Therapy for Helicobacter pylori in patients with nonulcer dyspepsia: a meta-analysis of randomised controlled trials

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Authors' objectives
To assess the effect of eradication therapy for Helicobacter pylori (H. pylori) on symptoms of nonulcer dyspepsia.

Searching
MEDLINE and HealthSTAR were searched from 1984 to 1999 with no language restrictions; the search terms were reported. Proceedings from the annual meetings of the American College of Gastroenterology, American Gastroenterological Association, and European H. pylori Study Groups (1995 to 1999), and reference lists of retrieved articles and reviews that met the inclusion criteria, were also searched. Manufacturers of H. pylori medications and experts in the field were contacted for unpublished research.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) with a minimum of 1 month' follow-up were eligible for inclusion.

Specific interventions included in the review
Studies of dual, triple or quadruple therapy for H. pylori compared with an ineffective control, such as no antibiotics or bismuth compounds, were eligible for inclusion. The therapies reported in the included studies were: a combination of omeprazole, amoxicillin, with or without either clarithromycin or metronidazole; a combination of colloidal bismuth subcitrate and amoxicillin with either tetracycline or metronidazole; a combination of ranitidine, metronidazole and amoxicillin, and a combination of amoxicillin, metronidazole and furazolidone. Drug doses were reported in the review.

Participants included in the review
Studies of patients with nonulcer dyspepsia and documented H. pylori infection were eligible for inclusion.

Outcomes assessed in the review
Studies reporting the symptoms of nonulcer dyspepsia were eligible for inclusion.

How were decisions on the relevance of primary studies made?
Titles and abstracts were assessed in duplicate. The authors did not report how the retrieved articles were assessed for relevance, or how many reviewers performed the assessment.

Assessment of study quality
Validity was assessed using the Jadad scale (see Other Publications of Related Interest). Two reviewers independently assessed study quality, with any differences resolved by consensus.

Data extraction
Two reviewers independently extracted the data from the included studies, with any differences resolved by consensus. Data were extracted on: diagnosis of H. pylori, definition and assessment of nonulcer dyspepsia, eradication therapy, control therapy, the use of therapeutic cointerventions, randomisation, blinding, analysis, attrition, duration and frequency of the follow-up, method of assessment, and definition of success.

Methods of synthesis
How were the studies combined?
Pooled odds ratios (ORs) and 95% confidence intervals (95% CIs) were calculated using a random-effects model.

How were differences between studies investigated?
Statistical heterogeneity was assessed using MA 2x2 statistical software. Sensitivity analyses were undertaken to determine the effect of study quality, the definition of dyspepsia used in the included studies, and the duration of follow-up.

Results of the review
Seven studies (n=1,444) and three abstracts (n=303) were included in the review.

People receiving therapy versus controls - 1 month after intervention.
Four full papers (quality: three scored 5/5, one 4/5) and three abstracts (quality: one scored 3/5, two 2/5) compared the success of therapy in the treatment and control groups. When pooled, there was no statistically significant difference in success between the control and therapy groups (OR 1.29, 95% CI: 0.89, 1.89). This was also the case when only studies of better quality were pooled (OR 1.41, 95% CI: 0.85, 2.33), and when one study was removed from the analysis because of a different definition of dyspepsia. Statistical heterogeneity was reported in three of the analyses; statistical homogeneity when the single study was removed from the analysis.

Patients cured of dyspepsia and those with persistent infection.
Three full papers (quality: all 5/5) and two abstracts (quality: one 3/5, one 2/5) compared the success of therapy in people cured of dyspepsia and those with persistent infection. When pooled, there was no statistically significant difference in success between the groups (OR 1.17, 95% CI: 0.87, 1.59) and no statistical heterogeneity.

Scale used to score dyspepsia.
Seven full papers (quality: three 5/5, one 4/5, two 3/5, one 1/5) compared the changes in the scale used to score dyspepsia between those receiving therapy and controls. Only the smallest study (quality score 1/5) reported a clinically significant benefit of H. pylori therapy.

Authors' conclusions
There was little support for the use of H. pylori eradication therapy in patients with nonulcer dyspepsia.

CRD commentary
The study question and inclusion criteria were clearly stated. The authors undertook a search to identify both published and unpublished data, without language restrictions, so minimising the potential for publication bias. The review methodology appears sound, with the title and abstract screening, quality assessment and data extraction processes being carried out in duplicate. However, how the retrieved articles were assessed for relevance was not reported, leaving some potential for the introduction of bias. The authors highlighted the effect of study quality on the results. Statistical heterogeneity was investigated. The authors' conclusions appear to follow from the evidence presented.

Implications of the review for practice and research
Practice: The authors stated that new therapeutic interventions are required for people with nonulcer dyspepsia.

Research: The authors suggested continued evaluation of the causes of nonulcer dyspepsia is needed.

Bibliographic details
PubMedID
11242496

Original Paper URL
http://www.annals.org/cgi/content/full/134/5/361

Other publications of related interest

Indexing Status
Subject indexing assigned by NLM

MeSH
Anti-Bacterial Agents /therapeutic use; Dyspepsia /drug therapy /microbiology; Helicobacter Infections /drug therapy; Helicobacter pylori; Humans; Odds Ratio; Organometallic Compounds /therapeutic use; Randomized Controlled Trials as Topic; Sensitivity and Specificity; Treatment Outcome

AccessionNumber
12001008097

Date bibliographic record published
30/04/2005

Date abstract record published
30/04/2005

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.