MINDFUL PRACTICE

PPIs to Prevent NSAID-Induced GI Ulceration

BY JON O. EBBERT, M.D., AND ERIC G. TANGALOS, M.D.

The Problem

A 57-year-old man with a history of coronary artery disease and severe degenerative joint disease status post right shoulder rotator cuff tear repair, right total knee arthroscopy, left knee meniscal tear repair, and three spinal fusions presents to you for pain management issues. He is on long-term narcotics with oxycodone. He presented 3 months earlier to the emergency department (ED) with dysphagia and odynophagia. His hemoglobin level was normal, and he denied gastrointestinal bleeding. At the time of presentation, he was taking naproxen sodium 440 mg in the morning and 220 mg in the evening for joint pain as he was trying to taper his narcotic regimen. Esophagogastroduodenoscopy (EGD) in the ED showed a normal-appearing esophagus with incidentally noticed gastric erosions. Esophageal biopsy revealed esophagitis. He was placed on omeprazole, instructed to discontinue the naproxen sodium, and dismissed. He improved over the next several months and became completely asymptomatic. He now presents with acute worsening of his shoulder pain and wishes to avoid increasing his dosage of narcotics because the drugs make him lethargic. He asks to go back on the naproxen for a short period of time. He remains on the omeprazole 20 mg per day and, given his recent history, you consider him to be at higher risk for gastrointestinal (GI) complications. You are aware of data for the cytoprotective effects of misoprostol for NSAID-induced GI complications but are not familiar with the data for proton-pump inhibitors (PPIs) for primary prevention of GI complications from NSAIDs.

The Question

In patients requiring NSAID treatment who are at higher risk for gastrointestinal complications, do PPIs prevent GI complications, compared with placebo?

The Search

You log on to PubMed (www.pubmed.gov) and go to the MeSH Database. You search for "anti-inflammatory agents, nonsteroidal" AND "proton-pump inhibitors"and limit results to randomized, controlled trials. You find a relevant study. (See box at right.)

Our Critique

This clinical trial was well designed and had appropriate randomization. Blinding may have been suboptimal due to the nonidentical appearance of the omeprazole placebo control capsule. The major limitation of this study is the short duration of medication (6.5 days of therapy). However, the findings are consistent with earlier trials. The findings are useful and generalizable to patients seen in the primary care setting who are placed on short-term NSAIDs for acute complaints. Clinicians can recommend that these patients start an over-the-counter dose of omeprazole to prevent complications.

Clinical Decision

You discuss the information with the patient. You agree to restart the naproxen 220 mg once per day and continue the PPI. He agrees to call you with any new symptoms and to call you in 3 weeks with an update on his pain and gastrointestinal symptoms.

DR. EBBERT *and* DR. TANGALOS *are with the Mayo Clinic in Rochester, Minn. They have no conflict of interest to report. To respond to this column or suggest topics for consideration, write to Dr. Ebbert and Dr. Tangalos at our editorial offices or e-mail them at imnews@elsevier.com.*

J.C. Desai, et al.

Primary prevention of adverse gastroduodenal effects from short-term use of non-steroidal anti-inflammatory drugs by omeprazole 20 mg in healthy subjects: A randomized, double-blind, placebo-controlled study. Dig. Dis. Sci. 2008; 53:2059-65.

► **Design:** Randomized, blinded, placebo-controlled clinical trial.

► **Setting:** Single academically affiliated, urban gastroenterology practice.

► **Subjects:** Potential subjects were eligible for inclusion if they were 50-75 years of age. Subjects were excluded if they had: 1) use of any NSAID (including aspirin) within past 2 weeks or history of chronic NSAID use; 2) use of antacids, histamine$_2$ blocker within past 2 weeks, or PPI within past 30 days; 3) use of any corticosteroid within the past 60 days; 4) history of bleeding tendencies or warfarin use within the past 60 days; 5) history of previous bleeding ulcer; 6) consumption of three or more alcoholic beverages a day; 7) hypersensitivity or allergy to NSAIDs or omeprazole, or other contraindications to their use; 8) baseline abdominal pain, nausea, and/or cramping; or 9) the presence of one or more gastroduodenal mucosal breaks (erosions or ulcerations) at baseline endoscopy.

► **Intervention:** Eligible subjects were randomly assigned to 6.5 days of naproxen (NPX) 500 mg twice per day plus omeprazole (OMP) 20 mg daily; or NPX 500 mg twice per day plus placebo. EGD was performed at baseline with biopsies for *Helicobacter pylori*. Study medication was started 7 days later to allow mucosa healing.

► **Outcomes:** The primary end point was the presence of any gastroduodenal ulceration on repeat EGD 14 days after randomization (and 7 days after EGD). Secondary end points included erosions and NSAID-related GI symptoms. GI symptoms were assessed using the Severity of Dyspepsia Assessment consisting of three subscales: pain intensity, nonpain symptoms, and satisfaction with dyspepsia-related health.

► **Results:** A total of 70 patients were randomized (average age 56 years). OMP was associated with fewer gastroduodenal ulcerations (NPX + OMP 11.8% vs. NPX + placebo 46.9%; relative risk = 0.25; $P = .002$). OMP was also associated with fewer gastroduodenal ulcerations and/or a decreased risk of more than five erosions (38.2% vs. 81.3%; RR = 0.47; $P = .001$). The NPX + placebo group was more likely to report increases in nonpain symptoms ($P = .01$).

Colorectal Screening Age Limit Criticized

BY DAMIAN McNAMARA

HOLLYWOOD, FLA. — Nearly 50% of patients who were diagn with colorectal cancer at two large tertiary-care hospitals in Michigan would fall outside recommendations that favor limiting routine screening to patients who are 50-75 years of age.

Last year, the U.S. Preventive Services Task Force released a recommendation statement following two studies that assessed expected health outcomes and resource utilization from screening with fecal occult blood testing, sigmoidoscopy, and colonoscopy (Ann. Intern. Med. 2008;149:627-37). This report recommends against routine screening of patients aged 76-85 years, but notes that screening may be warranted in some individuals outside of that age group. They also recommended against screening any adult older than 85 years.

Dr. Jason Shellnut and his associates launched a study to assess the appropriateness of these guidelines at William Beaumont Hospital System in Royal Oak, Mich. They identified 6,925 patients with colorectal cancer treated at one of their two referral hospitals with a total of 1,357 beds between January 1973 and December 2007. They divided patients into three groups by age at diagnosis—younger than 50 years, 50-75 years, or older than 75.

'Not screening those older than 75 and younger than 50 would miss 49% of our diagnosed patients.'

DR. SHELLNUT

They also evaluated the 35 years' worth of data in 5-year increments to assess trends over time.

"Not screening those older than 75 and younger than 50 would miss 49% of our diagnosed patients in the last 5-year period [2003-2007]," said Dr. Shellnut, a colorectal surgery fellow at William Beaumont Hospital. This 49% is a significant increase, compared with 36% in the first 5 years (1973-1978) of the tumor registry data. Most of the increase is attributed to the older patient group.

The percentage of patients who were older than 75 years at diagnosis rose from 29% (1973-1978) to 40% (2003-2007). This includes a significant increase in patients older than 85 years, from 6% to 12%. In contrast, the percentage of patients younger than 50 did not change significantly from 1973 to 2007, staying within a 6% to 8% range.

At the same time, the percentage of patients in the age range recommended for screening declined significantly. Specifically, patients in the age range of 50-75 years decreased from 64% (1973-1978) to 52% (2003-2007) of those diagnosed.

The researchers looked for any differences in pathologic stage and tumor location. "Pathologic stage data did not vary [significantly] across the years," Dr. Shellnut reported at the annual meeting of the American Society of Colon and Rectal Surgeons.

However, patients under 50 years old were significantly more likely to present with advanced disease. A total of 51% of these younger patients were diagnosed with either stage III or IV colorectal cancer, compared with 41% of the 50- to 75-year-olds and 35% of patients older than 75.

By age of diagnosis, there were significant differences in terms of rectal and left-sided cancer diagnoses. These tumors were most common in the younger age group, 68%, compared with 64% of the patients aged 50-75 years and 50% of the older group.

The retrospective design of the study is a potential limitation, Dr. Shellnut said, and applicability of the findings beyond their health system is unknown. In addition, the tumor registry data track only patients who underwent resection of their cancer.

Dr. Shellnut had no disclosures. ■