LOS ANGELES
COLON AND RECTAL SURGICAL ASSOCIATES
Norman N. Hoffman, MD | Gary H. Hoffman, MD | Eiman Firoozmand, MD | Liza M. Capiendo, MD

Peptic Ulcer:
Tailoring Management Strategies to H. pylori Status

Treatment for all peptic ulcer patient infected with H. pylori was strongly recommended by the 1994 National Institute of Health (NIH) Consensus Development Conference and the 1997 American Digestive Health Foundation (ADHF) International Update Conference on H. pylori. Recommended as appropriate goals for success of an eradication regimen were more than 90% on a “per-protocol” (PP) analysis and more than 80% on an “intent-to-treat” (ITT) analysis.

Bismuth-based triple therapy (BTT: bismuth subsalicylate 2 tablets qid, metronidazole 250 mg qid, and tetracycline 500 mg qid for 2 weeks, accompanied by a H2RA for 4 weeks) produced eradication rates of 77% and 82% in historical trials reviewed by the FDA for approval. BTT has had more limited success in clinical practice because of the regimen’s complexity, metronidazole resistance, and adverse effects. Compliance with BTT needs to be high; the chance of success is greatly reduced in patients who take 60% or less of the prescribed medication. Rates of metronidazole resistance vary widely among different countries and different regions of the same country. They are currently about 50% in the United States and are rapidly increasing.

The combination of omeprazole 40 mg qd and clarithromycin 500 mg tid for 2 weeks, followed by omeprazole 20 mg qd for a further 2 weeks, was the first regimen to the FDA-approved. In FDA pivotal trials, eradication rates were 64% and 74%. Ranitidine bismuth citrate (RBC) is a new chemical entity that is also FDA-approved as part of the treatment of H. pylori infection in patients with peptic ulcer. RBC 400 mg bid with clarithromycin 500 mg tid for 2 weeks, followed by RBC 400 mg bid alone for a further 2 weeks, produced eradication rates of 73% and 84% in FDA pivotal trials.

Increasing evidence suggests that a PPI or RBC plus two antibiotics (i.e., clarithromycin plus either amoxicillin or metronidazole) for 1 to 2 weeks is the best treatment for H. pylori infection. The first PPI-based triple combination to be FDA-approved is lansoprazole 30 mg bid with clarithromycin 500 mg bid and amoxicillin 1000 mg bid for 2 weeks. Eradication rates in a large US-based multicenter trial were 94% (PP) and 86% (ITT).

Although H. pylori infection is the single most common cause of peptic ulceration, it is not the sole cause - particularly in the United States. Recent reports have documented absence of H. pylori infection in up to 42% of patients with peptic

ulcer. Some of these cases may be explicable on the basis of false-negative tests for H. pylori infection, the surreptitious or overuse use of aspirin or NSAIDs, or Zollinger-Ellison syndrome. However, some patients have truly “idiopathic” H. pylori-negative peptic ulcer disease. These patients may have a particularly severe ulcer diathesis characterized by refractoriness to 2RAs, rapid recurrence after healing, and a high incidence of complications. Long-term medical treatment with a PPI is the most appropriate form of management. The FDA has approved omeprazole 20 mg qd and lansoprazole 15 mg qd for the short-term treatment of active duodenal ulcer to produce healing. Lansoprazole 15 mg qd is also FDA-approved as maintenance therapy of healed duodenal ulcer.

There is overwhelming evidence that cure of H. pylori infection eliminates the probability of recurrence of duodenal or gastric ulcer in those patients in whom the ulcer was truly H. pylori-related. True reinfection after cure of H. pylori infection is rare in adults but more frequent in very young children. A number of studies have shown substantial reduction in the rates of recurrent duodenal ulcer hemorrhage 1 to 2 years after cure of H. pylori infection. In patients found to have bleeding from a peptic ulcer, and in whom there is evidence of H. pylori infection, treatment for the infection should be started prior to hospital discharge.

The cumulative costs of different forms of therapy for duodenal ulcer have been modeled over a 15-year period. The total costs of elective surgery or either the continuous or intermittent use of an H2RA were considerably greater than those of antimicrobial treatment for H. pylori infection. Recent studies have also focused on the cost-effectiveness of different methods of diagnosing the presence of peptic ulcer and/or H. pylori infection. In general, treatment of H. pylori infection with some combination of antimicrobial agents and an antisecretory drug, as endorsed by the 1994 NIH conference and the 1997 ADHF conference, has been associated with the lowest cost per ulcer cured. Prompt, effective treatment of H. pylori infection in patients with peptic ulcer makes sound economic sense.

QUESTION:
What is the status of breath tests for diagnosing H. pylori infection?

In the urea breath tests, urea in which carbon 12 has been substituted with carbon 13 or 14 is given by mouth. In the presence of H. pylori infection, the urease of the bacterium splits the urea to produce ammonia and labeled carbon dioxide, which is detected in a breath sample. These commercially available tests are simple to perform and have excellent operating characteristics. They may be used either before or after treatment. Sensitivity of the urea breath tests may be

reduced in patients recently taking antibiotics, bismuth compounds, or acid-suppressing medicines.

QUESTION:
We hear much about metronidazole resistance, but what is the impact of resistance on therapy?

The impact is considerable. Eradication rates for otherwise effective regimens drop to 65% in the presence of metronidazole resistance. A realistic approach is to promote use of the regimens that are effective regardless of the problem of resistance. Adding a PPI to BMT therapy might suffice because with this quadruple regimen the mean eradication rate was reduced by only 2% in patients with resistance to metronidazole. A better and more cost effective approach is the use of PPI, amoxicillin, and clarithromycin. This combination was effective in more than 90% of patients with metronidazole resistance in a recent European trial.

QUESTION:
If a patient has a duodenal ulcer, is it necessary to test for H. pylori?

Although it has been argued that confirmation of H. pylori infection is unnecessary in patients with an endoscopic diagnosis of duodenal Ulcer, H. pylori-negative duodenal ulceration is a definite phenomenon in the United States that requires accurate diagnosis and evaluation. Routine treatment of patients with duodenal ulcer for H. pylori infection is not recommended without prior documentation of infection.

QUESTION:
What is the best way to test for H. pylori?

This method of testing for H. pylori infection depends on the clinical situation. If an ulcer is detected at upper gastrointestinal endoscopy, some form of biopsy urease test is recommended, with the potential caveat that the result may be false-negative. The urea breath test is the method of choice for diagnosing infection when endoscopy is not indicated and for documenting cure of infection after treatment. Serologic analysis may be used for confirming the presence of infection in patients with a previous diagnosis of peptic ulcer and in whom endoscopy is not otherwise necessary.

QUESTION:
What is the status of an H. pylori vaccine?

Vaccination against H. pylori infection is a possibility for the future. There are a number of potential H. pylori antigens that may be used for the purposes of vaccination, particularly urease and heat-shock proteins. These will have to be administered orally with a suitable and safe adjuvant. Preliminary trials of the use of a vaccine therapeutically (rather than prophylactically) have produced reduced colonization with H. pylori in some patients.