

## Implications for treatment: pH, *Helicobacter pylori* or alternative approaches?

W. D. CHEY

University of Michigan Medical Center, Ann Arbor, MI, USA

Accepted for publication 8 November 2004

### INTRODUCTION

There are three well-accepted management strategies for patients with non-investigated dyspepsia. These are the early endoscopy for all, empiric antisecretory therapy, or the *Helicobacter pylori* test and treat strategy, with benefits and limitations to each of these methods.

Although early endoscopy provides a precise diagnosis that guides treatment, its widespread use is limited by its cost (at least in countries such as the USA), availability, and risk for complications that is largely related to the need for conscious sedation. Therefore, it is generally reserved for those patients with onset of dyspepsia symptom after aged 45–50 years, those of all ages with concurrent alarm symptoms, and those who fail to respond to *H. pylori* test and treat strategies or empiric antisecretory therapy.

The test and treat strategy has the advantage of not requiring endoscopy, being less costly than endoscopy, and offers the potential for curative treatment in those found to be infected with *H. pylori*. Its clinical utility is probably greatest in younger patients without alarm symptoms in geographic regions where *H. pylori* prevalence remains robust but gastric cancer prevalence is low. The contribution of *H. pylori* infection to dyspeptic symptoms appears to vary based upon geographic and demographic factors.<sup>1,2</sup> A recent update of the Cochrane systematic review of *H. pylori* eradication therapy in patients with functional dyspepsia found a small but significant benefit associated with cure of the infection: 37% mean response rate in the active treatment group compared with 29% in those treated with placebo or a short course of PPI therapy.<sup>3</sup>

Empiric antisecretory therapy is a widely used, cost-effective, safe management strategy in those with dyspepsia. In a recent publication, two double-blind, randomized, placebo-controlled trials involving 921 patients with functional dyspepsia found that treatment with a proton-pump inhibitor (PPI; lansoprazole 15 mg or 30 mg once daily for 8 weeks) produced significantly ( $P < 0.001$ ) greater mean reductions in the percentage of days with upper abdominal discomfort and, as illustrated in Figure 1, significantly greater number of patients with complete symptom resolution compared with placebo-treated patients.<sup>4</sup> The finding of PPIs being superior to placebo in relieving symptoms is similar to that of a recently updated Cochrane meta-analysis of pharmacological interventions for functional dyspepsia.<sup>5</sup> The major disadvantage to this strategy is that it may, on rare occasions, mask serious disease and postpone timely investigation or subject patients with a curable disease (i.e. *H. pylori*-related ulcer disease) to long-term pharmacological therapy. A recent study reported that response to PPI treatment in functional dyspepsia was most reliable in patients with dyspepsia of short-duration (few days of heartburn during the first week and a history of symptoms for <3 months); low scores for bloating, epigastric pain and diarrhoea;<sup>6</sup> and in young patients with dyspepsia and no alarm symptoms.

### Workshop Consensus on Clinical Management Issues

*The prevalence of H. pylori infection and its contribution to dyspepsia may vary across different geographic regions. What are the current recommendations for testing for H. pylori infection among patients presenting with dyspepsia? Unfortunately, there is no general consensus or recommendations for H. pylori testing among patients with dyspepsia. Factors that influence patient*

Correspondence to: Dr W. D. Chey, University of Michigan Medical Center, Ann Arbor, MI, USA.

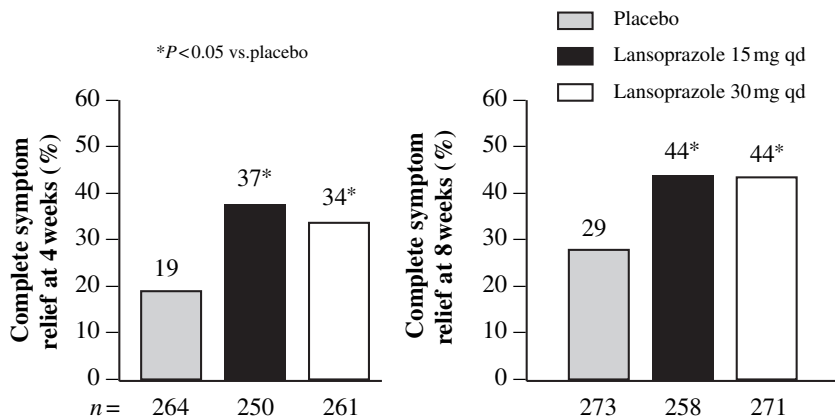


Figure 1. Placebo-controlled trials of lansoprazole in functional dyspepsia. Two identically designed trials found that treatment with lansoprazole 15 mg or 30 mg once daily produced complete symptom relief in significantly higher percentages of patients compared with placebo. Adapted from Peura *et al.*<sup>4</sup>

management strategies include the prevalence of *H. pylori* and the cost and effectiveness of diagnostic testing and treatment. For example, in Asia where the prevalence of *H. pylori* and gastric cancer are high and the costs of endoscopy are low, patients with dyspepsia often undergo endoscopy with *H. pylori* testing early in the management algorithm. On the contrary, in the USA and Europe where *H. pylori* prevalence is relatively low and the costs of endoscopy are relatively high, affected patients more often are treated empirically with antisecretory drugs. Most often patients with dyspepsia in a low *H. pylori* prevalence region have functional dyspepsia or an acid-related disorder such as reflux disease. The use of empiric PPI treatment is a more rational and cost-effective approach than the test and treat strategy or immediate endoscopy. Endoscopy should be performed in patients of any age with alarm symptoms (i.e. weight loss, gastrointestinal blood loss, anaemia, vomiting, severe or progressive symptoms), those >45–50 years of age with new onset symptoms, as well as for those who fail to respond to antisecretory therapy or the test and treat strategy. The cost-effectiveness and effect on clinical outcomes of combining empiric antisecretory therapy and the test and treat strategy before proceeding to endoscopy deserves further study. A recent decision analysis model found that such an approach before endoscopy might be more cost-effective than employing either strategy alone.<sup>7</sup>

*Is empiric PPI treatment a safe, rational and appropriate approach for patients with dyspepsia and without 'alarm features'?* More than 99% of workshop participants agreed (75% strongly and 24% with some reservation) that empiric PPIs are a safe, rational and appropriate strategy for the management of patients with dyspepsia and without alarm features.

*Is PPI treatment a preferred first-line approach for patients with NSAID-associated dyspepsia, assuming the absence of 'alarm features'?* About 59% agreed with reservations (e.g. age of the patient) and 29% strongly agreed that PPI therapy is a preferred first-line approach for patients with non-steroidal anti-inflammatory drug (NSAID)-associated dyspepsia. About 12% either disagreed with reservation (6%) or strongly disagreed (6%) with this strategy.

## REFERENCES

- Ladabaum U, Chey WD, Scheiman J, Fendrick M. Empiric therapy may be cost-effective compared to *H. pylori* testing and treatment in some populations with uninvestigated dyspepsia. *Aliment Pharmacol Ther* 2002; 16: 1491–501.
- Allison JE, Hurley LB, Hiatt RA, *et al.* A randomized controlled trial of test-and-treat strategy for *Helicobacter pylori*: clinical outcomes and health care costs in a managed care population receiving long-term acid suppression therapy for physician-diagnosed peptic ulcer disease. *Arch Intern Med* 2003; 163: 1165–71.
- Moayyedi P, Deeks J, Talley NJ, Delaney B, Forman D. An update of the Cochrane systematic review of *Helicobacter pylori* eradication therapy in nonulcer dyspepsia: resolving the discrepancy between systematic reviews. *Am J Gastroenterol* 2003; 98: 2621–6.
- Peura DA, Kovacs TOG, Metz DC, Siepmann N, Pilmer BL, Talley NJ. Lansoprazole in the treatment of functional dyspepsia: two double-blind, randomized, placebo-controlled trials. *Am J Med* 2004; 116: 740–8.
- Moayyedi P, Soo S, Deeks J, Delaney B, Innes M, Forman D. Pharmacological interventions for non-ulcer dyspepsia. *Cochrane Database Syst Rev* 2003; CD001960.
- Bolling-Sternevald E, Lauritsen K, Talley NJ, Junghard O, Glise H. Is it possible to predict treatment response to a proton pump inhibitor in functional dyspepsia. *Aliment Pharmacol Ther* 2003; 18: 117–24.
- Spiegel BM, Vakil NB, Ofman JJ. Dyspepsia management in primary care: a decision analysis of competing strategies. *Gastroenterology* 2002; 122: 1270–85.