Meta-analysis: comparing the efficacy of proton pump inhibitors in short-term use
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CRD summary
This review compared the effectiveness of different proton-pump inhibitors in the management of gastro-oesophageal reflux disease, peptic ulcer disease and Helicobacter pylori. The authors concluded that the differences found may be due to the high dose used and not the specific inhibitor. Given the lack of information on differences between the studies and the quality of the individual studies, it is difficult to verify the conclusions.

Authors' objectives
To compare the efficacy of proton-pump inhibitors (PPIs) in the short-term management of gastro-oesophageal reflux disease (GERD), peptic ulcer disease (PUD), and the eradication of Helicobacter pylori (H. pylori).

Searching
MEDLINE (from 1985 to 2002), EMBASE (from 1985 to 2002) and the Cochrane Library (whole period) were searched for English, Dutch, German and French articles; the keywords were provided. Abstracts of symposia poster presentations were excluded.

Study selection
Study designs of evaluations included in the review
Only randomised controlled trials (RCTs) were eligible.

Specific interventions included in the review
Studies comparing two or more PPIs for short-term management, under the same clinical conditions, were eligible. Short-term management was defined as a treatment duration of 4 weeks for GERD and PUD and between 7 and 14 days for H. pylori. Other treatment regimens were excluded. The included studies, which were pooled, were of esomeprazole 40 mg (E40), lansoprazole 30 and 60 mg (L30 and L60, respectively), omeprazole 20 and 40 mg (O20 and O40), pantoprazole 40 and 80 mg (P40 and P80), and rabeprazole 20 and 40 mg (R20 and R40). For H. pylori disease, the PPIs were given in conjunction with antibiotic treatment.

Participants included in the review
Patients with GERD or PUD as determined by endoscopy, or H. pylori as determined by urea breath test or endoscopy, were eligible. Studies of specific patient groups, such as the elderly, children or mentally ill, were excluded.

Outcomes assessed in the review
Only studies assessing the outcome after 4 weeks for GERD and PUD, and between 7 and 14 days for the eradication of H. pylori, were eligible. Studies assessing symptom improvement only for H. pylori were excluded, as were studies of pharmacokinetics, pharmacodynamics and pH measurement. Treatment success or failure was the outcome of interest. Success was defined as cured GERD or ulcer, as determined by endoscopy, and the eradication of H. pylori, as determined by urea breath test or endoscopy.

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

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
The data extraction was carried out in duplicate and a third reviewer was consulted if there were any disagreements. The numbers of treatment successes and failures for each intervention were extracted. The relative risk (RR) and 95% confidence interval (CIs) for each treatment comparison were estimated.

**Methods of synthesis**

How were the studies combined?
The studies were combined separately for each of the drug comparisons using the method of Mantel-Haenszel.

How were differences between studies investigated?
Differences between the studies were not investigated.

**Results of the review**

Forty-one RCTs were included. Of these, 16 considered GERD, 9 considered PUD and 9 considered H. pylori eradication.

**GERD.**

E40 was superior to O20 in endoscopic healing (2 trials, n=3,729); the RR was 1.18 (95% CI: 1.14, 1.23). No significant differences were found in the other comparisons: P40 versus O20 (4 trials, n=604), L30 versus O20 (6 trials, n=1,881) and R20 versus O20 (2 trials, n=409). The results of individual studies of other dosages were also presented in the paper, but could not be pooled as only one trial was identified.

**Peptic ulcer healing.**

P40 was superior to O20 in peptic ulcer healing (3 trials, n=760); the RR was 1.07 (95% CI: 1.02, 1.13). No significant differences were found in the other comparisons: L30 versus O20 (3 trials, n=504) and R20 versus O20 (2 trials, n=432).

**H. pylori eradication.**

No significant differences were found for the following treatment comparisons: L60 versus O40 (5 trials, n=860), L30 versus O40 (2 trials, n=196), R40 versus L60 (2 trials, n=354), R20 versus O40 (2 trials, n=314), R40 versus O40 (2 trials, n=311), P40 versus O40 (2 trials, n=213), P80 versus O40 (2 trials, n=349) and E40 versus O40 (2 trials, n=833).

**Authors’ conclusions**

Both significant differences were in favour of the highest dose of PPI. Therefore, the difference may be dose dependent and not PPI specific. All the PPIs appeared comparable, thus clinical choice may be based on other factors such as pharmaco-economic considerations.

**CRD commentary**

The review question was clear in terms of the interventions, participants, outcomes and study design of interest. Three relevant electronic databases were searched and the keywords used in the search strategy were given. However, the searches were restricted to four languages and only full-text articles were included; studies may therefore have been missed. Although the data extraction and analysis were carried out in duplicate, no information was provided on whether attempts were made to reduce error and bias during the study selection process. A validity assessment was not reported and the findings were not discussed in the context of study quality.

No details of the individual studies were given, thus it was not possible to assess whether the pooled studies were clinically homogeneous. Statistical heterogeneity was not investigated. Although the authors’ conclusions appear to follow from the evidence presented, the findings should be viewed with some caution given the lack of consideration of differences between the studies and study quality, and the lack of information on the individual studies.
Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: The authors stated that in relation to H. pylori, there is a requirement for large trials comparing all PPIs, which should be designed to include a correction for the effect of antibiotic resistance. They also stated that, in general, RCTs comparing three or more PPIs are needed.

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