Speed of healing and symptom relief in grade II to IV gastroesophageal reflux disease: a meta-analysis

Authors' objectives
To evaluate speed of healing and symptom relief in grade II to IV gastroesophageal reflux disease, treated with different drug classes.

Searching
MEDLINE was searched up to July 1999 using the MeSH terms 'gastroesophageal reflux' and 'randomized controlled studies', and using 'esophagitis' with the names of each respective drug. The European Journal of Gastroenterology and Hepatology was manually searched. The reference lists of all the retrieved articles were also checked.

Study selection
Study designs of evaluations included in the review
Single- or double-blind, randomised studies were included. Studies with less than 20 patients per arm were excluded. Abstracts and non-English articles were also excluded.

Specific interventions included in the review
Proton-pump inhibitors (including omeprazole, lansoprazole and pantoprazole); H2-receptor antagonists (including cimetidine, nizatidine, ranitidine and famotidine); sucralfate; prokinetics (cisapride); placebo.

Participants included in the review
Patients aged 16 years and over with endoscopically proven grade II to IV erosive or ulcerative esophagitis. The study patients were predominantly male (65%) with a mean age of 51 years.

Outcomes assessed in the review
Endoscopic healing of all erosions: the healing proportion (i.e. the number of patients healed per number treated, expressed as a percentage) and the healing rate (i.e. the percentage of patients healed per week).

Symptom relief: the number of patients who obtained complete relief of heartburn symptoms, and improvement in heartburn symptoms over time.

How were decisions on the relevance of primary studies made?
Each article was reviewed by two independent reviewers, and one arbitrator reviewed any discrepancies.

Assessment of study quality
Blinding of the study and randomisation were considered as the most important and second-most important criteria in the assessment of study validity. Other quality issues that were also mentioned were: patient selection; baseline characteristics; compliance; and definition of healing. Each article was reviewed by two independent reviewers, and any discrepancies were resolved by consensus.

Data extraction
The data were extracted by two independent reviewers.

Methods of synthesis
How were the studies combined?
The data were grouped by drug class, and the overall estimate for each drug class was calculated by combining the
results of individual arms across the studies. Linear regression analysis was used to estimate the healing rate (the percentage of patients healed per week).

How were differences between studies investigated?
The authors do not state how differences between the studies were investigated.

**Results of the review**
Forty-three studies (7,635 patients in total) were included.

The mean overall healing proportion irrespective of drug dose or treatment duration (12 weeks or shorter) was 83.6% (95% confidence interval, CI: 79.2, 88.1) with proton-pump inhibitors, 51.9% (95% CI: 46.9, 56.9) with H2-receptor antagonists, 39.2% (95% CI: 3.6, 74.8) with sucralfate, 37.9% (95% CI: not available) with prokinetics, and 28.2% (95% CI: 19.2, 37.2) with placebo.

Correcting for patients without baseline heartburn, the mean heartburn-free proportion was 77.4% with proton-pump inhibitors and 47.6% with H2-receptor antagonists.

Proton-pump inhibitors showed a significantly faster healing rate (11.7% per week) than H2-receptor antagonists (5.9% per week) or placebo (2.9% per week).

**Authors’ conclusions**
More complete oesophageal healing and heartburn relief was observed with proton-pump inhibitors than H2-receptor antagonists, which occurred nearly twice as fast. This semiquantitative expression of speed of healing and symptom relief permits comparisons for future economic evaluations and quality of life assessments.

**CRD commentary**
The review was systematic in terms of the literature search, clear inclusion criteria, and the validity assessment. The potential for publication bias should be stressed as the review excluded abstracts and non-English articles. The data from the included studies were tabulated. The comparison of different drug classes was made between studies, not within studies, and the advantage of randomisation was thus lost by this indirect comparison. The validity of this review may be equivalent to that of a review of observational studies, although it included only randomised controlled studies. It was unclear whether a standard error or a standard deviation followed the estimated overall proportion. The conclusion of this review should therefore be interpreted with great caution.

**Bibliographic details**

**PubMedID**
9178669

**Other publications of related interest**
This additional published commentary may also be of interest. Treatment effectiveness in reflux disease. Bandolier 2000;77:1-4.

**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
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Treatment Outcome; Wound Healing

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Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.