A meta-analysis: comparison of esomeprazole and other proton pump inhibitors in eradicating Helicobacter pylori

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CRD summary
The authors concluded that esomeprazole-based triple therapy may be as effective as omeprazole-based therapy in eradicating Helicobacter pylori, and was well tolerated. There were limitations to this review that appear to undermine the reliability of these conclusions.

Authors’ objectives
To compare the effects of esomeprazole-based therapy and alternative proton-pump inhibitor (PPI)-based therapy on Helicobacter pylori (H. pylori) eradication rates.

Searching
MEDLINE, EMBASE, the Cochrane Library and the Chinese Biomedical Database were searched from 2000 to 2005 using the reported search terms. In addition, abstracts from the International Workshop of Gastroduodenal Pathology and H. pylori, Chinese Core Periodicals, American Digestive Diseases Week and the United European Gastroenterology Week, as well as the reference lists of retrieved studies, were screened. National and pharmaceutical industry sources and consensus conferences were also examined. No language restrictions were applied.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) that were open-labelled or blinded were eligible for inclusion in the review.

Specific interventions included in the review
Studies that compared esomeprazole-based triple therapy with an alternative PPI-based triple therapy were eligible for inclusion. Studies had to use the same type and dose of antibiotic in both treatment arms and to report the duration of antibiotic therapy. All but one of the included studies compared esomeprazole (total daily dose 40 or 80 mg) with omeprazole (total daily dose 40 mg); one comparison was with pantoprazole (total daily dose 80 mg). The antibiotic regimens used were clarithromycin plus amoxicillin or clarithromycin plus metronidazole. The duration of treatment ranged from 1 week (most studies) to 4 weeks.

Participants included in the review
Studies of patients with peptic ulcer disease or non-ulcer disease with H. pylori infection were eligible for inclusion. H. pylori infection had to be diagnosed using the rapid urease test, C (14) or C (13) urea breath test, or histology.

Outcomes assessed in the review
Studies that reported the H. pylori eradication rate and H. pylori status 4 weeks after the completion of treatment were eligible for inclusion in the review.

How were decisions on the relevance of primary studies made?
Two reviewers independently selected the studies and resolved any disagreements by discussion.

Assessment of study quality
Two reviewers independently assessed validity using the following criteria: randomisation methods, allocation concealment, blinding of the investigator, reporting of withdrawals and drop-outs, and baseline comparability of the groups. Each study was assigned a quality score (from 0 to 5) using the Jadad scale, where studies scoring 3 or more points were classified as high quality. Any disagreements were resolved by consensus.

Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data
extraction. For each study, data on the eradication rate of H. pylori were extracted on an intention-to-treat (ITT) basis and, where possible, on a per-protocol (PP) basis. Authors of reports published as abstracts or reports with incomplete data were contacted for additional information.

**Methods of synthesis**

How were the studies combined?
The results from individual studies were combined using random-effects (DerSimonian and Laird) or fixed-effect (Peto) models to give a pooled odds ratio (OR) with 95% confidence intervals (CIs). The mean percentage and pooled weighted mean percentage of patients with H. pylori eradication, along with 95% CIs, were calculated on ITT and PP bases. A funnel plot was used to assess publication bias.

How were differences between studies investigated?
Statistical heterogeneity was assessed using the chi-squared and I-squared statistics, taking a p-value of less than 0.1 or I-squared greater than 50% to indicate significant heterogeneity. Subgroup analyses were performed to assess the influence of the comparison drug, the dose of esomeprazole and study quality.

**Results of the review**

Eleven RCTs (n=2,159) were included.

All 11 studies used ITT analysis, five were double-blind and three described withdrawals or drop-outs. Seven studies scored 3 or more out of 5 for validity.

There was a significant increase in the odds of H. pylori eradication with other PPIs compared with esomeprazole (OR 1.38, 95% CI: 1.09, 1.75, p=0.007); no statistically significant heterogeneity was detected (p=0.34; I-squared 10.6%). The results were similar and homogeneous when only studies that compared esomeprazole with omeprazole were included (OR 1.29, 95% CI: 1.01, 1.65).

The subgroup analysis of high-quality studies (6 RCTs, n=1,596) showed no statistically significant difference in eradication rates between esomeprazole-based and other PPI-based regimens (OR 1.17, 95% CI: 0.89, 1.54, p=0.25). No statistically significant heterogeneity was detected (p=0.87; I-squared 0%).

The subgroup analysis of low-dose (20 mg twice daily) esomeprazole (9 RCTs, n=1,666) and high-dose (40 mg twice daily) esomeprazole (2 RCTs) showed no significant differences in H. pylori eradication rates between esomeprazole-based and other PPI-based regimens (OR 1.20, 95% CI: 0.92, 1.56, p=0.17 and OR 3.21, 95% CI: 0.31, 32.93, respectively).

The asymmetrical funnel plot suggested the absence of some small negative studies.

**Authors’ conclusions**

Esomeprazole-based triple therapy was highly effective for the eradication of H. pylori and might be as effective as omeprazole-based therapy.

**CRD commentary**

The review addressed a clear question that was defined in terms of the participants, intervention, outcomes and study design. Several relevant sources were searched and attempts were made to minimise language bias. Only published studies appear to have been included, which raises the possibility of publication bias; this was assessed and some evidence of it was found. Validity was assessed using specified criteria and the results of this assessment reported. There was no information about the participants studied, which makes it difficult to generalise the review findings. Methods were used to minimise reviewer error and bias in the study selection and validity assessment processes, but it is unclear whether similar steps were taken when extracting the data.

The data were combined in a meta-analysis and differences between the studies explored. There appears to be inconsistencies in the reporting of the results, with forest plots for the main analysis showing benefit for other PPIs and
not for esomeprazole. Not all studies scoring 3 or more points on the Jadad scale were included in the analysis of higher quality studies. Furthermore, in some studies, treatments apart from the drug being investigated were not identical and the influence of this on the results was not examined. Collectively, these factors suggest there were limitations to this review. The authors’ conclusion about the probable comparability of esomeprazole and omeprazole does not appear to be supported by the evidence presented, and so may not be reliable.

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

Practice: The authors stated that esomeprazole-based triple therapy is as effective as other PPIs in the treatment of H. pylori infection.

Research: The authors did not state any implications for further research.

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