Meta-analysis: role of Helicobacter pylori eradication in the prevention of peptic ulcer in NSAID users


CRD summary
This review compared Helicobacter pylori eradication with either no eradication or treatment with a proton-pump inhibitor (PPI) in H. pylori-infected patients requiring non-steroidal anti-inflammatory drugs (NSAIDs). The authors concluded that eradication is more effective than no eradication, but is less effective than PPI treatment for preventing NSAID-associated ulcers. The conclusions appear generally reliable.

Authors' objectives
To determine whether the eradication of Helicobacter pylori (H. pylori) prevents peptic ulcer in users of non-steroidal anti-inflammatory drugs (NSAIDs).

Searching
MEDLINE, EMBASE and the Cochrane Controlled Trials Register were searched from January 1984 to December 2004; the search terms were reported. Abstracts submitted to the Digestive Diseases Week meeting between 1984 and 2004 were also searched, as were reference lists of retrieved studies and recent reviews.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion. The duration of follow-up in the included RCTs ranged from 1 to 6 months.

Specific interventions included in the review
Studies comparing H. pylori eradication with no eradication or treatment with a proton-pump inhibitor (PPI) were eligible for inclusion. The included studies compared eradication versus no eradication, placebo or PPI. The eradication rates ranged from 66 to 90% in the eradicated groups and from 0 to 22% in the non-PPI comparison groups. Details of eradication and PPI regimens were not reported.

Participants included in the review
Eligible studies included patients with H. pylori infection who required NSAID therapy. The patients had to have no ulcer, or their ulcer must have healed, at the start of follow-up. The NSAIDs used were naproxen (500 or 750 mg/day) and diclofenac (50 to 100 mg/day).

Outcomes assessed in the review
The primary outcome was the appearance of an endoscopically diagnosed peptic ulcer during follow-up. Development of an ulcer complicated by bleeding, perforation or obstruction was a secondary outcome.

How were decisions on the relevance of primary studies made?
Two reviewers independently assessed abstracts retrieved from the search.

Assessment of study quality
Validity was assessed using the criteria of Chalmers et al. (trial design and protocol, statistical analysis and presentation of results) and Jadad et al. (randomisation, double-blinding, and adequate description of withdrawals and drop-outs). Two reviewers independently assessed quality. Any disagreements were resolved by consensus.
Data extraction
Two reviewers independently extracted the data. In cases of disagreement, the papers were reviewed jointly until the differences were resolved. Data on the numbers of ulcers in each group were used to calculate the odds ratio (OR) and associated 95% confidence interval (CI) for each study.

Methods of synthesis
How were the studies combined?
The studies were combined in a meta-analysis. Peto ORs with 95% CIs were used for comparisons, but a random-effects model was used if significant heterogeneity was present.

How were differences between studies investigated?
Heterogeneity was assessed by means of a Q-test, with a P-value of less than 0.15 indicating significant heterogeneity. Subgroup analyses were performed to evaluate the effect of eradication in new versus previous NSAID users, its effect in patients with and without a previous history of ulcer, the protective effect of eradication for gastric and duodenal ulcers, and the effect of eradication on peptic ulcer complications.

Results of the review
Six RCTs (n=1,207) were included in the review.

In terms of the quality assessment, the Chalmers scores ranged from 0.25 to 0.88 (maximum score 1) and all studies met two or three of the Jadad criteria (not presented as a score).

A significant benefit of eradication was found in comparison with no eradication (5 RCTs, n=939; OR 0.43, 95% CI: 0.20, 0.93). Significant heterogeneity was present for this outcome.

The benefit of eradication was significant for new NSAID users (3 RCTs, n=532; OR 0.26, 95% CI: 0.14, 0.49) but not for previous users (2 RCTs, n=407). Eradication significantly benefited patients without a history of ulcer (3 RCTs, n=572), reduced the risk of both duodenal and gastric ulcers (4 RCTs), and reduced the risk of bleeding ulcers (4 RCTs).

Two RCTs (n=385) compared eradication with PPI treatment; the pooled analysis showed a significant benefit of PPI treatment (OR 7.43, 95% CI: 1.27, 43.64) without significant heterogeneity.

Authors' conclusions
H. pylori eradication reduces the incidence of peptic ulcer in patients receiving NSAIDs and appears to be especially effective in NSAID-naive patients. However, eradication seems to be less effective than treatment with a PPI for preventing NSAID-associated ulcers.

CRD commentary
The review's inclusion criteria for the interventions, participants and outcomes were clear, although few details of the participants and interventions were reported. The authors searched a reasonable range of sources but, since it was unclear whether language restrictions were applied, the potential for language bias could not be assessed. Publication bias was not investigated. Validity was assessed using standard methods and taken into account in the discussion. The study selection, validity assessment and data extraction processes were performed by two reviewers independently, thus reducing the risk of bias and errors during the review process. The results were combined in a meta-analysis. Significant heterogeneity was present for the main analysis but sources of heterogeneity were investigated in subgroup analyses. The authors' conclusions follow from the evidence presented and appear generally reliable, although the small number of studies involved in some analyses and the lack of long-term data should be noted.

Implications of the review for practice and research
Practice: The authors stated that cure of H. pylori infection does not remove the need for ulcer prophylaxis when indicated.

Research: The authors stated that there is a need for long-term studies of the effect of H. pylori eradication on ulcer complications in patients treated with NSAIDs.

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