

Review: On-demand maintenance therapy with proton pump inhibitors is as effective as continuous therapy for nonerosive GERD

Pace F, Tonini M, Pallotta S, Molteni P, Porro GB. Systematic review: maintenance treatment of gastro-oesophageal reflux disease with proton pump inhibitors taken "on-demand". *Aliment Pharmacol Ther.* 2007;26:195-204.

Clinical impact ratings: GIM/FP/GP ★★★★★☆ Gastroenterology ★★★★★☆☆

QUESTION

In patients with gastroesophageal reflux disease (GERD), is on-demand maintenance therapy with proton pump inhibitors (PPIs) effective for controlling symptoms and preventing relapse?

METHODS

Data sources: MEDLINE and Cochrane Controlled Trials Register (to December 2006), and reference lists.

Study selection and assessment: Studies published in English as full articles that compared on-demand maintenance therapy, using PPIs or H₂-receptor antagonists, with placebo or continuous maintenance therapy in patients with GERD, with or without erosive esophagitis. 17 articles reporting on 16 studies ($n = 14\ 142$) met the selection criteria. All studies used PPIs (esomeprazole, 20 or 40 mg; lansoprazole, 15 or 30 mg; omeprazole, 10 or 20 mg; pantoprazole, 20 or 40 mg; or rabeprazole, 10 or 20 mg); 1 study also included an H₂-receptor antagonist (ranitidine, 300 mg). In the 14 randomized controlled trials (RCTs), symptomatic patients were first given a short course (4 to 8 wk) of continuous treatment, and then responding patients were randomized to the different maintenance treatment groups.

Outcomes: Willingness to continue with treatment as assigned, symptom relief, or endoscopic remission at 6 months; mean

number of doses of study drug taken per day; and costs.

MAIN RESULTS

Because of differences in outcome measures among studies, meta-analysis was not done. On-demand PPI therapy was more effective than placebo for all levels of GERD severity (Table). It was more effective than continuous PPI therapy in patients with nonerosive GERD but not in patients with erosive or uninvestigated GERD (Table). 1 RCT ($n = 6017$) showed that continuous PPI therapy provided better quality of life than on-demand PPI therapy in patients with nonerosive or mildly erosive GERD. 2 pharmacoeconomic studies based on RCTs

showed that total costs were lower with on-demand treatment than with continuous or physician-directed intermittent treatment.

CONCLUSIONS

In patients with gastroesophageal reflux disease (GERD), on-demand maintenance therapy with proton pump inhibitors (PPIs) is more effective than placebo for controlling symptoms. On-demand PPI therapy is as effective as continuous PPI therapy in patients with nonerosive GERD but not in those with more severe disease.

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Randomized controlled trials of on-demand maintenance therapy with proton pump inhibitors (PPIs) for gastroesophageal reflux disease (GERD) at 6 months

Comparisons	Severity of GERD	Number of trials (n)	Willingness to continue with treatment	Mean number of study drug doses/d
On-demand PPI vs placebo	Nonerosive	4 (2009)	70% to 94% vs 48% to 72%*	0.25 to 0.43 vs 0.40 to 0.47
	Nonerosive or mildly erosive	2 (987)	98% vs 89%*; 88% vs 64%*	0.34 vs 0.35
	Uninvestigated	1 (181)	81% vs 61%*	0.22 vs 0.18
On-demand PPI vs continuous PPI	Nonerosive	1 (622)	93% vs 88%*	0.30 vs 0.80
	Nonerosive or mildly erosive	1 (176)	75% vs 86%†	0.31 vs 0.96
	Uninvestigated	1 (1292)	52% vs 83%‡	—
	Erosive	1 (477)	58% vs 81%‡§	—

*Statistically significant difference in favor of on-demand PPI.

†Outcome is symptom relief.

‡Statistically significant difference in favor of continuous PPI.

§Outcome is endoscopic remission.

COMMENTARY

GERD is a chronic condition necessitating long-term therapy in most patients, with continuous PPI use being the most common prescription pattern (1). Because of cost and safety issues, several alternatives to this approach have been suggested, including intermittent therapy (sustained periods of continuous therapy followed by discontinuation until symptoms recur) and on-demand therapy (patient-driven use based on day-to-day symptoms). Many experts recommend the use of on-demand therapy for nonerosive GERD (2), a view that is supported by the review by Pace and colleagues. The designs, outcomes, and even patient populations (as evidenced by varying placebo response rates) of the included studies are heterogeneous; thus, the authors have appropriately refrained from doing a meta-analysis.

For the practicing clinician, considerable support now exists for recommending on-demand therapy for nonerosive GERD and continuous therapy for complicated GERD (e.g., ulcers, strictures, and Barrett esophagus). The findings of this review also have implications for the pharmaceutical industry: Over-the-counter drugs may be preferred for on-demand regimens because of cost and availability.

How to approach mildly erosive GERD remains a matter of contro-

versy, at the heart of which lies the question of whether GERD is a "categorical" disease with phenotypically stable patterns (nonerosive, mildly erosive, and complicated) or is more of a spectrum with both regression and progression among these subtypes (3). If it is the former, then on-demand therapy is appropriate for mildly erosive GERD because inadequate treatment carries little risk for disease progression. For now, however, a reasonable alternative is to treat such patients continuously but at one half the dosage once complete symptomatic and endoscopic remission has been achieved (4).

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