Somatostatin or octreotide compared with H2 antagonists and placebo in the management of acute nonvariceal upper gastrointestinal hemorrhage: a meta-analysis

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Authors' objectives
To determine the efficacy of somatostatin or octreotide for the treatment of acute nonvariceal upper gastrointestinal haemorrhage.

Searching
MEDLINE was searched from January 1966 to October 1996, and EMBASE from 1980 to October 1996, for English language publications using the headings 'somatostatin', 'octreotide' and 'gastrointestinal hemorrhage'. Manual searches were undertaken using references from retrieved studies. Included studies were limited to those of human participants.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) or randomised clinical trials. Studies were excluded if they pertained to other research questions, review articles, editorials or letters to editors.

Specific interventions included in the review
Somatostatin, octreotide, H2 blockers and placebo, with treatment intervals ranging from 48 to 120 hours.

Participants included in the review
Participants with a clinical or endoscopic diagnosis of acute nonvariceal upper gastrointestinal haemorrhage. Participants were excluded if they suffered from bleeding related to portal hypertension or cancer, presence of coagulopathy, renal insufficiency, pregnancy, or trivial or massive bleeding.

Outcomes assessed in the review
Continued bleeding, re-bleeding during treatment period, need for surgery and transfusion requirements.

How were decisions on the relevance of primary studies made?
[A: Two independent reviewers, with discrepancies resolved through discussion]

Assessment of study quality
The quality of the studies was assessed on:

investigator blinding;

definition of the inclusion and exclusion criteria;

baseline comparability of the treatment and control groups;

standard and similar doses of the intervention agents;

clearly-defined outcome variables; and

appropriate timing of outcome in relation to treatment.

Blinding of allocation was assessed after analysis. Two independent reviewers [A: with discrepancies resolved through discussion].
Data extraction
Two independent reviewers [A: with discrepancies resolved through discussion].

Methods of synthesis
How were the studies combined?
The studies were combined by pooling the relative risks (RRs) using a random-effects model. Summary point estimates of effect were computed using weighted averages of stratum-specific RRs, with weights derived from the reciprocals of the variances adjusted for statistical heterogeneity; 95% confidence intervals (CIs) were calculated on the basis of the adjusted weights. Where RRs were significant, numbers-needed-to-treat (NNT) and 95% CIs were calculated.

How were differences between studies investigated?
Assuming heterogeneity was present, differences between studies were investigated using a random-effects model to combine studies. Graphical displays of continued bleeding and the need for surgery were also utilised to help assess heterogeneity, and the DerSimonian and Laird method (see Other Publications of Related Interest) was applied for each planned analysis. Subgroup analyses were also undertaken, based on exclusion of statistical outliers, investigator-blinded trials and source of bleeding.

Results of the review
Fourteen RCTs (1,829 patients) were included.

For continued bleeding or rebleeding (assessed in 14 RCTs), somatostatin reduced the RR to 0.53 (95% CI: 0.43, 0.63). The NNT was 5 patients (95% CI: 3.2, 9.1). Analysis revealed that heterogeneity was significant (P<0.005).

In the 12 RCTs measuring continued bleeding alone, somatostatin reduced the RR to 0.55 (95% CI: 0.33, 0.55). The NNT was 5 patients (95% CI: 3.1, 9.3). Analysis revealed that heterogeneity was significant (P<0.005).

The RR of surgery was reduced by somatostatin to 0.71 (95% CI: 0.61, 0.81). The NNT was 8 patients (95% CI: 4.5, 40.0). Analysis revealed that heterogeneity was significant (P<0.005).

Subgroup analyses of investigator-blinded trials indicated that somatostatin remained efficacious for continued bleeding alone (RR 0.6, 95% CI: 0.53, 0.70) and with rebleeding (RR 0.73, 95% CI: 0.64, 0.81). In addition, it showed that somatostatin or octreotide was more effective for peptic ulcer bleeding (RR 0.48, 95% CI: 0.39, 0.59) than non-peptic ulcer bleeding (RR 0.62, 95% CI: 0.39, 1.002).

Authors’ conclusions
Intravenous somatostatin reduces the risk for persistent, acute nonvariceal upper gastrointestinal haemorrhage caused by peptic ulcer disease, and may have a therapeutic role in initial management of the clinical problem. By slowing and halting bleeding, somatostatin may be useful in the resuscitative phase of management, enhancing the clinical utility of endoscopy by improving visualisation of lesions.

CRD commentary
This is a good quality systematic review. It provides clear descriptions of the objective, interventions, participants, outcomes, study designs, other inclusion criteria, sources used, quality criteria, methods used to combine studies and to assess heterogeneity, and details of the primary studies. Additional information from the authors on the processes used for applying inclusion criteria, quality criteria and for data extraction, indicate a rigorous methodology was followed. Results are clearly stated and issues concerning interpretation of the results are discussed.

Implications of the review for practice and research
Further research is required to clarify the effect of somatostatin in clinically-distinct patient subgroups.
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Other publications of related interest

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Record Status
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