Systematic review of proton pump inhibitors for the acute treatment of reflux oesophagitis

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Authors' objectives
To compare the effectiveness of esomeprazole with the recommended dose of proton-pump inhibitors (PPIs) in the healing of reflux oesophagitis, using omeprazole as a common comparator.

Searching
EMBASE, MEDLINE, BIOSIS Previews and AstraZeneca's internal database were searched in December 2000. The search terms and strategy are reported in detail in the review.

Study selection
Study designs of evaluations included in the review
The review specified randomised controlled trials (RCTs) with omeprazole (20 mg).

Specific interventions included in the review
Direct comparisons of any currently UK-licensed PPI with 20 mg omeprazole. The PPIs included in the review were esomeprazole (40 mg), lansoprazole (30 mg), pantoprazole (40 mg) and rabeprazole (20 mg).

Participants included in the review
The inclusion criteria relating to the participants were not pre-specified. For the primary analysis, the review included participants with acute reflux oesophagitis.

Outcomes assessed in the review
The specified outcome was endoscopic healing rates at 4 and/or 8 weeks.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the reviewers performed the selection.

Assessment of study quality
The methodological quality of the included studies was assessing using the Jadad scoring system. The scoring covered elements of study design, level of blinding, method of randomisation and the proportion of patients lost to follow-up. The scale ranges from 0 (low quality) to 5 (high quality). Studies were only included in the primary analysis if the quality score was greater than 2 on the Jadad scale. The authors do not state how the papers were assessed for quality, or how many of the reviewers performed the quality assessment.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the reviewers performed the data extraction. Four- and 8-week healing data were taken from qualifying trials and recalculated if not presented in an intention-to-treat format.

Methods of synthesis
How were the studies combined?
The pooled relative risks (RRs) with 95% confidence intervals (CIs) were calculated using the Mantel-Haenszel fixed-effect model. The DerSimonian and Laird random-effects model was also used for supplementary analyses.

How were differences between studies investigated?
A chi-squared test was carried out to investigate possible heterogeneity. Further sensitivity analyses were performed to test the effects of including studies with a quality score of 2 or less on the Jadad scale.

Results of the review
Eighteen RCTs (total number of participants not given) met the inclusion criteria. However, a further 6 RCTs were excluded from the primary analysis due to a quality score of 2 or lower. Twelve RCTs were included in the primary analysis (number of participants not reported).

Jadad quality scores: six RCTs scored 2 points or less, five scored 3 points, three scored 4 points, and four scored 5 points.

Endoscopic healing rates of esomeprazole (40 mg) compared with omeprazole (20 mg): the RR was 1.14 (95% CI: 1.10, 1.18) at 4 weeks (n=3) and 1.08 (95% CI: 1.05, 1.10) at 8 weeks (n=3).

The endoscopic healing rates of other PPIs compared with omeprazole (20 mg) were as follows:

for lansoprazole (30 mg) compared with omeprazole, the RR was 1.02 (95% CI: 0.97, 1.08) at 4 weeks (n=5) and 1.01 (95% CI: 0.97, 1.06) at 8 weeks (n=4);

for pantoprazole (40 mg) compared with omeprazole, the RR was 0.99 (95% CI: 0.91, 1.07) at 4 weeks (n=3) and 0.98 (95% CI: 0.93, 1.04) at 8 weeks (n=3);

for rabeprazole (20 mg) compared with omeprazole, the RR was 1.00 (95% CI: 0.87, 1.14) at 4 weeks (n=1) and 0.98 (95% CI: 0.91, 1.05) at 8 weeks (n=1).

Pooling the data for lansoprazole, pantoprazole and rabeprazole compared with omeprazole showed no statistically-significant difference in treatment at 4 weeks (RR 1.01, 95% CI: 0.97, 1.06) and at 8 weeks (RR 1.07, 95% CI: 1.01, 1.13).

For the comparison of esomeprazole with omeprazole, the chi-squared test indicated significant heterogeneity; there was no evidence of heterogeneity in any of the other comparisons. The random-effects calculations made no significant difference to the results stated above for the fixed-effect calculations.

The sensitivity analysis, which was performed to include all 18 trials regardless of quality score, did not make a significant difference to any of the comparisons carried out in the primary analysis.

Authors' conclusions
Esomeprazole has demonstrated higher healing rates than omeprazole at 4 and 8 weeks. Other PPIs (lansoprazole, pantoprazole and rabeprazole) have not shown higher healing rates when compared with omeprazole.

CRD commentary
In this review, the research question was clearly stated. There was some detail of the inclusion criteria for study design, intervention and outcomes, but the criteria for participants were not stated. The review included searches of several databases, but language restrictions were not mentioned. A further limitation of the literature search was that there was no analysis of possible publication bias or the effects on the review of not performing additional searches beyond the electronic databases mentioned. The review does not report who, or how many of the authors, performed the selection of studies, quality assessment or data extraction processes. Data relating to the participants' characteristics were missing from the review. The included studies were assessed for quality and the results of the assessment were used to exclude studies in the meta-analysis; the authors conducted further sensitivity analyses to check whether such exclusions affected the results of the review. Given a stated lack of heterogeneity, the fixed-effect statistical pooling was appropriate.

The conclusions of this review appear to follow from the results. However, it should be noted that further detail on the
process of the review, and of individual studies included in the review, would have helped to deflect comment concerning possible biases.

**Implications of the review for practice and research**

The authors did not state any implications for further research and practice.

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