan FK, To KF, Wu JC, et al. Eradication of Helicobacter pylori and risk of peptic ulcers in patients starting long-term treatment with non-steroidal anti-inflammatory drugs: a randomised trial. Lancet 2002;359:9–13.

Study Overview

Objective. To determine if eradicating *Helicobacter pylori* before initiating chronic nonsteroidal anti-inflammatory drug (NSAID) therapy reduces the risk of peptic ulcers in persons with dyspepsia or prior ulcer.

Design. Randomized double-blind, allocation-concealed, controlled trial with 6-month follow-up. Analyses were by intention-to-treat.

Setting and participants. NSAID–naive arthritis patients in Hong Kong who required initiation of NSAID therapy were screened. Patients were included if they had a positive urea breath test (indicating *H. pylori* infection) and dyspepsia or a history of ulcer disease. Patients were excluded if they were treated with steroids, anticoagulants, or anti-ulcer drugs; had significant renal impairment; received prior treatment for *H. pylori;* or had a history of gastric surgery.

Intervention. All patients received slow-release diclofenac 100 mg daily for 6 months. The intervention group received omeprazole 20 mg, amoxicillin 1 g, and clarithromycin 500 mg, each given twice daily for 1 week; the control group received omeprazole only.

Main outcome measures. The primary endpoint was gastric or duodenal ulcers seen on endoscopy at 6 months or sooner if severe dyspepsia or bleeding developed. The secondary endpoint was complicated ulcers (bleeding ulcers or ulcers found in the presence of severe dyspepsia).

Main results. 51 patients were assigned to each group; 33% of the patients were men, and the mean age was 63 years. 2 patients in the control group withdrew consent after randomization, and they were excluded from the analysis. 5 intervention patients (12.1%) and 15 control patients (34.4%) developed ulcers ($P = 0.0085$). Complicated ulcers occurred in 2 (4.2%) patients in the intervention group and 9 (27.1%) in the control group ($P = 0.0026$). None of the patients in the intervention group and 3 in the placebo group developed bleeding ulcers.

Conclusion. For patients infected with *H. pylori* who also are starting NSAID therapy, triple drug therapy decreases the risk of peptic ulcers.

Commentary

This well-done study helps inform the debate over the interaction between the 2 leading causes of peptic ulcer disease: *H. pylori* infection and NSAID use. Eradication of *H. pylori* before NSAID exposure led to clear reductions in symptomatic ulcers as well as ulcers detected by endoscopy. These findings coincide nicely with a meta-analysis of observational studies appearing in the same *Lancet* issue. Huang et al found that *H. pylori* and NSAIDs independently increased ulcer risk and that these effects were approximately additive when both risk factors were present [1].

Chan et al's study addresses a specific facet of the relationship between NSAIDs and *H. pylori*. The participants in this trial all had either a history of a documented ulcer or symptoms consistent with ulcer disease prior to initiating NSAID therapy. Also, patients with certain kinds of prior NSAID use were excluded. These selection criteria made it likely that *H. pylori*–induced ulcer disease was already present in many of the study patients at entry. (In fact, patients with these characteristics for reasons unrelated to NSAID use can be considered for *H. pylori* screening and treatment regardless of planned NSAID use.) The selection criteria used in this study differed from an earlier trial conducted with patients already using NSAIDs who had preexisting ulcer disease or dyspepsia. For that group, *H. pylori* eradication did not reduce the ulcer risk and may have impaired the healing of existing ulcers [2]. Neither of these 2 studies helps define the role of screening for and treating *H. pylori* in asymptomatic patients undergoing NSAID treatment, particularly among demographic groups where *H. pylori* infection may be less prevalent.

Regardless of whether *H. pylori* infection is present, long-term NSAID users face considerable risk from ulcer

"Outcomes Research in Review" is edited by Harvey J. Murff, MD, Stephen D. Persell, MD, Josh F. Peterson, MD, Eric G. Poon, MD, and David R. Spigel, MD, all from the Department of Medicine, Brigham and Women's Hospital, Boston, MA.

disease. As recently as 1997, mortality in the United States from complications of NSAIDs was comparable to deaths from AIDS [3]. For NSAID users at high risk (such as the elderly, those with prior ulcer disease, serious systemic illness, or steroid or anticoagulant use), strategies in addition to the treatment of concomitant *H. pylori* are needed. Approaches may include long-term therapy with a proton-pump inhibitor, misoprostol, or the substitution of a cyclooxygenase-2 (COX-2) selective NSAID [3].

Applications for Clinical Practice

Identifying and treating *H. pylori* infection seems worthwhile for patients beginning prolonged NSAID therapy if they have a history of a prior ulcer or ulcer-type dyspepsia. For the broader population of NSAID users, the precise role, if any, for *H. pylori* screening and treatment is less clear, and the availability of antisecretory therapy and COX-2 selective NSAIDs along with their high costs makes decision making even more complex.

–Review by Stephen D. Persell, MD

References

1. Huang JQ, Sridhar S, Hunt RH. Role of *Helicobacter pylori* infection and non-steroidal anti-inflammatory drugs in peptic-ulcer disease: a meta-analysis. Lancet 2002;359:14–22.
2. Hawkey CJ, Tulassay Z, Szczepanski L, et al. Randomised controlled trial of *Helicobacter pylori* eradication in patients on non-steroidal anti-inflammatory drugs: HELP NSAIDs study. *Helicobacter* Eradication for Lesion Prevention [published erratum appears in Lancet 1998;352:1634]. Lancet 1998;352:1016–21.
3. Wolfe MM, Lichtenstein DR, Singh G. Gastrointestinal toxicity of nonsteroidal antiinflammatory drugs [published erratum appears in N Engl J Med 1999;341:548]. N Engl J Med 1999;340:1888–99.