Review: Somatostatin analogues reduce blood products used in acute bleeding esophageal varices but do not reduce mortality

QUESTION

Is somatostatin or its analogues more effective than placebo or no treatment for patients with suspected acute bleeding from esophageal varices?

DATA SOURCES

Published and unpublished studies were identified by searching MEDLINE and the Cochrane Controlled Trials Register (last searched August 2001) with combinations and various forms of the terms somatostatin, octreotide, variceal, varices, bleed, hemorrhage, esophag, hematemesis, and melena; reviewing abstracts of conference proceedings and bibliographies of relevant studies; and contacting authors.

STUDY SELECTION

Studies were selected if they were randomized controlled trials (RCTs) that compared somatostatin or its analogues with placebo or no treatment in patients with suspected or verified, acute or recently bleeding esophageal varices.

DATA EXTRACTION

Data were extracted on the nature, dosage, and duration of treatment; number of randomized patients; randomization and blinding procedures; exclusions after rando-mization; loss to follow-up; and outcomes (mortality, blood transfusions, balloon tamponade, failed initial hemostasis, and rebleeding).

MAIN RESULTS

12 trials (n = 1452) were included in the intention-to-treat analysis. Meta-analysis showed no difference between somatostatin or analogues and placebo or no treatment for mortality (12 trials, n = 1452), balloon tamponade (6 trials, n = 736), or rebleeding (9 trials, n = 937) (Table). Similar results were found when somatostatin or analogues were given for 5 days (7 trials) rather than for a shorter period. Patients in the somatostatin or analogue group received fewer units of blood products (10 trials, n = 1172; weighted mean difference 0.94 units, 95% CI 0.65 to 1.2), and fewer had failure of initial hemostasis (11 trials, n = 1232) (Table).

CONCLUSION

Somatostatin or its analogues reduced the number of blood products given and failure of initial hemostasis in patients with suspected acute bleeding esophageal varices but did not affect mortality, balloon tamponade, or rebleeding.

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Somatostatin or analogues vs placebo or no treatment (control) for acute or recently bleeding esophageal varices (follow-up ranged from 5 d to 6 wk)*

Outcomes	Weighted event rates		RRR (95% CI)	NNT (CI)
	Somatostatin	Control		
Mortality	18%	19%	7% (−14 to 25)	Not significant
Balloon tamponade†	9.1%	14%	32% (−24 to 63)	Not significant
Failure of initial hemostasis†	27%	37%	32% (8 to 50)	10 (6 to 44)
Rebleeding†	9.8%	17%	39% (−9 to 65)	Not significant

*Abbreviations defined in Glossary; RRR, NNT, and CI calculated from data in article.
†Calculated using a random-effects model.

COMMENTARY

Somatostatin and its analogues reduce portal pressure in animal experiments and healthy patients (1), but this effect is less certain in portal hypertension or esophageal variceal pressure or during active bleeding. The facile, immediate administration and lack of important side effects, however, have made somatostatin a popular choice for expedient treatment of bleeding varices.

Gøtzsche's timely and excellent meta-analysis assessed the efficacy of somatostatin in bleeding esophageal varices. The inclusion of complete data from preliminary communications avoided publication bias and conferred a balanced evaluation. From this large patient sample, the outcome measures of mortality, rebleeding, and the use of balloon tamponade to control bleeding did not differ between treatment and control groups. The reduced transfusion requirement of about 1 unit of blood in the treated group was a minor benefit. The relative risk for failure of initial hemostasis was lower in the somatostatin group. 10 patients will need treatment to achieve benefit in 1 additional patient.

Some limitations should be considered. A precise definition of hemostasis, not apparent in the studies, is essential for the interpretation of failure of initial hemostasis. The lack of benefit in rebleeding may be limited because definitive treatment was offered after drug or placebo infusion in 10 trials: sclerotherapy in 8 and either sclerotherapy or band ligation in 2 trials. In evaluating transfusion requirements, threshold parameters for blood replacement may be different in the various centers. Last, heterogeneity of studies, an inherent and confounding problem in studies of bleeding varices, was noted in this meta-analysis, particularly in the secondary outcome measures.

Further controlled trials of somatostatin and analogues in the acute treatment of bleeding varices are not justified. Although one cannot strongly recommend the use of this drug in acute variceal hemorrhage, clinicians may continue to use it initially while the patient is stabilized for definitive therapy. The 5-day somatostatin infusion regimen has no evidence of effectiveness and will only delay definitive therapy. Somatostatin, similar to vasopressin, has been proved minimally effective for acute bleeding varices. Unlike vasopressin, however, this conclusion is based on the meta-analysis of a large number of patients from several controlled trials.

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Reference

1. **Hanisch E, Doertenbach J, Usadel KH.** Somatostatin in acute bleeding oesophageal varices. Pharmacology and rationale for use. Drugs. 1992;44 Suppl:24-35.