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

Shukla VK, Otten N, Dubé C, Moher D. **Use of cisapride in patients with non-ulcer dyspepsia: a meta-analysis of randomized trials.** Ottawa: Canadian Coordinating Office for Health Technology Assessment (CCOHTA); Feb 2000.

QUESTION

Is cisapride as effective as placebo, H_2 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 H_2 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 H_2 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.

For correspondence: CCOHTA, 110-955 Green Valley Crescent, Ottawa, Ontario K2C 3V4, Canada. FAX 613-226-5392. Web site http://www.ccohta.ca/pubs/index.asp.

Cisapride vs placebo for adults with nonulcer dyspepsia*

Symptoms after 2 to 6 wk	Weighted event rates		RBI (95% CI)	NNT (CI)
	Cisapride	Placebo		
Excellent resolution	19%	17%	152% (64 to 287)	5 (3 to 12)
Excellent or good resolution	77%	40%	90% (70 to 110)	3 (3 to 4)

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

COMMENTARY

This meta-analysis published by the Canadian Coordinating Office for Health Technology Assessment of the effectiveness of cisapride in NUD reaches conclusions that are similar to those of a recently published Cochrane review (1). Because cisapride has been linked with adverse reactions in patients with cardiac disease (2) and is one of the more costly treatments for dyspepsia, it is particularly important to establish clear evidence of benefit.

Meta-analysis is not only a method of pooling individual trial results to obtain an overall estimate of effect, it is also a process of critical evaluation of the studies to detect bias. A reliable estimate of the overall effect can only be obtained if the individual studies are similar.

In this study, strong evidence showed that the trials were not similar (expressed as significant heterogeneity). An excess of small trials with results in favor of cisapride were identified. This excess could be caused by publication bias. Small negative trials may not be published, whereas the favorable ones may appear in journal supplements. Poor-quality trials have also been shown to exaggerate treatment effects (3).

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.

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References

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