Acid suppression in peptic ulcer haemorrhage: a 'meta-analysis'

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Authors' objectives
To evaluate the efficacy of acid-decreasing agents in the management of acute bleeding from peptic ulcers.

Searching
MEDLINE was searched between 1980 and 1999, and the reference lists from relevant studies were reviewed. No search terms were reported.

Study selection
Study designs of evaluations included in the review
Randomised placebo-controlled trials were included.

Specific interventions included in the review
The inclusion criterion was treatment with an acid-decreasing agent compared with placebo. The acid-decreasing agents studied were omeprazole, famotidine, ranitidine, cimetidine and balancid. In one trial, however, the control group received conventional treatment.

Participants included in the review
Studies were included if they did not contain a large fraction of patients receiving potentially effective additional therapies, e.g. endoscopic therapy, and did not contain a large number of excluded patients, e.g. those with severe bleeding. Studies were also excluded if they included patients who did not have bleeding due to peptic ulcer disease. No other details regarding the participants' characteristics were reported.

Outcomes assessed in the review
Re-bleeding, surgery, and mortality rates were reported as the primary outcomes.

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

Assessment of study quality
No formal assessment of quality was undertaken.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the reviewers performed the data extraction.

The extracted data included details relating to study details, treatment type, and outcomes.

Methods of synthesis
How were the studies combined?
A meta-analysis was performed using the Mantel-Haenszel fixed-effect model. This generated a combined odds ratio (OR) along with 95% confidence interval (CIs) for all studies. The meta-analysis was also subdivided to show results for studies using H2-antagonists and those assessing proton-pump inhibitors.

How were differences between studies investigated?
Heterogeneity was assessed using the chi-squared statistic. This was also used to assess the significance of a negative association between the treatment and control groups.

Results of the review
Twenty-one randomised controlled trials involving a total of 3,566 participants (treatment n=1,775) were included.

A significant reduction in re-bleeding rates (OR 0.727, 95% CI: 0.618, 0.855, P<0.001) and surgery rates (OR 0.707, 95% CI: 0.582, 0.859, P<0.001) was demonstrated when acid-reducing agents were used to treat acute peptic ulcer haemorrhage. Mortality rates, however, appeared to be unaffected (OR 1.140, 95% CI: 0.818, 1.588, P=0.49).

The subdivided meta-analysis showed that the H2-antagonists significantly reduced the need for surgery (OR 0.751, 95% CI: 0.593, 0.950, P=0.019) but not re-bleeding rates (OR 0.837, 95% CI: 0.688, 1.019, P=0.084) or mortality (OR 1.059, 95% CI: 0.71, 1.578, P=0.86). In addition, the meta-analysis produced more favourable results for proton-pump inhibitors, demonstrating a significant reduction in re-bleeding rate (OR 0.513, 95% CI: 0.377, 0.699, P<0.001) and the need for surgery (OR 0.583, 95% CI: 0.408, 0.833, P=0.0036); mortality was again, unaffected (OR 1.344, 95% CI: 0.739, 2.444, P=0.41).

No side-effects were reported in the studies included.

Authors' conclusions
The meta-analysis demonstrated a significant beneficial effect of acid-decreasing agents in the reduction of re-bleeding and surgery rates in patients with ulcer haemorrhage; however, no effect upon mortality was demonstrated.

CRD commentary
The review question was stated clearly and was well supported by the study inclusion criteria. The pooling of studies was appropriate. The literature search was limited in that only one database was searched, only English language publications appear to have been included, no search terms were provided, and no attempts to identify unpublished literature were reported. It seems very unlikely that the review included all the available studies. Of the studies that were included, no formal quality assessment was undertaken. In addition, some potentially important study-specific details were not reported, including drug dosage, duration of treatment, and characteristics of the participants such as age and gender.

The extent to which the results of the review were generalisable were limited by the failure to report adequate details pertaining to the interventions and patients' profiles.

Many details of the review process were not reported, such as how the data were extracted or how many of the reviewers performed the data extraction. The extent to which bias played a role in the review is, therefore, unknown.

The authors' conclusions do follow from the results presented, but should be treated cautiously given the limitations of the review.

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

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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.