A meta-analysis of somatostatin versus vasopressin in the management of acute esophageal variceal hemorrhage

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Authors' objectives
To compare the efficacy and toxicity of somatostatin and vasopressin in short-term treatment of hemorrhage from oesophageal varices.

Searching
MEDLINE was searched for English language trials from January 1985 to March 1994, using the search terms 'somatostatin', 'vasopressin', 'oesophageal/gastric varices', 'clinical trials' and 'human'. In addition, the reference lists of retrieved reports, review articles and chapters from textbooks were searched. Fifty references were obtained from the MEDLINE search and 45 reports were excluded. Manual searching produced one additional report.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were included. Articles pertaining to a different research question, review articles, editorials and letters to the editor were excluded from the review.

Specific interventions included in the review
Somatostatin, vasopressin and somatostatin bolus plus octreotide. Length of treatment in the included studies ranged from 18-72 hours. Dosage for vasopressin ranged from 0.1 U/min to 0.4 U/min; for somatostatin the dosage was 250 microg/h; for somatostatin plus octreotide the bolus dose of somatostatin was 100 microg/h, followed by 25 microg/h/octreotide (two studies).

Participants included in the review
Patients with acute oesophageal variceal bleeding and clinical evidence of hypertension. All except one subject included in the studies were classified by Child's class. Proportions of Child's A, B and C class were 13%, 34% and 54% respectively.

Outcomes assessed in the review
Initial control of bleeding (defined as clinical absence of continued bleeding within 6-12 hours); sustained control of bleeding (24-72 hours); adverse drug effects leading to discontinuation of treatment and all cause mortality.

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 authors performed the selection.

Assessment of study quality
Quality of the trials were evaluated on the basis of investigator blindness; well-defined study population; baseline condition established; baseline equivalence of treatment groups; adequate potency of the of the principal treatments; clearly-defined outcome variables. One point was given for each of these six criteria, except adequate potency of the principal treatments, which was worth 2 points (1 point for each treatment). A quality score was generated which potentially ranged from 0 to 7. Two reviewers independently evaluated the quality of each trial. All trials scored 6 out of a possible score of 7 on aspects of quality.

Data extraction
Two reviewers independently abstracted data regarding the number of patients in both treatment groups and the number
with each outcome.

Methods of synthesis
How were the studies combined?
Summary points estimations of effect were computed using precision-based weighted averages of stratum-specific relative risk (RR), with the weights derived from the reciprocals of the variances. 95% confidence intervals (CI) were calculated by the Taylor series method (see Other Publications of Related Interest). For subgroup analysis of initial control of bleeding by Child class, the Mantel-Haenszel method was used to calculate the estimator of RR. For adverse drug effects, aggregate analyses were performed using either the chi-squared statistic or Fisher's Exact Test.

How were differences between studies investigated?
Test for heterogeneity were performed for outcomes of initial and sustained control of bleeding. Subgroup analysis of initial control of bleeding by Child class was performed. A sensitivity analysis was performed for the outcome of initial control of bleeding, excluding one trial in which a low dose of vasopressin was used.

Results of the review
Six studies were included with a total of 275 patients. Somatostatin was the comparative treatment in four studies; in two studies somatostatin was given as a bolus followed by treatment with octreotide. All six studies measured initial control of bleeding, adverse drug effects requiring discontinuation of treatment and all-cause hospital mortality. Four studies measured sustained control of bleeding (203 patients).

Tests for heterogeneity were not statistically-significant.

Initial control of bleeding:
RR of achieving initial control of bleeding with somatostatin compared with vasopressin was 1.62 (95% CI: 1.37, 1.93) and the number need to treat (NNT) was 3.7 (95% CI: 2.7, 6.0). Exclusion of the trial in which a low dose of vasopressin was used had no significant effect on the results. Subgroup analysis of treatments across each Child's class: no difference in efficacy in Child's A patients (RR = 1.06, 95% CI: 0.67, 1.67), a significant difference in Child's B patients (RR = 1.36, 95% CI: 1.05, 1.96), and in Child's C patients somatostatin was twice as effective as vasopressin (RR = 2.02, 95% CI: 1.33,3.06).

Sustained control of bleeding:
RR of achieving sustained control of bleeding with somatostatin compared with vasopressin was 1.28 (95% CI: 1.00, 1.65) and the NNT was 8.8 (95% CI: 4.0, 46).

Adverse effects and mortality:
The risk of adverse effects requiring discontinuation of treatment was greater with vasopressin (10% vs 0%, p = 0.00007). Adverse effects included left ventricular failure, severe abdominal pain, dysrhythmias, severe diarrhoea, pulmonary oedema and chest pain. All-cause mortality was 31% for somatostatin and 40% for vasopressin (p=0.14).

Authors' conclusions
The meta-analysis suggest that somatostatin is more effective in controlling acute haemorrhage from oesophageal varices and has a lower risk of adverse effects than vasopressin.

CRD commentary
This is a good systematic review with the methods and inclusion criteria clearly stated. One limitation, however, is the search strategy did not extend to searching electronic databases apart from MEDLINE. Furthermore, only English language trials were included. The authors reported on six aspects of quality, but should also have included concealment of allocation and method of randomisation. It is not clear whether octreotide is another name for somatostatin, or
perhaps a derivative with similar therapeutic properties.

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