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


**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the field of dyspepsia, and pharmaceutical companies with an interest in gastroenterology were contacted for details of unpublished trials.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 [H2RAs], 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), H2RAs (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 H2RAs, antacids and H1RAs, and H2RAs and the antimuscarinic pirenzepine did not show statistically significant differences. Prokinetics and H1RAs 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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**For correspondence:** Dr. S. Soo, 30-32 Hyde Terrace, Leeds LS2 9LN, England, UK. FAX 44-113-233-6778.

### Drug classes vs placebo for improvement in dyspeptic symptom scores*

<table>
<thead>
<tr>
<th>Drug class</th>
<th>Number of trials</th>
<th>Number of patients</th>
<th>Weighted event rates</th>
<th>RBI (95% CI)</th>
<th>NNT (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prokinetics†</td>
<td>12</td>
<td>829</td>
<td>75%</td>
<td>44%</td>
<td>50% (30 to 65)</td>
</tr>
<tr>
<td>H2RAs</td>
<td>8</td>
<td>1225</td>
<td>71%</td>
<td>51%</td>
<td>30% (4 to 48)</td>
</tr>
<tr>
<td>Antimuscarinics (pirenzepine)</td>
<td>2</td>
<td>163</td>
<td>79%</td>
<td>58%</td>
<td>50% (19 to 69)</td>
</tr>
</tbody>
</table>

*H2RAs = histamine-2 receptor antagonists. Treatment duration was 2 to 6 weeks for prokinetics and H2RAs 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 endoscopic evaluation is indicated, then which therapies, recruitment source, diagnostic criteria, dyspeptic symptoms, intervention and dosage, outcomes (dichotomous and continuous variables), and study quality.

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.

Mark D. Schwartz, MD
New York University School of Medicine
New York, New York, USA

**References**