Review: Somatostatin and its analogues do not reduce mortality in acute bleeding esophageal varices

Gøtzsche PC, Hróbjartsson A. **Somatostatin analogues for acute bleeding oesophageal varices.** Cochrane Database Syst Rev. 2005;(1):CD000193. **Clinical impact ratings:** Hospitalists ★★★★★★☆ Gastroenterology ★★★★★★☆

QUESTION

In patients with suspected acute bleeding from esophageal varices, are somatostatin or its analogues more effective than placebo or no treatment?

METHODS

Data sources: MEDLINE (1966 to February 2004), the Cochrane Library, abstracts from conference proceedings, reference lists of trials, and contact with authors.

Study selection and assessment: Randomized controlled trials (RCTs) in any language that compared somatostatin or its analogues with placebo or no treatment in patients with suspected or recently bleeding esophageal varices. Quality assessment of individual studies included allocation concealment and blinding.

Outcomes: Mortality, blood transfusion, rebleeding, failed initial hemostasis, and balloon tamponade.

MAIN RESULTS

20 RCTs (n = 2518) met the selection criteria. 9 trials were high-quality, having concealed allocation and blinding of clinicians and patients. Somatostatin did not reduce mortality in all trials in which it was assessed (14 RCTs) or in high-quality trials (7 RCTs) (Table). Patients receiving somatostatin required fewer units of blood products (Table). Rebleeding rates were lower with somatostatin in low-quality trials but did not differ from placebo or no treatment in high-quality trials (Table). Fewer patients receiving somatostatin had failure of hemostasis (Table). Groups did not differ for balloon tamponade (Table).

CONCLUSIONS

In patients with suspected acute bleeding from esophageal varices, somatostatin or its analogues do not reduce mortality. Patients who receive somatostatin require fewer units of blood products and have a lower failure rate of hemostasis.

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Somatostatin or its analogues vs placebo or no treatment for suspected acute or recently bleeding esophageal varices*

Outcomes	Number of trials (n)	Study quality	Weighted event rates		RRR (95% CI)	NNT (CI)
			Somatostatin	Placebo or no treatment		
Mortality†	14 (2002)	All	17%	20%	13% (–4 to 28)	Not significant
	7 (967)	High	18%	19%	4% (–24 to 26)	Not significant
Rebleeding	7 (739)	Low	14%	28%	64% (49 to 74)	8 (5 to 25)
	5 (538)	High	20%	25%	22% (–5 to 42)	Not significant
Failed initial hemostasis	16 (1861)	All	28%	38%	33% (14 to 47)	10 (7 to 25)
	8 (979)	High	28%	41%	35% (23 to 45)	8 (5 to 17)
Balloon tamponade	6 (736)	All	9%	14%	32% (–24 to 63)	Not significant
	4 (610)	High	10%	13%	21% (–20 to 48)	Not significant
			Weighted mean difference (CI)			
Transfusions	14 (1589)	All	–0.98 (–1.35 to –0.61)			
	8 (1105)	High	–0.77 (–1.06 to –0.47)			

*Abbreviations defined in Glossary; weighted event rates, RRR, NNT, and CI calculated from data in article using a random-effects model. Follow-up ranged from 48 hours to 6 weeks.

†A fixed-effects model was used.

COMMENTARY

The meta-analysis by Gøtzsche and Hróbjartsson updates their previous meta-analysis (1), attempting to determine benefits of somatostatin analogues for bleeding esophageal varices. 8 recent studies added to their previous analysis showed no significant differences. All studies to date were subdivided on the basis of high- versus low-quality; high-quality studies included concealed allocation and double-blind design. In the high-quality studies, differences between somatostatin and placebo were even less significant—about a half unit of blood was saved per patient with somatostatin treatment.

Research in the treatment of bleeding esophageal varices is complex and fraught with confounding variables that contribute to both the *intra-* and *inter-*center differences seen in this review: 1) endoscopic criteria for diagnosis (affected by the extent of the hemorrhage and visibility), 2) differing drug dosage and duration of infusion, 3) varying protocols for intervention with definitive therapy, 4) definition of rebleeding or failure of hemostasis (appearance of blood in nasogastric tube vs endoscopic proof), 5) threshold for transfusion, 6) use of such alternative therapies as endoscopic therapy or transjugular intrahepatic portalsystemic shunt (TIPS) in patients who may or may not be potential liver transplantation candidates (in whom earlier intervention is desirable), and 7) timing of assessment of mortality (5 to 42 d). In addition, the degree of the decompensation of cirrhosis at presentation and the severity of coagulopathy contributing to the bleeding episodes were often not satisfactorily quantified in the included studies. Of interest, even studies done after the Baveno II Consensus Workshops (2) had some of these limitations, attesting to the difficult nature of the problem.

Somatostatin analogues have only marginal benefit in the management of bleeding varices, as concluded in this meta-analysis. In my view, this is the final nail in the coffin of their efficacy, and there is no basis to use or study this class of drug further for bleeding varices. However, if the practicing physician chooses to use these drugs as a temporizing measure while the patient is resuscitated during acute variceal hemorrhage, it should not be done at the expense of delaying definitive treatment.

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References

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