A meta-analysis comparing eradication, healing and relapse rates in patients with Helicobacter pylori-associated gastric or duodenal ulcer

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Authors' objectives
To compare the efficacy of Helicobacter pylori (H. pylori) eradication on healing and ulcer relapse rates in H. pylori-infected patients with gastric ulcer and duodenal ulcer.

Searching
MEDLINE and other unspecified databases via DIMDI were searched for the period ending on December 1998 using the following search terms: 'gastric ulcer', 'duodenal ulcer' and 'pylori' in combination with 'eradication', 'recurrence', 'relapse' and 'healing'. The reference lists of all the included and excluded studies were also examined. Abstracts were not included in the analysis.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs), and non-randomised studies with or without a control group, were included in the review. Studies had to evaluate gastric and duodenal ulcers, and have at least ten patients per study arm.

Specific interventions included in the review
For studies evaluating H. pylori eradication and ulcer healing, the therapy regimens must have used proton-pump inhibitors and antibiotics (dual, triple or quadruple) exclusively (the names of the drugs were tabulated). The additional use of bismuth and other protective agents were included for studies that examined ulcer relapse rates. Maintenance treatment with proton-pump inhibitors or histamine antagonists had to be no longer than 12 weeks after the start of treatment. Studies were excluded if there was concomitant treatment with non-steroidal anti-inflammatory drugs (NSAIDs); studies without explicit statements regarding the use of NSAID intake were included.

Participants included in the review
H. pylori-infected patients with gastric or duodenal ulcer. To be included, the initial assessment of H. pylori infection status had to be made using at least one biopsy-based test, and the assessment of ulcer diagnosis had to be made using endoscopy. The characteristics of the participants were not reported.

Outcomes assessed in the review
There were three main outcomes:

- eradication of H. pylori after a minimum of 4 weeks, as assessed by diagnostic test(s) based on biopsy or the urea breath test;

- ulcer healing at 4 to 12 weeks after treatment, as assessed by endoscopy; and

- the number of patients with no ulcer relapse at 12 months after treatment, as assessed by endoscopy.

How were decisions on the relevance of primary studies made?
One author performed the study selection based on predefined inclusion criteria.

Assessment of study quality
The quality of each study was assessed using two quality scores: the 3-item, 5-point Jadad scale (see Other Publications of Related Interest); and a 9-point scale developed to evaluate reproducibility, baseline comparability of groups, compliance and statistical analysis. The results from both scales were summed. The median of this total score was chosen as a cut-off point for determining high-quality studies. Two reviewers independently performed the quality
assessment, with any disagreements resolved by discussion.

Data extraction
The data were extracted on pre-tested forms. When important data were lacking, the authors of the primary studies were contacted for further details. The completed forms were independently checked for completeness and inconsistencies. The information collected for these forms included: study identification and country; language of publication; study type; sample size; whether the treatment was abandoned; quality assessment; ulcer type; treatment regimens and dosages; the type of diagnostic test used; time point for investigation of H. pylori status after therapy; time point to assess healing and ulcer relapse; use of proton-pump inhibitor or histamine receptor antagonists during the follow-up period; previous eradication therapy; and consumption of nicotine, alcohol and concurrent NSAIDs. The following data were tabulated: study identification; sample size; study design; treatment; evaluated outcomes; Jadad score; and the total quality score. Intention to treat data were used whenever available, otherwise an all-patients-treated analysis was performed. The individual odds ratios (ORs) were calculated for each study.

Methods of synthesis
How were the studies combined?
The data were pooled using a meta-regression (logistic regression). Publication bias was examined by funnel plots.

How were differences between studies investigated?
Heterogeneity was assessed using a chi-squared statistic. Subgroup analyses were conducted according to the therapeutic regimen (dual and triple therapy), co-medication (use of NSAIDs prohibited versus no information in this respect), and trial design (RCTs versus other designs). The relapse rates were analysed separately for patients who, at the end of treatment, were H. pylori-negative and H. pylori-positive. Sensitivity analyses of quality were also performed by weighting quality scores (above a specific threshold) in the logistic regression analysis.

Results of the review
Twenty-four studies with 3,996 participants were included in the review: 8 RCTs, 3 controlled trials and 13 other (unspecified) study designs. Of the included studies, 15 were analysed for eradication rates, 11 for healing rates, and 12 for ulcer relapse rates.

The total quality scores ranged from 1.5 to 11, out of a possible 14.

The authors suggested that the funnel plots (not presented) showed an acceptable distribution for studies examining H. pylori eradication and ulcer relapse rates.

When all the studies were included, the results for eradication, and ulcer remission in H. pylori-positive and -negative patients were non-heterogeneous (results not presented). Healing data in gastric ulcer and duodenal ulcer studies failed the test for heterogeneity (not presented) and, therefore, were not comparable.

No statistical differences were found between gastric ulcer and duodenal ulcer patients with regard to eradication rates (OR 1.23, 95% confidence interval, CI: 0.99, 1.55) or ulcer relapse rates, whether in successfully H. pylori eradicated patients (OR 0.69, 95% CI: 0.26, 1.84) or unsuccessfully H. pylori eradicated patients (OR 1.48 95% CI: 0.85, 2.56).

The data regarding subgroup analyses were presented in figures. Heterogeneity was found for eradication rates in trials involving dual therapy regimen, and in RCTs. For subgroup analysis of trials that explicitly excluded NSAID intake, there was a small change in ORs, but no significant differences were observed between gastric ulcer and duodenal ulcer with regard to H. pylori eradication and ulcer relapse rates. There was also no significant difference between gastric and duodenal ulcers in studies with a quality score better than the median score for all studies.

Authors' conclusions
The data indicated that H. pylori eradication cures H. pylori-associated gastric and duodenal ulcer disease at similar rates. This suggests that H. pylori is the key factor in peptic ulcer disease independent of the ulcer site.
CRD commentary
The review question was clearly stated, and the inclusion and exclusion criteria were detailed. While more than one database was searched to identify the primary studies, there does not appear to have been a search for unpublished studies. It is possible, therefore, that some studies may have been missed. The authors constructed funnel plots, but it may have been helpful to have included them in the review. The quality of the included studies was adequately assessed, although using a median cut-off point to determine high-quality studies appears to be rather subjective.

The authors stated that detailed information was extracted from each study; more of this information could have been presented in the review. For example, details on the study type, participants and control groups were lacking. Only one reviewer performed the study selection, whereas two reviewers independently checked the data extraction forms. The studies appear to have been summarised appropriately, but the results were largely presented in figures only, and the exact effect sizes were difficult to extrapolate. In addition, the statistical tests for heterogeneity were not reported.

The conclusions appear to follow the results. However, the conclusions should be treated with caution given that a number of studies did not appear to be of a high quality.

Implications of the review for practice and research
Practice: The authors state that the strong recommendation that H. pylori eradication therapy should be used to cure H. pylori-associated peptic ulcer disease applies equally to duodenal and gastric ulcers.

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

Bibliographic details

PubMedID
11736726

Other publications of related interest

Indexing Status
Subject indexing assigned by NLM

MeSH
Anti-Bacterial Agents /therapeutic use; Duodenal Ulcer /drug therapy /microbiology /prevention & control; Helicobacter Infections /drug therapy /microbiology /prevention & control; Helicobacter pylori /drug effects /isolation & purification; Humans; Odds Ratio; Proton-Translocating ATPases /antagonists & inhibitors; Randomized Controlled Trials as Topic; Recurrence; Stomach Ulcer /drug therapy /microbiology /prevention & control

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Record Status
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