Review: prokinetics, histamine H2 receptor antagonists, antimuscarinics, and proton pump inhibitors improve global symptoms in non-ulcer dyspepsia

Richard J Saad and William D Chey

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Review: prokinetics, histamine H2 receptor antagonists, antimuscarinics, and proton pump inhibitors improve global symptoms of non-ulcer dyspepsia


Q In patients with non-ulcer dyspepsia (NUD), do antacids, histamine H2 receptor antagonists (H2RAs), proton pump inhibitors (PPIs), prokinetics (PROK), mucosal protecting agents (MPAs), and antimuscarinics improve symptoms?

**METHODS**

**Data sources:** Medline (1966 to January 2006), CINAHL (1982 to January 2006), EMBASE/Excerpta Medica (1988 to January 2006), Cochrane Central Register of Controlled Trials (Cochrane Library, Issue 4, 2005), SIGLE, bibliographies of relevant studies, experts in the field, and pharmaceutical companies.

**Study selection and assessment:** randomised controlled trials (RCTs) that compared antacids, H2RAs, PPIs, PROK, MPAs, or antimuscarinics with placebo or other drugs in patients with symptoms of NUD and no significant findings on endoscopy or barium studies. Studies of patients who had peptic ulcer disease, pancreato-biliary disease, neoplastic disease, or genetic or psychosocial factors were excluded. 73 RCTs met selection criteria: 19 RCTs (n = 3178) evaluated PROK, 12 RCTs (n = 2183) evaluated H2RAs, and 10 RCTs (n = 3347) evaluated PPIs. Quality assessment was based on randomisation, allocation concealment, and blinding. Funnel plot analyses suggested possible publication bias in RCTs that evaluated PROK.

**Outcomes:** improvement in individual or global symptoms of NUD.

**MAIN RESULTS**
The table shows the results.

**CONCLUSION**
Prokinetics, histamine H2 receptor antagonists, antimuscarinics, and proton pump inhibitors improve global symptoms of non-ulcer dyspepsia.

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**Commentary**

**NUD or functional dyspepsia (FD) remains a challenge for clinicians.** The review by Moayyedi et al provides the most up-to-date analysis of medical options for this condition. The central problem with FD is its heterogeneity. FD can present as abdominal pain or discomfort, postprandial fullness, bloating, early satiety, belching, or nausea and/or vomiting. Its postulated pathophysiology includes abnormal motor and reflex functions, visceral hypersensitivity, altered brain-gut interactions, disrupted gut-immune interactions, and genetic or psychosocial factors. No single mechanism is universally responsible, and it is likely that several contribute in most cases. Consequently, no single therapy has been universally effective for FD.

This review suggests that specific drug classes such as PPIs or PROKs are effective in subsets of FD patients. The challenge is to identify clinical factors that predict response. PPIs appear most effective in patients with heartburn or epigastric burning, which suggest an acid-related aetiology. Conversely, PROKs are no more effective than placebo in patients with symptoms that suggest abnormal sensorimotor function, including nausea, postprandial fullness, or early satiety. Unfortunately, methods to define such subgroups remain imperfect. The Rome III criteria subclassify FD into epigastric pain syndrome and postprandial distress syndrome. It remains to be proven whether this scheme is physiologically valid or, more importantly, clinically useful.

Unless we identify symptoms or biomarkers that predict drug response, empirical therapy will remain the primary approach to FD. Clinicians can expect more studies with marginal therapeutic gains, as well as continued return visits from patients with FD.

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<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Number of trials (n)</th>
<th>Comparisons</th>
<th>Weighted event rates</th>
<th>RRR [95% CI]</th>
<th>NNT [CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Global symptoms</td>
<td>19 (3178)</td>
<td>PROK v H2RA</td>
<td>32% v 53%</td>
<td>33% (18 to 45)</td>
<td>5 (4 to 10)</td>
</tr>
<tr>
<td></td>
<td>12 (2183)</td>
<td>H2RA v PLAC</td>
<td>44% v 60%</td>
<td>23% (8 to 35)</td>
<td>7 (4 to 15)</td>
</tr>
<tr>
<td></td>
<td>10 (3347)</td>
<td>PPI v PLAC</td>
<td>66% v 75%</td>
<td>13% (4 to 20)</td>
<td>12 (7 to 50)</td>
</tr>
<tr>
<td></td>
<td>2 (163)</td>
<td>AMSCs v PLAC</td>
<td>21% v 42%</td>
<td>50% (19 to 69)</td>
<td>5 (3 to 13)</td>
</tr>
</tbody>
</table>

**RRI [CI] NNNH [CI]**

**Epigastric pain and discomfort**

<table>
<thead>
<tr>
<th>Number of trials (n)</th>
<th>RRI [CI]</th>
<th>NNNH [CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (138)</td>
<td>55% v 35%</td>
<td>58% (8 to 133)</td>
</tr>
</tbody>
</table>

*Abbreviations defined in glossary; weighted event rates, RRR, RRI, NNT, NNH, and CI based on a random effects model.*