Clinical practice guideline for the eradicating therapy of Helicobacter pylori infections associated to duodenal ulcer in primary care

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Authors' objectives
The authors' objectives were three-fold:

- to assess the efficacy of triple therapy (consisting of a proton-pump inhibitor plus clarithromycin and one other antibiotic) for the eradication of Helicobacter pylori (H. pylori) infection associated with duodenal or gastric ulcer;
- to assess the effect of triple therapy versus any other intervention not containing clarithromycin on ulcer healing; and
- to assess the safety of triple therapy in comparison with any other intervention not containing clarithromycin.

Searching
MEDLINE (from 1988 to 1997), Current Contents (1998), HealthSTAR (from 1992 to 1997), the Cochrane Library (Issue 4, 1997), Indice Medico Espanol (from 1970 to 1997), and the bibliographic databases of Laboratories PENSA and Abbott Laboratories S.A. were searched. The reference lists of selected articles were examined and grey literature and the Internet were searched using the Cyber 411 search engine. The search terms were not reported. Studies in English and Spanish were selected.

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

Specific interventions included in the review
Studies that compared triple therapy (proton-pump inhibitor plus clarithromycin plus one other antibiotic) with a therapeutic schedule that did not include clarithromycin were eligible for inclusion. In studies which assessed the H. pylori eradication rate, the control therapy had to include at least one antibiotic. Details of the drug combinations in the included studies were not reported. The duration of therapy in the included studies ranged from 7 to 28 days.

Participants included in the review
Studies of patients with gastric or duodenal ulcers, diagnosed by endoscopy or radiographic examination with barium contrast, were eligible for inclusion. No further details of the included participants were reported.

Outcomes assessed in the review
The primary outcome measures were defined as follows.

Eradication: the proportion of patients with newly diagnosed gastric or duodenal ulcer who had H. pylori eliminated during the first month after the end of therapy.

Healing: the proportion of patients with a healed ulcer during the first month after the end of therapy.

Safety: the number of patients with adverse effects reported in the studies, regardless of type and severity, in relation to the total number of treated patients.

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
Validity was assessed according to the Jadad criteria, which assesses the method of randomisation, blinding and the handling of withdrawals. Studies scoring 0 on the Jadad scale were excluded from the review. The authors did not state how the papers were assessed for validity, or how many reviewers performed the validity assessment.

**Data extraction**

Two reviewers independently extracted the data onto a specially designed data extraction sheet. Any disagreements were resolved by consensus.

**Methods of synthesis**

*How were the studies combined?*

Fixed-effect and random-effect models were used to generate pooled odds ratios (ORs) and 95% confidence intervals (CIs) for the outcomes infection eradication and ulcer healing.

*How were differences between studies investigated?*

Differences between the studies, in terms of therapeutic schedules and duration of therapy, were discussed. Statistical heterogeneity does not appear to have been assessed formally.

**Results of the review**

Eleven RCTs were included in the review. The number of participants was not reported (it was likely to be less than 2,000, as only 2 of the 11 studies had a sample size of more than 200).

The quality of the studies was low with none scoring more than 2 on the Jadad scale.

Eradication of *H. pylori* (7 trials, n=1,143): triple therapy was significantly more effective than comparator therapy (random-effects OR 3.25, 95% CI: 1.79, 5.89; fixed-effect OR 3.01, 95% CI: 2.17, 4.17). Visual examination of the forest plot indicated possible heterogeneity.

Ulcer healing (7 trials, n=802): triple therapy was significantly more effective than comparator therapy (random-effects OR 2.04, 95% CI: 1.29, 3.25; fixed-effect OR 2.11, 95% CI: 1.33, 3.35).

Adverse effects (8 trials, n=1,500): no significant differences were seen between triple therapy and comparator therapy (fixed- and random-effects OR 1.3, 95% CI: 0.99, 1.73).

**Cost information**

The cost-effectiveness of empirically eradicating *H. pylori* infection in people with duodenal ulcers in primary care was compared with the cost-effectiveness of giving therapy after *H pylori* infection had been confirmed, in a clinical decision analysis model. The empiric eradication therapy of non-complicated duodenal ulcer was found to be the most cost-effective strategy. For strategies involving diagnostic tests, the serum test gave the highest cost-effectiveness ratio, followed by the urease and breath tests. The strategies with the worst cost-effectiveness ratio were those requiring culture and histology.

**Authors' conclusions**

The authors' conclusions appear to be that triple therapy shows higher efficacy (than comparators) in the eradication of *H. pylori* and the healing of newly diagnosed gastric or duodenal ulcers.

**CRD commentary**

This was an English publication based on a full report in Spanish; missing details of the review may well be found in the Spanish publication. The review question was clearly stated and the literature search appears to have been comprehensive, although inclusion was restricted to reports published in English or Spanish. The effects of potential
publication or language bias do not appear to have been assessed. Details of the review process were not reported, apart from the data extraction, so it is unclear whether bias could have been introduced into the review process at this stage.

Details of the included studies, particularly the comparator regimens, were not reported. It is therefore difficult to assess whether it was appropriate to combine the studies in a meta-analysis. Statistical tests for heterogeneity do not appear to have been carried out, although some differences between the studies were discussed in the text. The impact of the poor quality of the included trials was not explored or discussed. The authors used the OR as the summary statistic in the meta-analysis. However, this approximates to the relative risk only when the outcome is rare, and it may have been more appropriate to use the relative risk statistic.

There was insufficient detail in this report to be confident that the authors’ conclusions were based on reliable evidence.

**Implications of the review for practice and research**
Practice: The authors proposed a clinical practice guideline that recommends 7-day triple therapy with proton-pump inhibitor (standard dose), clarithromycin (500 mg/12 hours) and either amoxicillin (1,000 mg/12 hours) or metronidazole (500 mg/12 hours) as first choice therapy. The choice of antibiotics should be based on the local and national profile of bacterial resistance.

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

**Bibliographic details**

**Indexing Status**
Subject indexing assigned by CRD

**MeSH**
Amoxicillin /therapeutic use; Anti-Bacterial Agents /administration & dosage; Anti-Ulcer Agents /administration & dosage; Clarithromycin /therapeutic use; Duodenal Ulcer /drug therapy; Helicobacter Infections /drug therapy; Helicobacter pylori; Metronidazole /therapeutic use

**AccessionNumber**
12000008043

**Date bibliographic record published**
31/08/2004

**Date abstract record published**
31/08/2004

**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.