Systematic review and meta-analysis: is 1-week proton pump inhibitor-based triple therapy sufficient to heal peptic ulcer?

Gisbert J P, Pajares J M

CRD summary
This review concluded that prolonging therapy with proton-pump inhibitor (PPI) after 1-week triple therapy with PPI and two antibiotics is not necessary to induce ulcer healing. The conclusion is weakened by poor reporting of the methods and limited details of the study participants.

Authors' objectives
To determine the efficacy of 1-week combination of proton-pump inhibitor (PPI) and two antibiotics on ulcer healing; and to determine whether 1-week PPI-based triple therapy is sufficient to heal peptic ulcer.

Searching
MEDLINE, EMBASE, CINAHL and the Cochrane Library (Issue 3, 2004) were searched up to August 2004 using the reported search terms. The reference lists of selected studies and relevant articles were also searched. Studies published in any language except Japanese were eligible.

Study selection
Study designs of evaluations included in the review
To meet the first objective, clinical trials were eligible for inclusion. To meet the second objective, randomised controlled trials (RCTs) were eligible for inclusion.

Specific interventions included in the review
Studies of 1-week triple therapy (PPI plus two antibiotics) were eligible for inclusion. Studies in which all patients were taking non-steroidal anti-inflammatory medication were excluded. To meet the second objective, studies that compared 7-day PPI triple therapy with the same 7-day triple therapy but prolonging PPI treatment were eligible for inclusion. In these studies, PPIs were prolonged for 2 to 4 weeks. Details of treatment combinations were reported.

Participants included in the review
Studies of participants requiring treatment for Helicobacter pylori (H. pylori) eradication and healing of peptic ulcer disease were eligible for inclusion. The presence of the ulcer had to be documented endoscopically. Most studies that evaluated the effects of prolonged treatment with PPI were in patients with duodenal ulcers.

Outcomes assessed in the review
The outcome of interest was ulcer healing success. To be eligible for inclusion, studies had to clearly report the numbers of patients who were treated and the number with ulcer healing success. Studies included in the second objective assessed ulcer healing at 4 to 9 weeks.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
Studies that met inclusion criteria for the first objective did not undergo a validity assessment. Studies that met inclusion criteria for the second objective were assigned a quality score (from 0 to 5) based on the Jadad tool, which is used to assess the reporting of randomisation, blinding, description of withdrawals and drop-outs.

The authors did not state how many reviewers performed the validity assessment, or how any discrepancies were resolved.
Data extraction
Data were extracted using a pre-defined data extraction form. However, it was unclear how many reviewers performed the data extraction, or how any discrepancies were resolved. For the first objective, data on overall ulcer healing and ulcer healing in patients with H. pylori eradication success were extracted. For the second objective, the numbers of patients with a healed ulcer in each comparison group were extracted to enable the calculation of an odds ratio (OR) with 95% confidence intervals (CIs).

Methods of synthesis
How were the studies combined?
For the first objective, results of studies reporting on the efficacy of ulcer healing with 7-day triple-based therapy were tabulated and expressed as a weighted mean with 95% CIs.

For the second objective, studies were combined using a DerSimonian and Laird random-effects model to calculate a pooled OR with 95% CIs.

How were differences between studies investigated?
In the meta-analysis, heterogeneity was assessed using the chi-squared test (significance threshold of p>0.1). Subgroup analyses were performed on the basis of ulcer type (duodenal or gastric) and methodological quality, where appropriate.

Results of the review
Twenty-four studies (n=2,342) were included in the review of efficacy, of which 6 (n=862) were included in the meta-analysis.

Ulcer healing with 7-day combination of a PPI plus two antibiotics.

The overall ulcer healing rate was 86% (95% CI: 84, 87), based on 2,342 patients in 24 studies. Ulcer healing in patients with H. pylori eradication success was 95% (95% CI: 94, 96), based on 1,327 patients in 17 studies. Similar results were shown when the analysis was based on studies of patients with duodenal ulcer only, and on studies of patients with duodenal and/or gastric ulcer disease.

Prolongation of PPI therapy following 7-day PPI plus two antibiotics.

One study scored 5 for methodological quality, 4 studies scored 4 and 1 study scored 3 out of a maximum of 5. Five studies were double-blinded.

No statistically significant difference was shown on the likelihood of ulcer healing between the 7-day combination of PPI and prolonged PPI (OR 1.11, 95% CI: 0.71, 1.74, p=0.66). There was no evidence of statistical heterogeneity (p=0.98). Similar results were shown when the analysis was based on studies of higher methodological quality only (quality score of 3 or more) and on studies of patients with duodenal ulcer only.

Authors’ conclusions
Prolongation of therapy with PPI following triple therapy for 7 days with a PPI and two antibiotics is not required to induce ulcer healing.

CRD commentary
The review appeared to address two research questions: the first considered the efficacy of 1-week PPI-based triple therapy on ulcer healing; the second considered whether 1-week PPI-based triple therapy is sufficient to heal peptic ulcer. Inclusion criteria were defined for both review questions. However, the rationale of the decision to address the first question was unclear, given that it did not appear to influence the authors’ conclusion. Furthermore, the included studies did not appear to have comparison groups, so it is not possible to comment on the relative efficacy of 7-day PPI-based triple therapy.
Several sources were searched to identify relevant studies and attempts were made to limit language bias, but there were no specific attempts to minimise publication bias. There were also no details on whether steps were taken to minimise reviewer error and bias in the study selection, data extraction and validity assessment processes. Studies that addressed the efficacy of a PPI plus two antibiotics were not subject to validity assessment, and study designs and patient populations were not defined. Given these limitations, any conclusions based on this part of the review should be viewed cautiously.

The review of studies to determine whether 7-day PPI-based triple therapy is sufficient to heal ulcers did undergo a validity assessment, and this was considered in the analysis. Details of the intervention were documented and statistical heterogeneity was assessed. These suggested that the studies were sufficiently similar to combine using statistical pooling. However, details of patient demographics were limited, it was unclear how H. pylori was diagnosed in the included studies, and there were no details of ulcer characteristics or definitions used to determine ulcer healing. This means it is difficult to comment on the generalisability of the evidence presented.

In summary, the strength of the authors’ overall conclusion is weakened by poor reporting of the review methodology and limited details of the patients evaluated in the included studies.

Implications of the review for practice and research
Practice: The authors stated that prolonging therapy with PPI after triple therapy for 7 days with a PPI and two antibiotics in patients with uncomplicated duodenal peptic ulcer and H. pylori infection is not necessary.

Research: The authors stated that additional RCTs are required to evaluate the effects of prolonged PPI treatment in all or some patients with gastric ulcers.

Funding
Instituto de Salud Carlos III, grant number C03/02.

Bibliographic details

PubMedID
15801914

DOI
10.1111/j.1365-2036.2005.02418.x

Other publications of related interest
This additional published commentary may also be of interest. Veldhuyzen van Zanten S. Review: 7-day proton-pump inhibitor-based triple therapy is as effective as >7 days of the same regimen for healing H. pylori-associated peptic ulcer. ACP J Club 2005;143:49.

Indexing Status
Subject indexing assigned by NLM

MeSH
Anti-Bacterial Agents; Anti-Ulcer Agents /administration & dosage; Double-Blind Method; Drug Administration Schedule; Drug Therapy, Combination /administration & dosage; Helicobacter Infections /drug therapy; Helicobacter pylori; Peptic Ulcer /drug therapy; Proton Pump Inhibitors; Randomized Controlled Trials as Topic; Treatment Outcome
AccessionNumber
12006008067

Date bibliographic record published
30/04/2007

Date abstract record published
30/04/2007

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.