

# Omeprazole was effective in the short term for uninvestigated dyspepsia

Rabeneck L, Soucek J, Wristers K, et al. A double blind, randomized, placebo-controlled trial of proton pump inhibitor therapy in patients with uninvestigated dyspepsia. *Am J Gastroenterol.* 2002;97:3045-51.

## QUESTION

In patients with uninvestigated dyspepsia, is a proton-pump inhibitor (PPI) (omeprazole) effective?

## DESIGN

Randomized (allocation concealed\*), blinded (patients and clinicians),\* placebo-controlled trial with 12-month follow-up.

## SETTING

A Veterans Affairs outpatient clinic in Houston, Texas, USA.

## PATIENTS

140 patients who were  $\geq 18$  years of age (mean age 51 y, 95% men), had  $\geq 1$ -week history of dyspepsia, and had not had a diagnostic workup with either endoscopy or barium swallow in the past 6 months. Exclusion criteria were a single complaint of heartburn, history of documented peptic ulcer, previous gastric surgery, dysphagia, unintentional weight loss of  $> 10$  lb, melena or hematemesis in previous 3 months, use of anticoagulants or oral corticosteroids, confusion, homelessness, or need for hospitalization. Follow-up was 84%.

## COMMENTARY

Empirical acid suppression is a popular initial dyspepsia management strategy; a Cochrane review concluded that PPIs are significantly better than  $H_2$ -antagonists or antacids for dyspepsia in the short term (1). Rabeneck and colleagues found that a short empirical PPI course was beneficial at 2 weeks but did not succeed at 1 year (based on a score defining the need for endoscopy). This is not surprising; the patients had uninvestigated dyspepsia, which probably comprised predominantly nonulcer dyspepsia (NUD) and gastroesophageal reflux disease (GERD), or (less likely) undiagnosed peptic ulcer disease (PUD). Endoscopy in those with treatment failure showed that 13% had PUD and 36% had esophagitis. Patients with GERD and PUD respond adequately to PPI but often relapse off therapy; any benefit of acid suppression in NUD is controversial (2). Adenocarcinoma of the stomach or distal esophagus would be unlikely because patients with alarm features were excluded. Although risk for cancer increases with age (with the threshold for its consideration usually set at 50 years) and older patients were included in this trial, no cancer was observed.

*Helicobacter pylori* status was not considered, although 50% of patients were infected. In places where this infection is still relatively common, it cannot be ignored. Chiba and colleagues randomized *H. pylori*-positive patients with uninvestigated dyspepsia to either empirical triple therapy or omeprazole for 7 days; at 1 year, 50% of patients in the eradication arm (versus 36% in the PPI arm) had no or minimal dyspepsia, and eradication therapy reduced costs (3).

Empirical acid suppression has other disadvantages. Many patients continue inappropriate treatment. Pharmacy billing data suggest that

## INTERVENTION

Patients were allocated to oral omeprazole, 20 mg twice daily ( $n = 71$ ) or placebo ( $n = 69$ ) for 6 weeks. Patients were told to discontinue any nonsteroidal anti-inflammatory drugs except aspirin, 325 mg/d. Patients were given acetaminophen as an analgesic and Gelusil tablets (Pfizer Canada Inc., Arnprior, ON, Canada) for dyspepsia, if needed.

## MAIN OUTCOME MEASURES

Treatment failure, which was defined as SODA (Severity of Dyspepsia Assessment) Pain Intensity Score  $\geq 29$  at any follow-up. The SODA Pain Intensity scale has 6 items, and scores range from 2 to 47 (more severe pain).

## Treatment failure rates for omeprazole vs placebo in uninvestigated dyspepsia†

Follow-up	Omeprazole	Placebo	RRR (95% CI)	NNT (CI)
2 wk	17%	35%	51% (12 to 74)	6 (4 to 30)
6 wk	30%	45%	34% (-1.8 to 58)	Not significant
1 y	52%	59%	12% (-18 to 35)	Not significant

†Abbreviations defined in Glossary; RRR, NNT, and CI calculated from data in article.

## MAIN RESULTS

Analysis was by intention to treat. Fewer patients in the omeprazole group than in the placebo group had treatment failure at 2 weeks (Table). The difference was not statistically significant at 6 weeks or 1 year (Table).

## CONCLUSION

In patients with uninvestigated dyspepsia, a proton-pump inhibitor (omeprazole) was effective in the short term.

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\*See Glossary.

3% of the population take acid suppressants, but less than two thirds have a relevant indication and few have had diagnostic testing (4). Acid suppression may mask some diagnoses and reduce the diagnostic yield if endoscopy becomes indicated (5).

Empirical PPI treatment for 4 to 8 weeks is still reasonable in younger dyspeptic patients with no alarm features who are *H. pylori*-negative. For patients in whom PPI then fails, optimal long-term management remains poorly defined.

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