Meta-analysis: the influence of pre-treatment with a proton pump inhibitor on Helicobacter pylori eradication

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CRD summary
This review assessed the effects of pre-treatment with a proton-pump inhibitor on triple and quadruple therapies for Helicobacter pylori eradication. The authors concluded that pre-treatment had no effect on Helicobacter pylori eradication. Differences between the studies mean that the reliability of the results is uncertain.

Authors' objectives
To evaluate the effect of pre-treatment with a proton-pump inhibitor (PPI) on Helicobacter pylori (H. pylori) eradication.

Searching
The Cochrane Controlled Trials Register, MEDLINE, Current Contents and CINAHL were searched without language restrictions to August 2004; the search terms were reported. The reference lists of all identified trials and reviews were screened. In addition, abstracts of four named major gastroenterology meetings (1994 to August 2004) were handsearched.

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 the same triple or quadruple therapy with and without pre-treatment with a PPI were eligible for inclusion. The included studies used various triple or quadruple regimens for 2 to 14 days. The PPIs used for pre-treatment also varied and their duration ranged from 3 to 49 days. Full details of the drugs and dosages were reported.

Participants included in the review
Studies of participants diagnosed with H. pylori infection before treatment using the urea breath test, faecal antigen test, biopsy-based urease test, histology or culture were eligible for inclusion. The included studies were in patients with peptic ulcer disease and functional dyspepsia.

Outcomes assessed in the review
Studies that confirmed cure of H. pylori infection using the urea breath test or two biopsy-based tests (CLO/histology/culture) at least 4 weeks after the completion of treatment were eligible for inclusion. The studies also had to report the number of patients treated and the number cured.

How were decisions on the relevance of primary studies made?
Two reviewers independently selected the studies and resolved any disagreements on inclusion through consultation with a third author. In the event of several publications on the same trial, only the most recent was included.

Assessment of study quality
Validity was assessed and scored using the Jadad scale, which considers reporting of randomisation, blinding and withdrawals. The maximum possible score was 5 points. Two reviewers independently assessed the validity of each included study and the results were compared for consistency.
Data extraction
Two reviewers independently extracted the data and the results were compared for consistency. For each study, the numbers of patients treated and cured were extracted and used to calculate the risk difference (RD) with 95% confidence intervals (CIs).

Methods of synthesis
How were the studies combined?
Individual RDs were weighted by the inverse variance and combined to give a pooled RD with 95% CIs. A funnel plot was used to assess publication bias.

How were differences between studies investigated?
Statistical heterogeneity was assessed using the chi-squared statistic and through visual examination of a forest plot. A subgroup analysis was used to examine the influence of the underlying condition of the patients (peptic ulcer disease versus both peptic ulcer disease or functional dyspepsia), treatment regimen ('quadruple therapy' only versus 'modern triple therapies') and the type of triple therapy (PPI, clarithromycin plus amoxicillin versus PPI, a macrolide plus a nitroimidazole). The authors reported that there were too few studies to conduct meta-regression analyses.

Results of the review
Nine RCTs (n=773) were included.

The quality scores ranged from 1 to 3 out of a possible 5: six studies scored 3; two scored 2; and one study scored 1.

No statistically significant difference was observed in H. pylori eradication between pre-treatment and no pre-treatment (RD 0.1%, 95% CI: -5, 5). Statistically significant heterogeneity was found. Heterogeneity was largely due to two studies that reported the largest RDs (-18% and 33%, respectively); other studies reported RDs ranging from -8 to 10%.

There were no statistically significant differences for subgroup analyses of studies of patients with peptic ulcer disease or either peptic ulcer disease or functional dyspepsia, or for studies using different regimens ('quadruple therapy', 'modern triple therapies', PPI, clarithromycin plus amoxicillin, and PPI, a macrolide plus a nitroimidazole).

The authors reported that the funnel plot was 'fairly symmetrical' with smaller studies showing more variation.

Authors' conclusions
Pre-treatment with a PPI had no effect on H. pylori eradication.

CRD commentary
The review addressed a clear question that was defined in terms of the participants, intervention, outcomes and study design. A number of relevant sources were searched and attempts were made to minimise language and publication bias; publication bias was assessed. Two reviewers independently selected studies, assessed validity and extracted the data, thus reducing the potential for reviewer bias and errors. Validity was assessed, although only the composite score was presented; this makes it difficult to comment independently on the reliability of the evidence presented.

Since details of the demographics of participants in the included studies were limited, it may be difficult to generalise the review findings. The details given highlighted considerable clinical variation, and statistical heterogeneity was also found. The authors explored possible sources of variation, although were limited by small numbers of patients. However, the pooling of heterogeneous data makes the reliability of the results uncertain.

Implications of the review for practice and research
The authors did not state any implications for practice or further research.
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