Review: Cisapride reduces overall and global symptoms in adults with nonulcer dyspepsia, but study quality is poor


QUESTION
Is cisapride as effective as placebo, H2 antagonists, and proton-pump inhibitors for relief or reduction of symptoms in patients with nonulcer dyspepsia (NUD)?

DATA SOURCES
Studies were identified by searching MEDLINE, HealthSTAR, TOXLINE, EMBASE/Excerpta Medica, Current Contents Online, and the Cochrane Library up to the end of 1999. Lists of conference abstracts in Gastroenterology, 1989 to 1998, were hand searched, and the manufacturer of cisapride was contacted.

STUDY SELECTION
Randomized controlled trials were selected if adults with NUD were studied, endoscopy had eliminated esophagitis or peptic ulcer, cisapride was compared with control treatments, treatment duration was ≥2 weeks, and outcomes of improvement in global dyspepsia or specific symptoms (epigastric pain, early satiety, nausea, belching, and bloating) were recorded.

DATA EXTRACTION
Data were extracted on study quality, patient and study characteristics, symptoms at baseline, and symptom resolution at the end of treatment. “No symptoms” was considered to be an excellent outcome, and “improvement in symptoms” was considered to be a good outcome.

MAIN RESULTS
15 studies (1681 patients) compared cisapride with placebo, 2 (526 patients) compared cisapride with H2 antagonists, and 1 studied both. No studies evaluated proton-pump inhibitors. 1 study had high-quality scores, 16 had moderate-quality scores, and 1 had a low-quality score. More patients reported excellent outcomes (Peto odds ratio [OR] using fixed effects 4.58, 95% CI 3.58 to 5.85) and excellent or good outcomes (OR 4.25, CI 3.42 to 5.27) with cisapride than with placebo (Table). Significant heterogeneity was present and may have affected the findings of decreased epigastric pain (OR 5.34, CI 2.60 to 10.9), early satiety (OR 2.85, 1.54 to 5.24), belching (OR 4.13, CI 1.96 to 8.69), and bloating (OR 3.13, CI 1.68 to 5.81) but not nausea (OR 1.39, CI 0.73 to 2.62). Sensitivity analysis showed that the results may have been biased because of the presence of poor-quality trials published in supplements and non–English-language journals. Cisapride and H2 antagonists did not differ for symptomatic resolution (OR for excellent outcome 1.43, CI 0.98 to 2.08, and OR for excellent or good outcome 1.13, CI 0.6 to 2.13).

CONCLUSION
Although cisapride appears to improve symptoms more than does placebo in adults with nonulcer dyspepsia, this effect may be caused mainly by bias in individual studies.

Source of funding: Federal and provincial Departments of Health.


Cisapride vs placebo for adults with nonulcer dyspepsia*

<table>
<thead>
<tr>
<th>Symptoms after 2 to 6 wk</th>
<th>Weighted event rates</th>
<th>RBI (95% CI)</th>
<th>NNT (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cisapride</td>
<td>Placebo</td>
<td></td>
</tr>
<tr>
<td>Excellent resolution</td>
<td>19%</td>
<td>17%</td>
<td>152% (64 to 287)</td>
</tr>
<tr>
<td>Excellent or good resolution</td>
<td>77%</td>
<td>40%</td>
<td>90% (70 to 110)</td>
</tr>
</tbody>
</table>

*Abbreviations defined in Glossary; RBI, NNT, and CI calculated from data in article using a fixed-effects model.

The effect of cisapride in NUD may well be subject to bias. Therefore, no reliable evidence is available to support its efficacy. Dubious efficacy combined with serious toxicity should lead to cisapride’s timely withdrawal from our therapeutic offerings.

Brendan Delaney, MD, BMBCh
University of Birmingham Medical School
Birmingham, England, UK

References