Systematic review and meta-analysis: Helicobacter pylori eradication therapy after simple closure of perforated duodenal ulcer

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CRD summary
This review found significantly less recurrence of ulcers when patients were treated with Helicobacter pylori eradication therapy after surgery for perforated duodenal ulcers compared to treatment with antisecretory non-eradication therapy. The review was well conducted, but the small number and size of the included trials means the authors’ conclusions should be interpreted with some caution.

Authors’ objectives
To evaluate the effectiveness of Helicobacter pylori eradication therapy for the prevention of ulcer recurrence in patients with simple closures of perforated duodenal ulcers.

Searching
MEDLINE, EMBASE and Cochrane Central Register of Controlled Trials (CENTRAL) were searched from inception to December 2010 without language restrictions; search terms were reported.

Study selection
Eligible studies were randomised controlled trials (RCTs) that evaluated Helicobacter pylori eradication therapy compared with antisecretory non-eradication therapy in patients who underwent surgery for simple closures of duodenal ulcers. The primary outcome was ulcer recurrence at 12 months post-surgery. Healing of ulcers had to be confirmed by endoscopic examination early in the post-surgical period, with ulcer recurrence and Helicobacter pylori positivity determined by endoscopic examination at one year post-surgery.

Studies were conducted in Hong Kong, Egypt and Thailand. Confirmation of ulcer healing was provided at two to four months of follow-up post-surgery. The proportion of patients positive for Helicobacter pylori ranged from 80.6 to 92.8%. All the trials enrolled at least one patient who was using non-steroidal anti-inflammatory drugs. The Helicobacter pylori eradication regimes included omeprazole with other drugs including bismuth subcitrate, metronidazole, tetracycline, amoxicillin or clarithromycin. The duration of eradication therapy ranged from two to five weeks. The comparator treatment was omeprazole administered in doses from 20 to 40mg for durations of two to four weeks.

Two reviewers performed the study selection.

Assessment of study quality
Methodological quality was assessed using Downs and Black criteria and the Jadad five-point composite scale.

Two reviewers assessed study quality; any discrepancies were resolved by consensus.

Data extraction
Data were extracted to calculate relative risks (RR) and 95% confidence intervals (CI) for the outcomes. Study authors were contacted for further information where necessary.

Data were extracted by two independent reviewers; disagreements were resolved by consensus.

Methods of synthesis
Pooled relative risks and 95% confidence intervals were calculated using a DerSimonian and Laird random-effect model. Statistical heterogeneity was assessed using $I^2$. The reviewers evaluated the potential for publication bias using the Egger test and by visual appraisals of funnel plots. Numbers-needed-to-treat (NNT) for benefit was also calculated.

Results of the review
Three RCTs (183) were included in the review. The quality of the three studies using the Jadad scale scores were one
point, two points and five points. One trial reported double-blinding and allocation concealment was reported to be adequate in all three RCTs.

Statistically significant reductions in the pooled incidence of one-year ulcer recurrence were observed with *Helicobacter pylori* eradication therapy compared with the control group (RR 0.15, 95% CI 0.06 to 0.37; $I^2=0\%$; NNT=4).

There was no evidence of publication bias identified for these results.

**Authors' conclusions**
Treatment with *Helicobacter pylori* eradication therapy was associated with a statistically significant reduction in the recurrence of ulcers in patients who underwent simple closures of duodenal ulcers.

**CRD commentary**
The review addressed a clear question and criteria for the inclusion of studies were defined and reproducible. Appropriate databases were searched without language restriction for relevant studies. There were no attempts to identify unpublished studies, but the authors evaluated the potential for publication bias using validated methods. Steps were taken at each stage of the review process to minimise errors and bias by the authors.

The methodological quality of the studies was evaluated and quality ranged from very good to poor. The decision to combine the results in a meta-analysis appeared to be justified, particularly given the lack of statistical heterogeneity observed in the results. The authors correctly acknowledged the limitations of the review due to very small numbers of patients included in the trials. In general, the review was well conducted but the small number and size of the included studies means that a cautious interpretation of the conclusion is warranted.

**Implications of the review for practice and research**

**Practice:** The authors stated that all patients with duodenal ulcer perforations should be tested for *Helicobacter pylori* infection, and eradication therapy was required in all infected patients.

**Research:** The authors stated that recurrence of *Helicobacter pylori* infection was common in developing countries and studies from these regions were required to determine the optimal treatment approaches.

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