Meta-analysis. Proton pump inhibitors vs. H2-receptor antagonists: their efficacy with antibiotics in Helicobacter pylori eradication

CRD summary
This meta-analysis assessed the effectiveness of proton-pump inhibitors and H2-receptor antagonists, both co-prescribed with antibiotics, in Helicobacter pylori eradication. The authors concluded that proton-pump inhibitors are more effective than H2-receptor antagonists when prescribed at usual doses. The authors' conclusion is consistent with the evidence reviewed, and is likely to be reliable.

Authors' objectives
To perform a meta-analysis comparing the efficacy of proton-pump inhibitors (PPIs) and H2-receptor antagonists (H2RAs) when administered in conjunction with antibiotics, in the eradication of Helicobacter pylori (H. pylori) infection.

Searching
PubMed and the Cochrane Controlled Trials Register were searched from inception until January 2002. No language restrictions were imposed and the search terms were reported. In addition, abstracts from 1995 to 2001 from the International Workshop on Gastroduodenal Pathology and Helicobacter pylori and American Digestive Disease Week were handsearched. The references of reviews on H. pylori treatment and of articles selected for the review were also examined.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion.

Specific interventions included in the review
Studies that compared treatment with a PPI (omeprazole, lansoprazole, pantoprazole, rabeprazole or esomeprazole) with an H2RA (cimetidine, ranitidine, famotidine or nizatidine), and which were administered with the same antibiotics, were included. The duration of therapy ranged from 7 to 15 days. Studies that evaluated these therapies as second-line treatment for previous eradication failures were excluded.

Participants included in the review
Participants with functional dyspepsia or peptic ulcers were eligible for inclusion. Almost all of the included studies assessed participants with peptic ulcer disease, some combined with functional dyspepsia. Only two included studies assessed participants with functional dyspepsia alone.

Outcomes assessed in the review
Studies that reported the H. pylori eradication rates were included.

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 quality of the included studies was assessed using the scoring system of Jadad et al., which assesses the methods of randomisation and blinding, and the description of withdrawals and drop-outs. The authors assessed the studies using the quality checklist developed by Jadad et al. However, they did not state how many reviewers performed the quality assessment, or how any discrepancies were resolved.
Data extraction
Two reviewers extracted the data independently. Data on study demographics, type of disease, type of treatment, use of high H2RA doses (defined as greater than 300 mg/12 hours of ranitidine, or equivalent with other H2RAs), duration of treatment, and Helicobacter pylori eradication rates were extracted on both an 'intention-to-treat' and 'per protocol' basis. Odds ratios (ORs) were calculated and analyses were carried out.

Methods of synthesis
How were the studies combined?
The studies were combined using a random-effects meta-analysis (DerSimonian and Laird). Publication bias was not formally assessed.

How were differences between studies investigated?
Heterogeneity of effects was assessed using the chi-squared test (significance level, P=0.1). Subgroup analyses were planned a priori to examine the effects of the number of antibiotics prescribed (double or triple therapies), the duration of therapy, short-term (7 days) versus long-term (10 to 14 days) antibiotic use, and the dose of H2RAs.

Results of the review
Twenty RCTs were included (total randomised n=2,374: 1,193 to PPIs and 1,181 to H2RAs).

No significant heterogeneity between the studies was detected when the studies were pooled using either intention-to-treat or per-protocol data.

In the intention-to-treat analyses, the mean H. pylori eradication rates with PPIs and H2RAs plus antibiotics were 74% (95% confidence interval, CI: 71, 76) and 69% (95% CI: 66, 71), respectively. The OR was 1.31 (95% CI: 1.09, 1.58). The number-needed-to-treat (NNT) with PPIs to achieve one eradication success, compared with H2RAs, was 25.

In the per-protocol analyses, the mean H. pylori eradication rate was 82% (95% CI: 80, 84) with PPIs and 78% (95% CI: 75, 80) with H2RAs. The OR was 1.32 (95% CI: 1.00, 1.74). The NNT with PPIs to achieve one eradication success was 25.

Two studies used high-dose H2RAs. When these two studies were excluded from the analyses, the ORs increased: to 1.37 (95% CI: 1.13, 1.66) by intention-to-treat and to 1.5 (95% CI: 1.15, 1.97) by per protocol. The NNT with PPIs to achieve one eradication success, compared with H2RAs, also decreased to 20 for both the intention-to-treat and per protocol analyses. No further subgroup analyses were undertaken.

Authors’ conclusions
PPIs are more effective than H2RAs when both antisecretors are prescribed at their usual doses with antibiotics for the eradication of H. pylori infection.

CRD commentary
The review question was well defined in terms of the study design, intervention, participants and outcomes. An adequate number of sources was searched for relevant studies, and efforts were made to reduce both language and publication bias. The methods used to select the studies and assess their quality were not described, so it is not known whether any efforts were made to reduce bias and errors. This is particularly pertinent as some studies included in the review were reported in abstract form only, where it is difficult to accurately assess the quality of the study. Methods were used to minimise bias in the data extraction process.

The data were appropriately combined in a meta-analysis, and statistical heterogeneity was assessed. All subgroup analyses were appropriate and pre-specified a priori. Overall, the authors’ conclusion is consistent with the evidence reviewed, and would appear to be robust.
Implications of the review for practice and research
The authors did not state any implications for practice or further research.

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