Helicobacter pylori eradication: proton pump inhibitor versus ranitidine bismuth citrate plus two antibiotics for 1 week. A meta-analysis of efficacy


Authors' objectives
To compare the efficacy of proton-pump inhibitors (PPI) versus ranitidine bismuth citrate (RBC) with two antibiotics for 1 week in Helicobacter pylori (H. pylori) eradication.

Searching
Searches were performed in the PubMed database up to October 1999. The search strategies are reported in the paper. A manual search of abstracts from 1995 to 1999 was also undertaken from the following congresses: International Workshop on Gastroduodenal Pathology and Helicobacter pylori and American Digestive Disease Week. References of reviews and from the articles selected for the study were examined. There were no language restrictions.

Study selection
Study designs of evaluations included in the review
Comparative randomised trials were included.

Specific interventions included in the review
PPI (omeprazole, 20 mg b.d., i.e. twice daily; lansoprazole, 30 mg b.d.; or pantoprazole, 40 mg b.d.) plus two antibiotics (clarithromycin, 250 or 500 mg b.d.; amoxycillin, 1 g b.d.; or a nitroimidazole, 250 or 500 mg b.d.) versus RBC (400 mg b.d.) plus the same antibiotics for 1 week. Only studies evaluating these therapies as first-line treatment were eligible for inclusion.

Participants included in the review
Participants with either peptic ulcer or non-ulcer dyspepsia were eligible for inclusion.

Outcomes assessed in the review
The primary outcome was eradication of H. pylori. Control of eradication had to be performed by histology or 13C-urea breath test at least 4 weeks after therapy for a study to be eligible for inclusion.

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 authors do not state that they assessed validity.

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. Specific data were extracted on: format (abstract or journal article), disease (peptic ulcer or non-ulcer dyspepsia), RBC versus PPI (type and dose), dose of antibiotics, and percentage eradication (intention to treat (ITT) or per protocol (PP)).

Methods of synthesis
How were the studies combined?
Meta-analysis was performed combining the Peto odds ratio (OR) of the individual studies using a fixed-effect model.
How were differences between studies investigated?
Separate comparisons, depending on the type of antibiotics prescribed (either clarithromycin plus amoxycillin or clarithromycin plus a nitroimidazole), were performed. Heterogeneity was assessed using the chi-squared test.

Results of the review
Twelve studies were eligible for inclusion: 9 studies (ITT, n=677; PP, n=842) compared PPI versus RBC plus clarithromycin and amoxycillin, and 5 studies (ITT, n=493; PP, n=550) compared PPI versus RBC plus clarithromycin and a nitroimidazole.

PPI versus RBC plus clarithromycin and amoxycillin. Mean H. pylori eradication with RBC was 76.6% (95% confidence interval, CI: 72, 81) by ITT and 83.3% (95% CI: 79, 86) by PP analysis. With a PPI, the mean H. pylori eradication rates were 73.7% (95% CI: 69, 78) and 81% (95% CI: 77, 85), respectively. The corresponding ORs were 1.15 (95% CI: 0.80, 1.64) by ITT, and 1.08 (95% CI: 0.75, 1.55) on a PP basis. The chi-squared homogeneity test was 12.2 (p=0.1) by ITT and 14.3 (p=0.07) by PP analysis; there was evidence of significant heterogeneity in both cases.

PPI versus RBC plus clarithromycin and a nitroimidazole. Mean H. pylori eradication with RBC was 87.2% (95% CI: 83, 91) by ITT and 93.5% (95% CI: 91, 96) by PP analysis. With a PPI, the mean eradication rates were 79.4% (95% CI: 74, 84) and 85% (95% CI: 81, 89) by ITT and PP analysis, respectively. The corresponding ORs were 1.76 (95% CI: 1.08, 2.85) by ITT, and 2.43 (95% CI: 1.42, 4.18) on a PP basis. The chi-squared homogeneity test was 6.24 (p=0.18) by ITT and 1.6 (p=0.8) by PP analysis.

The overall efficacy of the two regimens was not shown to be different by either ITT (OR 1.37, 95% CI: 0.93, 2.05) or PP (OR 1.37, 95% CI: 0.88, 2.02) analysis. However, RBC-clarithromycin-nitroimidazole combinations were more effective than RBC-clarithromycin-amoxycillin regimens, both by ITT (87.2 versus 76.6%; OR 2.08, 95% CI: 1.33, 3.26) and PP (93.5 versus 83.3%; OR 2.88, 95% CI: 1.67, 4.97).

Authors' conclusions
RBC and PPI have similar efficacy for H. pylori eradication when given with clarithromycin and amoxycillin for 1 week, but RBC seems to have a higher efficacy than PPI when clarithromycin and a nitroimidazole are the co-prescribed antibiotics.

CRD commentary
On the whole this was a poor review. The review question and the selection criteria were well reported, but the authors failed to report on a number of methodological factors. No details were given regarding who carried out, and the procedures for, study inclusion, validity assessment and data extraction. The search strategy was adequate but may have benefited from searching additional databases; it is possible some studies may have been missed. Details of the included studies were reported but some important study characteristics were omitted, e.g. patient characteristics and drop-out rates.

The authors appear to have reported incorrectly that assessment of heterogeneity was undertaken prior to combination of the effect sizes of the individual studies, as this is impossible to do in Review Manager. Furthermore, they set a p-value of 0.20 as a threshold for homogeneity and although both of the reported meta-analyses gave lower p-values, indicating heterogeneity, data were still pooled. In addition, the authors did not investigate the possible sources of heterogeneity or undertake sensitivity analyses.

The overall efficacy of the regimens (PPI-clarithromycin-amoxycillin versus PPI-clarithromycin-nitroimidazole, and RBC-clarithromycin-amoxycillin versus RBC-clarithromycin-nitroimidazole) were not explored in a randomised comparison. The authors appear to have undertaken a simple indirect comparison and consequently the power of randomisation is lost. Any perceived difference in efficacy may be due to different patient characteristics or other prognostic factors across the trials.
The authors’ conclusions should be viewed with caution given the problems outlined above.

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

Practice: The authors did not state any implications for practice.

Research: The authors state that further randomised clinical trials with a larger number of patients comparing PPI and RBC triple therapies are clearly needed.

**Bibliographic details**


**PubMedID**

10971230

**Other publications of related interest**


**Indexing Status**

Subject indexing assigned by NLM

**MeSH**

Amoxicillin /administration & dosage /therapeutic use; Anti-Bacterial Agents /administration & dosage /therapeutic use; Anti-Ulcer Agents /administration & dosage /therapeutic use; Bismuth /administration & dosage /therapeutic use; Clarithromycin /administration & dosage /therapeutic use; Drug Therapy, Combination; Helicobacter Infections /drug therapy; Helicobacter pylori /drug effects; Humans; Nitroimidazoles /administration & dosage /therapeutic use; Proton Pump Inhibitors; Randomized Controlled Trials as Topic; Ranitidine /administration & dosage /analogs & derivatives /therapeutic use

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