Authors' objectives
To compare treatment of Helicobacter pylori infection with ranitidine bismuth citrate- and proton pump inhibitor-based triple therapies.

Searching
The authors searched MEDLINE and Current Contents, and manually reviewed abstracts submitted to meetings of the American Gastroenterological Association (Digestive Disease and the United European Gastroenterology weeks) and the European Helicobacter Study Group, for the period 1996 to 1999.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials were included.

Specific interventions included in the review
Proton-pump inhibitor (PPI)-based triple therapies compared with ranitidine bismuth citrate (RBC)-based triple therapies.

Interventions included:
All patients received clarithromycin (C; 250 or 500 mg b.d.) and amoxycillin (A; 1000 mg b.d.).

Patients were randomised to receive RBC (400 mg b.d.) or a PPI: nitroimidazoles (I), i.e. omeprazole (20 mg b.d.), lansoprazole (15 or 30 mg b.d.) or pantoprazole (40 mg b.d.).

Treatment duration was 7 or 10 days.

Participants included in the review
Patients with duodenal ulcer or non-ulcer dyspepsia being treated for Helicobacter pylori infection. One study included patients with insulin dependent diabetes.

Outcomes assessed in the review
Eradication rates were assessed.

How were decisions on the relevance of primary studies made?
Two reviewers independently assessed the relevance of studies.

Assessment of study quality
The quality of the studies was not formally assessed, although blinding was discussed.

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.

Data were extracted for the categories: study identification and year of publication, numbers of participants in RBC- and PPI-based treatment regimens (intention to treat (ITT) and per protocol (PP)), and therapy (dosages) administered.
The difference in eradication rates between the treatment modalities and 95% confidence intervals (CIs) were calculated.

**Methods of synthesis**

How were the studies combined?
The eradication rates, weighted for effect size, were pooled based on the chi-squared statistic for comparative analysis of two rates. In order to compare tolerability, the authors calculated the percentage of patients not finishing the study protocol as an objective measure of side-effects.

How were differences between studies investigated?
The authors do not report a method for assessing heterogeneity.

**Results of the review**

Seventeen studies were included in the review. Three of the studies were published in a full report, whilst the remainder were abstracts only. The median number of participants per treatment arm was 30 (range: 15-150).

Eradication rates in an ITT analysis ranged from 51 to 94%.

**RBC-A-C versus PPI-A-C (11 studies):**

Pooled ITT eradication rates were 78.5% (576 out of 734; range: 51-94%) for RBC-based triple therapy, compared to 78.7% (605 out of 769; range: 60-88%) for PPI-based triple therapy. The difference between the pooled eradication rate was not statistically significant (weighted difference 0.8%, 95% CI: -3.1, 4.7).

Pooled PP eradication rates (8 out of 11 studies) were 85.8% (327 out of 381; range: 66-98%) for RBC-based triple therapy, compared to 82.9% (344 out of 415, range: 62-95%) for PPI-based triple therapy. The difference between the pooled eradication rate was not statistically significant (weighted difference 3.3%, 95% CI: -0.8, 7.4). Drop-out rates were 10.4% (44 out of 425) for RBC-A-C and 10.0% (46 out of 461) for PPI-A-C.

**RBC-I-C versus PPI-I-C (7 studies):**

Pooled ITT eradication rates were 85.6% (338 out of 395; range: 70-95%) for RBC-based triple therapy, compared to 78.9% (355 out of 442; range: 70-93%) for PPI-based triple therapy. The difference between the pooled eradication rate was statistically significant in favour of RBC-I-C (weighted difference 6.4%, 95% CI: 1.6, 11.1).

Pooled PP eradication rates (4 out of 7 studies) were 91.5% (161 out of 176; range: 91-93%) for RBC-based triple therapy, compared to 86.9% (152 out of 175; range: 77-92%) for PPI-based triple therapy. The difference between the pooled eradication rate was not statistically significant (weighted difference 2.0%, 95% CI: -4.1, 8.0). Drop-out rates were 12.9% (26 out of 202) for RBC-I-C and 12.9% (26 out of 201) for PPI-I-C.

No definite conclusions could be made about the impact of metronidazole or clarithromycin resistance since only three studies performed a formal resistance analysis.

No serious side-effects were reported , and drop-out rates were equal for the two regimens.

**Authors’ conclusions**

The authors state that both RBC- and PPI-based triple therapies using amoxycillin or an imidazole in combination with clarithromycin are effective and safe therapies. In this review, no large difference in cure rates between the different regimens was demonstrated, although the RBC-I-C combination was somewhat better. From the studies reviewed here, no final conclusions can be drawn about the impact of bacterial resistance.

**CRD commentary**
The authors stated the research question and inclusion and exclusion criteria. The literature search was limited in its scope and search terms were not reported. It is unclear whether the search was restricted to English language publications. It is possible that additional relevant studies may have been missed and that publication bias exists.

The authors reported who selected the articles for the review. The quality of the included studies was not formally assessed, although blinding was discussed, and the authors have not reported who performed the data extraction.

The data extraction was reported in tables and discussed in the text of the review. The studies were combined in a statistical meta-analysis, but since heterogeneity was not investigated it may not have been appropriate to pool results.

The authors' conclusions appear to follow from the results, but should be viewed with caution because of methodological limitations of the review.

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

Practice: The authors state that if an imidazole and clarithromycin combination is preferred, the evidence presented in this review suggests that RBC-based therapy should be used instead of a PPI-based therapy.

Research: The authors state that larger studies comparing both forms of triple therapy, using proper resistance analysis, are needed before final conclusions can be reached regarding efficacy in the setting of bacterial resistance.

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