Triple vs. quadruple therapy for treating Helicobacter pylori infection: a meta-analysis
Gene E, Calvet X, Azagra R, Gisbert J P

CRD summary
This review compared triple versus quadruple therapy for the first-line treatment of H. pylori infection. The authors’ concluded that triple and quadruple therapies seem to be roughly equivalent in terms of effectiveness, compliance and side-effects profile. Although the review has some methodological limitations, the conclusions are supported by the evidence presented.

Authors’ objectives
To compare the effectiveness of triple versus quadruple therapy for the first-line treatment of Helicobacter pylori (H. pylori) infection.

Searching
PubMed was searched from 1995 to August 2002; the search terms were reported. Abstracts of the American Gastroenterological Association congresses (1998 to 2002) and the European Helicobacter pylori Study Group congresses (1998 to 2001) were manually searched, as were the bibliographies of selected studies.

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 of triple therapy (proton-pump inhibitor, clarithromycin and amoxicillin or an imidazole) compared with quadruple therapy (proton-pump inhibitor, bismuth salt, tetracycline and an imidazole) were eligible for inclusion. Trials in which amoxicillin or clarithromycin was part of both therapies (i.e. triple and quadruple) were excluded. Only studies where the two therapies had been administered for the same number of days were eligible. The duration of treatment was 7 days in three of the studies, 10 days in one study, and not reported in another study. The specific drug regimens varied between the studies.

Participants included in the review
Patients with H. pylori infection confirmed by histology, urease or breath test were eligible. The included patients were treated for peptic ulcer, chronic active gastritis and duodenal ulcer.

Outcomes assessed in the review
Studies reporting eradication confirmed by histology or C-urea breath test were eligible. Adverse events were also reviewed.

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
Studies were assessed for design, statistical analysis and presentation of results using a published checklist. The minimum and maximum possible scores were 0 and 1, respectively. The authors did not state how the papers were assessed for validity, or how many reviewers performed the validity assessment.

Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction.
Methods of synthesis
How were the studies combined?
The studies were combined in a meta-analysis using Peto's fixed-effect method.

How were differences between studies investigated?
The chi-squared test was used to investigate statistical heterogeneity between the studies.

Results of the review
Five RCTs were reported in an updated meta-analysis (see Other Publications of Related Interest). There were 1,119 participants, though this may be inaccurate due to small discrepancies between the stated total number of participants and the number of participants in the individual studies in the updated paper.

A quality rating was available for only two of the 5 studies; these scored 0.7 and 0.72 out of a maximum 1.0.

The updated meta-analysis based on 5 RCTs found similar levels of effectiveness for triple and quadruple therapy in the initial treatment of H. pylori (OR 1.00, 95% CI: 0.64, 1.57, P=1). These findings were similar to the meta-analysis based on 4 RCTs in the original publication. With the addition of the new study, there was evidence of statistical heterogeneity (P=0.068). There was no statistically significant difference between triple and quadruple therapy in the incidence of side-effects (OR 1.14, 95% CI: 0.76, 1.71, P=0.54).

Authors' conclusions
When administered as first-line treatment for H. pylori infection, the triple and quadruple therapies were roughly equivalent in terms of their effectiveness, compliance and side-effects profile.

CRD commentary
The review question was clear in terms of the inclusion criteria of interest. Relevant searches were carried out, though they could have been more extensive. It is also possible that studies may have been missed, particularly unpublished studies, thereby introducing publication bias. No information on the review processes was provided; therefore, it is unclear whether appropriate strategies were taken to reduce error and bias. A quality assessment was carried out, although the authors were limited in how they could use this: two studies could not be assessed since they were abstracts.

With the exception of the new study in the updated meta-analysis, appropriate details on the individual studies were provided. Given that this new study appears to have introduce heterogeneity, it would have been useful to have had information on the treatment regimen and length of treatment. It may not have been appropriate to add the new study to this particular group of studies. The authors' conclusions appear to follow from the evidence presented. However, the review has some limitations, in particular, compliance was not assessed.

Implications of the review for practice and research
Practice: The authors stated that the evidence was insufficient to change the current policy of triple therapy as the first-line treatment for H. pylori. However, in areas that do not achieve optimal results with triple therapy, giving quadruple therapy first may be a useful alternative.

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

Funding
Instituto de Salud Carlos III, grant number C03/02.

**Bibliographic details**

**PubMedID**
12752350

**Other publications of related interest**

**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Amoxicillin /administration & dosage; Antacids /administration & dosage; Anti-Bacterial Agents /administration & dosage; Bismuth /administration & dosage; Clarithromycin /administration & dosage; Ditiocarb /administration & dosage; Drug Resistance, Bacterial; Drug Therapy, Combination /administration & dosage; Helicobacter Infections /drug therapy; Helicobacter pylori; Humans; Metronidazole /administration & dosage; Proton Pump Inhibitors; Randomized Controlled Trials as Topic; Tetracycline /administration & dosage

**AccessionNumber**
12003001010

**Date bibliographic record published**
30/11/2004

**Date abstract record published**
30/11/2004

**Record Status**
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.