Proton pump inhibitors versus H2-antagonists: a meta-analysis of their efficacy in treating bleeding peptic ulcer


Authors' objectives
To evaluate whether proton-pump inhibitors are more effective than H2-antagonists (H2-A) for the treatment of bleeding peptic ulcer.

Searching
MEDLINE (via PubMed) was searched up to January 2000 using the keywords 'bleeding', 'proton pump inhibitor', 'peptic ulcer, and each of the drug names. The references of reviews and the retrieved articles were also examined.

Study selection
Study designs of evaluations included in the review
Only randomised controlled trials (RCTs) were eligible.

Specific interventions included in the review
Trials that compared an H2-A (cimetidine, ranitidine or famotidine) with a proton-pump inhibitor (omeprazole, lansoprazole or pantoprazole) were eligible for inclusion. Of the included studies, most (7 studies) compared omeprazole with ranitidine. Two studies compared omeprazole with cimetidine, while another compared lansoprazole with ranitidine. There were no eligible studies of famotidine or pantoprazole.

Participants included in the review
Patients with bleeding gastroduodenal ulcer.

Outcomes assessed in the review
The outcomes of interest for the review were persistent or recurrent bleeding, the need for surgery, or mortality.

How were decisions on the relevance of primary studies made?
The selection was performed independently by two different reviewers.

Assessment of study quality
The quality of the studies was assessed according to the Jadad score (see Other Publications of Related Interest). The authors do not state how the papers were assessed for quality, or how many of the reviewers performed the quality assessment.

Data extraction
The authors do not state how the data were extracted, how many of the reviewers performed the data extraction, or if there was independent checking. The following categories of data were extracted: the bibliographic details; drug name; indication; whether endoscopic therapy was given; the quality of the trial; and the results for the outcome measures.

Methods of synthesis
How were the studies combined?
The studies were combined in a meta-analysis, which combined the Peto odds ratios (ORs) using a fixed-effect model.

How were differences between studies investigated?
Heterogeneity was investigated using the chi-squared test; a significance level of 0.20 was taken.
Results of the review
Eleven studies were included in the review. The number of patients overall was unclear (possibly 1,365). However, 1,352 were included in an analysis of the effect on persistent or recurrent bleeding, 1,239 were included in an analysis of the need for surgery, and 1,239 were included in an analysis of mortality.

Overall, the quality of the trials was limited: out of a maximum score of 5, one study scored 4, four studies scored 3, three scored 2, and two scored only 1.

Effect on persistent or recurrent bleeding (10 studies included in the analysis): the pooled OR was 0.4 (95% confidence interval, CI: 0.27, 0.59) favouring proton-pump inhibitors, but there was statistically-significant heterogeneity (chi-squared 18, p=0.09).

Effect on the need for surgery (8 studies included in the analysis): the pooled OR was 0.7 (95% CI: 0.43, 1.13), but was not statistically significant. There was no heterogeneity (chi-squared 3.98, p=0.68).

Effect on mortality (8 studies included in the analysis): the pooled OR was 0.69 (95% CI: 0.31, 1.57), but was not statistically significant. There was no heterogeneity (chi-squared 3.44, p=0.63).

The subanalyses found no significant effect on persistent or recurrent bleeding between treatments administered by bolus injection. However, they found statistically-significant differences for high-risk patients (those with Forrest classification Ia, Ib or IIA ulcers) (pooled OR 0.28, 95% CI: 0.16, 0.48) in favour of proton-pump inhibitors, and for those not having endoscopic therapy (pooled OR 0.24, 95% CI: 0.13, 0.43).

Authors' conclusions
Proton-pump inhibitors were more effective than H2-A in preventing persistent or recurrent bleeding from peptic ulcers, although this advantage seemed more evident in patients not having adjunct endoscopic therapy. This beneficial effect appeared similar or even more marked in patients with Forrest classification Ia, Ib or IIA ulcers. However, proton-pump inhibitors were not more effective than H2-A for reducing surgery or mortality rates. Nevertheless, the data are too scarce and heterogeneous to draw definitive conclusions. Further comparative trials are clearly warranted.

CRD commentary
This review addressed an appropriate question with well-defined inclusion criteria for the participants, intervention and outcome measures. The literature search was limited to only a single database, and although this was supplemented with some handsearches, it is likely that some published studies were missed. In addition, there was no attempt to identify unpublished material. The quality of the included studies was assessed appropriately and the findings were reported in the review. A sensitivity analysis based on this assessment was not performed. The individual studies were reported in a fair amount of detail in the review. The meta-analyses were appropriate, although the source of heterogeneity within the studies pooled for the effect on the need for surgery could have been explored further. The authors' conclusions are supported by the review's findings, particularly as they stress these conclusions cannot be considered definitive.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: The authors state that further randomised clinical trials comparing proton-pump inhibitors and H2-antagonists are clearly warranted.

Bibliographic details
Other publications of related interest

Indexing Status
Subject indexing assigned by NLM

MeSH
Anti-Ulcer Agents /pharmacology; Endoscopy; Enzyme Inhibitors /pharmacology; Histamine H2 Antagonists /pharmacology; Humans; Peptic Ulcer /drug therapy /pathology /surgery; Peptic Ulcer Hemorrhage /drug therapy; Proton Pump Inhibitors; Recurrence; Treatment Outcome

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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.