Review: Prokinetics and histamine-2 receptor antagonists improve symptom scores in nonulcer dyspepsia

Soo S, Moayyedi P, Deeks J, et al. **Pharmacological interventions for non-ulcer dyspepsia.** Cochrane Database Syst Rev. 2000;(2):CD001960 (latest version 22 Feb 2000).

QUESTION

In patients with nonulcer dyspepsia, what is the relative effectiveness of 6 classes of drugs in improving symptom scores and quality of life?

DATA SOURCES

Studies were identified by searching the Cochrane Controlled Trials Register, MEDLINE (1966 to 1999), EMBASE/Excerpta Medica (1988 to 1999), CINAHL (1982 to 1999), and SIGLE. Members of the Cochrane Upper Gastrointestinal and Pancreatic Diseases Group, experts in the field of dyspepsia, and pharmaceutical companies with an interest in gastroenterology were contacted for details of unpublished trials.

STUDY SELECTION

Studies were selected if they were randomized controlled trials that included adult patients with dyspepsia symptoms and compared 1 of 6 drug classes (antacids, histamine-2 receptor antagonists [H_2RAs], proton-pump inhibitors, prokinetics, mucosal protection agents, and antimuscarinics) with placebo or a drug of a different class.

DATA EXTRACTION

Data were extracted on patient characteristics, recruitment source, diagnostic criteria, dyspeptic symptoms, intervention and dosage, outcomes (dichotomous and continuous variables), and study quality.

MAIN RESULTS

57 trials were included. In comparisons with placebo, trials of prokinetics (12 trials), H_2RAs (8 trials), and antimuscarinics (2 trials) showed improvement in dyspeptic symptoms with the active drugs (Table). No other drug classes differed from placebo, irrespective of whether they were analyzed as dichotomous or continuous variables. Trials with direct comparisons between prokinetics and H_2RAs, antacids and H_2RAs, and H_2RAs and the antimuscarinic pirenzepine did not show statistically significant differences. Prokinetics and H_2RAs were more effective than was placebo in reducing individual dyspeptic symptoms. The prokinetics trials were considered most subject to potential publication bias.

CONCLUSION

In patients with nonulcer dyspepsia, prokinetics and histamine-2 receptor antagonists are the most effective of 6 classes of drug in improving symptom scores and quality of life.

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Drug classes vs placebo for improvement in dyspeptic symptom scores*

Drug class	Number of trials	Number of patients	Weighted event rates		RBI (95% CI)	NNT (CI)
			Active drug	Placebo		
Prokinetics†	12	829	75%	44%	50% (30 to 65)	4 (3 to 6)
H_2RAs	8	1225	71%	51%	30% (4 to 48)	6 (5 to 9)
Antimuscarinics (pirenzepine)	2	163	79%	58%	50% (19 to 69)	5 (3 to 14)

*H_2RAs = histamine-2 receptor antagonists. Treatment duration was 2 to 6 weeks for prokinetics and H_2RAs and 4 weeks for pirenzepine. Other abbreviations defined in Glossary; RBI, NNT, and CI calculated from data in article.
†11 of the 12 prokinetics trials evaluated cisapride.

COMMENTARY

Dyspepsia is a common disorder with a prevalence of 20% to 50%, more than half of which is nonulcer dyspepsia (1). Clinicians must first determine whether endoscopic evaluation is indicated, then whether *Helicobacter pylori* status should be tested, and finally which treatment to offer.

A consensus panel described criteria for nonulcer dyspepsia (2). However, nonulcer dyspepsia is multifactorial, and differences in case definition not only account for much of the variability of prevalence estimates but also create heterogeneity among trials. These factors limit the confidence we can place in pooled estimates of effect. Soo and colleagues did a careful systematic review of data from 57 trials after excluding 50 studies that did not meet eligibility requirements and 37 eligible studies for which data extraction was not possible. They included trials in which case definition and outcome assessment methods were clear. This filter, although important for a meta-analysis, risks excluding potentially important studies. In fact, the authors caution that the prokinetic effect may be subject to publication bias and is therefore hard to interpret (3). They also warn that the quality of the H_2RA studies was poor.

The findings show that 50% of patients get better on placebo, whereas 25% have persistent symptoms. Clearly, we need to better understand the underlying mechanisms of this disorder. Some patients improve dramatically with therapy, but typical patients require long-term treatment. Until larger, long-term, high-quality trials are done, clinicians should continue to individualize therapy, searching for the most effective, safe, and economical choice over the long term.

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