

Esomeprazole was not better than omeprazole for resolving heartburn in endoscopy-negative reflux disease

Armstrong D, Talley NJ, Lauritsen K, et al. The role of acid suppression in patients with endoscopy-negative reflux disease: the effect of treatment with esomeprazole or omeprazole. *Aliment Pharmacol Ther.* 2004;20:413-21.

QUESTION

In patients with endoscopy-negative reflux disease (ENRD), is esomeprazole more effective than omeprazole for resolving heartburn?

METHODS

Design: 3 randomized controlled trials with similar design.

Allocation: {Concealed}†.*

Blinding: Blinded {patients, clinicians, data collectors, outcome assessors, data analysts, and monitoring committee}†.*

Follow-up period: 4 weeks (immediately at the end of therapy).

Setting: 10 countries (Canada, England, and Ireland [study A]; France, Germany, and Switzerland [study B]; and Denmark, Finland, Norway, and Sweden [study C]).

Patients: Patients with ENRD who were symptomatic, had heartburn as their main symptom for ≥ 6 months and for ≥ 4 days in the week before starting the study, and had normal results on endoscopy.

Intervention: In study A ($n = 1282$, mean age 48 y, 57% women), patients received esomeprazole, 40 mg ($n = 425$) or 20 mg

($n = 423$), or omeprazole, 20 mg ($n = 434$).

In study B ($n = 693$, mean age 50 y, 55% women), patients received esomeprazole, 40 mg ($n = 347$), or omeprazole, 20 mg ($n = 346$). In study C ($n = 670$, mean age 49 y, 51% men), patients received esomeprazole, 20 mg ($n = 336$), or omeprazole, 20 mg ($n = 334$). All doses were taken orally in the morning, once daily for 4 weeks.

Outcome: Resolution of heartburn (no heartburn symptoms in the previous 7 d).

Patient follow-up: 100% (intention-to-treat analysis) for all 3 studies.

MAIN RESULTS

Groups did not differ for resolution of heartburn among the 3 studies (Table).

CONCLUSION

In patients with endoscopy-negative reflux disease, esomeprazole was not better than omeprazole for resolving heartburn.

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*See Glossary.

†Information provided by author.

Esomeprazole, 40 or 20 mg, vs omeprazole, 20 mg, for resolution of heartburn in endoscopy-negative reflux disease at 4 weeks ‡

Study	Comparisons	Event rates	RBR (95% CI)	NNH
A	Esomeprazole 40 mg vs omeprazole	57% vs 58%	2% (-10 to 13)	Not significant
	Esomeprazole 20 mg vs omeprazole	61% vs 58%	4% (-7 to 17)	Not significant
B	Esomeprazole 40 mg vs omeprazole	70% vs 68%	4% (-6 to 14)	Not significant
	Esomeprazole 20 mg vs omeprazole	62% vs 60%	4% (-8 to 17)	Not significant

‡RBR = relative benefit reduction. Other abbreviations defined in Glossary; RBR, RBI, NNH, NNT, and CI calculated from data in article.

COMMENTARY

Patients present to family physicians with a constellation of upper gastrointestinal symptoms rather than a single complaint (1). If heartburn is predominant, these patients are considered to have gastroesophageal reflux disease (GERD). After endoscopy, these patients can be divided into those with erosive disease and those without (ENRD). However, because patients in practice are rarely investigated before receiving empiric drug treatment, the results of the study by Armstrong and colleagues are not generalizable to primary care.

The overall low rate of heartburn resolution (about 60% of patients in this study) reminds one of how arbitrary the designation of ENRD really is compared with that of erosive disease, which has better symptom resolution with proton-pump inhibitors (PPIs). Although the hypothesis of this study was that greater acid suppression with esomeprazole would result in greater heartburn relief than that achieved with omeprazole, the low rate of symptom resolution reflects the heterogeneity of the ENRD population. The benefit of esomeprazole over omeprazole is most apparent when healing the most severe grades of esophagitis. Patients in these studies may have a milder form of GERD or they may have had functional dyspepsia, in which rates of symptom relief with PPIs are known to be lower. It is noteworthy that extending

the treatment duration from 2 to 4 weeks in these studies improved heartburn resolution.

The authors did not provide a sample size calculation, so no estimate is provided of the power of these studies to show either equivalence or differences among groups. However, because a total of 2645 patients were included, a clinically relevant difference would be unlikely.

Thus, while symptoms are clearly not very diagnostic, it is reasonable to accept PPIs as the most effective agents for front-line therapy and to propose that patients should receive them for a minimum of 4 weeks as a therapeutic trial. More work is needed to determine what causes heartburn in the remaining 40% of patients who do not improve with PPIs.

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Reference

1. Thomson AB, Barkun AN, Armstrong D, et al. The prevalence of clinically significant endoscopic findings in primary care patients with uninvestigated dyspepsia: the Canadian Adult Dyspepsia Empiric Treatment Prompt Endoscopy (CADET-PE) study. *Aliment Pharmacol Ther.* 2003;17:1481-91.