Proton pump inhibitor therapy for suspected GERD-related chronic laryngitis: a meta-analysis of randomized controlled trials


CRD summary
This review compared proton-pump inhibitors (PPIs) with placebo for treating suspected gastroesophageal reflux disease-related chronic laryngitis in adults. The authors concluded that PPI therapy had a modest but non-significant effect over placebo. This was a well-conducted systematic review and the conclusion appears reliable.

Authors' objectives
To evaluate the efficacy of proton-pump inhibitors (PPIs) for treating suspected gastroesophageal reflux disease (GERD)-related chronic laryngitis.

Searching
MEDLINE, EMBASE, the Cochrane Controlled Trials Register and ClinicalTrials.gov were searched for English language reports. The search dates covered 1966 to August 2005 and the keywords were reported. The authors also handsearched meetings of the American Gastroenterological Association, the American College of Gastroenterology and the Triology Society (1999 to 2005) for additional papers.

Study selection
Study designs of evaluations included in the review
Double-blind, randomised controlled trials (RCTs) were eligible for inclusion.

Specific interventions included in the review
Studies of PPIs versus placebo were eligible for inclusion. The PPIs in the included studies were esomeprazole, pantoprazole, lansoprazole, rabeprazole and omeprazole administered once or twice daily. The dosages varied from 20 to 40 mg twice daily. The duration of therapy ranged from 8 to 16 weeks.

Participants included in the review
Studies of adults of at least 18 years of age with suspected GERD-related chronic laryngitis were eligible for inclusion. Suspected GERD-related chronic laryngitis was defined as one or more of the following symptoms: presence of hoarseness, globus sensation, frequent throat clearing, excessive phlegm, chronic cough, plus the presence of GERD-attributed signs of laryngitis on laryngoscopy including edema, erythema, contact ulcer, pachydermia and/or granuloma. Trials that enrolled participants with only chronic cough who did not undergo laryngoscopic evaluation for GERD-related laryngitis were excluded. The mean age of the participants ranged from 38 to 62 years. The proportion of men ranged from 29 to 95% of the study sample.

Outcomes assessed in the review
The outcome assessed was the proportion of participants with at least 50% reduction in self-reported laryngeal symptoms compared with baseline.

How were decisions on the relevance of primary studies made?
Three authors independently assessed the papers, which were then selected by consensus.

Assessment of study quality
Study quality was assessed in relation to randomisation, sequence generation, allocation concealment, blinding, and descriptions of withdrawals and drop-outs. Two authors independently assessed the validity and then reached consensus.
Data extraction
Three authors independently extracted the data from the studies. For each study, the proportion of participants who reported an at least 50% reduction in laryngeal symptoms compared with baseline was extracted. Investigators were contacted for missing information. When available, data from the non-crossover period of crossover trials were used.

Methods of synthesis
How were the studies combined?
A meta-analysis was used to estimate the pooled relative risk (RR) with 95% confidence intervals (CIs), using a random-effects model. Analyses were performed on an intention-to-treat basis. Publication bias was tested using Egger's method and assessed visually using a funnel plot.

How were differences between studies investigated?
A chi-squared test was used to test for statistical heterogeneity (at the p<0.10 level). Heterogeneity was investigated using meta-regression, in which several study variables were assessed. Sensitivity analyses were performed using different statistical methods (fixed-effect versus random-effects) and by examining the contribution of each study.

Results of the review
Eight RCTs (n=344) were included.

Six of the 8 included studies were considered to be of a high quality.

There was no significant difference between PPI and placebo in the proportion of patients with an at least 50% reduction in laryngeal symptoms (RR 1.28, 95% CI: 0.94, 1.74; 8 studies). No significant statistical heterogeneity was observed between the studies.

Meta-regression did not identify any significant clinical predictors of response to PPIs. There was evidence of publication bias.

Authors' conclusions
In comparison with placebo, PPI therapy may offer a modest, but non significant, clinical benefit.

CRD commentary
The inclusion criteria concerning the participants, interventions and study design were clearly defined. Several databases were searched, and the authors included both published and unpublished studies to minimise publication bias. The authors restricted their search to English language publications, thus potentially introducing language bias. Steps were taken to minimise reviewer bias and errors in the study selection, data extraction and quality assessment processes. The authors provided clear information about what quality criteria were reported for each study (e.g. allocation generation, allocation concealment), but did not explicitly state if these criteria were adequately applied. The number of participants in the included studies, and the overall number of participants this review was based on, was very small. Standard statistical methods were used to pool the data and potential sources of heterogeneity were explored. The authors also examined publication bias. The review appears to be well-conducted, and the authors' conclusion seems reliable based on the evidence presented.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: The authors stated that future RCTs should use validated guidelines for the diagnosis of GERD-related chronic laryngitis when assessing the effectiveness of PPI treatment.
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