Has the impact of Helicobacter pylori therapy on ulcer recurrence in the United States been overstated: a meta-analysis of rigorously designed trials

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Authors' objectives
To assess the effect of Helicobacter pylori (H. pylori) eradication on ulcer recurrence in North American duodenal ulcer patients.

Searching
MEDLINE was searched from 1983 onwards using the following keyword search strategies: ‘pylori, ulcer, treatment’, ‘pylori, ulcer, eradication’; ‘pylori, ulcer, recurrence’; ‘pylori, double-blind’. An additional search was conducted with these keyword combinations, but substituting ‘pyloridis’ for ‘pylori’. The reference lists of the identified articles, as well as other recent overviews of H. pylori therapy, were also examined.

Unpublished material were obtained by contacting pharmaceutical companies that manufacture medications used for H. pylori therapy in the USA (e.g. Abbott Laboratories, Astra Merck, Glaxo Wellcome, Procter and Gamble) and investigators in the field of H. pylori. The authors also reviewed open presentations made to the US Food and Drug Administration, and abstracts from annual meetings (1988 to 1996) of the American Gastroenterological Association, the American College of Gastroenterology, and the European Helicobacter pylori Study Group.

Study selection
Study designs of evaluations included in the review
Double-blind randomised controlled trials (RCTs) were considered for inclusion. Only North American trials were included in the review.

Specific interventions included in the review
The interventions included: omeprazole (20 to 40 mg); clarithromycin (500 mg); omeprazole and clarithromycin; ranitidine bismuth citrate (RBC; 400 mg); RBC and clarithromycin; amoxicillin (500 mg); RBC and amoxicillin; omeprazole and amoxicillin; placebo.

Participants included in the review
Patients with duodenal ulcers (documented by endoscopy) and H. pylori infection (documented by endoscopic biopsy), who did not use non-steroidal anti-inflammatory drugs and who had ulcer healing at post-treatment endoscopy.

Outcomes assessed in the review
The outcomes assessed were H. pylori eradication and ulcer recurrence over a 6-month follow-up period. H. pylori eradication was documented by at least 2 endoscopic biopsy tests performed at least 4 weeks after the completion of all medications active against H. pylori. Ulcer recurrence, as documented by endoscopy, was defined in all studies as endoscopic evidence of a break of the mucosa of any size with perceptible depth, irrespective of symptoms.

How were decisions on the relevance of primary studies made?
The authors independently reviewed the titles and abstracts of all studies, and retrieved all the articles that met the inclusion criteria.

Assessment of study quality
Since the authors only included those studies that achieved the highest methodological quality (i.e. randomised and double-blind studies), no methodological quality assessment was performed. The authors independently assessed whether the studies met the methodological quality inclusion criteria.
Data extraction
The authors independently abstracted the data and any disagreements were resolved by consensus.

In order to obtain missing data and to identify erroneous assessments, for each study, an author or sponsor was contacted and asked to provide full information regarding the methods and any updated results.

Methods of synthesis
How were the studies combined?
The pooled ulcer occurrence odds ratio (OR) was calculated, along with the 95% confidence intervals (CIs) and the number-need-to-treat.

How were differences between studies investigated?
The method of Breslow and Day (see Other Publications of Related Interest) was used to test for homogeneity under the null hypothesis that the ORs were consistent across studies. The corrected Mantel-Haenszel chi-squared test (d.f.=1, two-tailed) was used to test whether the ORs differed systematically from the value 1.

Results of the review
Seven studies involving 619 patients who met the inclusion criteria were included.

The common OR for ulcer recurrence in patients with H. pylori eradication, as compared with those with persistent infection, was 0.20 (95% CI: 0.13, 0.31); 2.8 patients would need to be successfully treated to prevent an ulcer recurrence at 6 months. There was no evidence of significant statistical heterogeneity among studies. The pooled ulcer recurrence rate at 6 months in patients with H. pylori eradication was 20%.

In a sensitivity analysis that included the best-case scenario, no patients with H. pylori eradication who were lost to follow-up had a recurrent ulcer, whereas all patients with H. pylori persistence who were lost to follow-up had a recurrent ulcer; the common OR was 0.12 (95% CI: 0.08, 0.19). In the worst-case scenario, all patients with H. pylori eradication who were lost to follow-up had a recurrent ulcer, whereas no patient with H. pylori persistence had a recurrent ulcer; the common OR was 0.57 (95% CI: 0.40, 0.80), although statistical heterogeneity was present (p=0.006). In the most positive scenario in this sensitivity analysis, 2.2 patients would need to be successfully treated to avert one ulcer recurrence at 6 months; in the most negative scenario, 7.3 patients would need to be successfully treated.

Authors’ conclusions
Eradication of H. pylori in North American patients with duodenal ulcer disease significantly decreases ulcer recurrence: the odds of developing a recurrent ulcer is five times greater if H. pylori infection persists than if H. pylori infection has been cured. However, the pooled results from the studies of the highest methodological quality revealed that about 20% (95% CI: 14, 26) of patients will develop a recurrent ulcer within 6 months after therapy. Although knowledge of H. pylori has led to a revolution in our management of ulcer disease and, overall, patients with H. pylori-associated ulcer disease will benefit greatly from antibacterial therapy, a significant minority of patients fail to be cured of their ulcer disease despite eradication of H. pylori.

CRD commentary
This was a thorough well-conducted review that included clear objectives and used specific inclusion and exclusion criteria. However, although the authors were only looking for North American studies, MEDLINE was the only database that was searched; a more extensive literature search may have uncovered further relevant studies. The authors’ conclusions seem to follow from the results presented.

Implications of the review for practice and research
The authors did not state any implications for practice or further research.
Bibliographic details

PubMedID
9732917

DOI
10.1111/j.1572-0241.1998.452_a.x

Other publications of related interest

These additional published commentaries may also be of interest. Peterson WL. Review: successful Helicobacter pylori eradication prevents ulcer recurrence. ACP J Club 1999;130:63. Peterson WL. Review: successful Helicobacter pylori eradication prevents ulcer recurrence. Evid Based Med 1999;4:81.

Indexing Status
Subject indexing assigned by NLM

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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.