# Review: Octreotide reduces rebleeding more than does vasopressin or terlipressin in patients with esophageal varices

Corley DA, Cello JP, Adkisson W, Ko WF, Kerlikowske K. **Octreotide for acute esophageal variceal bleeding: a meta-analysis.** Gastroenterology. 2001 Mar;120:946-54.

## QUESTIONS

In patients with upper gastrointestinal (GI) hemorrhage who have endoscopically confirmed esophageal varices as the probable cause of hemorrhage, does octreotide reduce all-cause mortality or control bleeding, and what are the major complications resulting from its use?

## DATA SOURCES

Clinical trials of the use of octreotide in patients with GI hemorrhage were identified by searching MEDLINE, the Cochrane Library, and EMBASE/Excerpta Medica (1985 to 1999). Conference abstracts and bibliographies were hand searched, and the manufacturer of octreotide (Novartis) was contacted.

## STUDY SELECTION

Randomized controlled trials (RCTs) were selected if octreotide was studied in patients with acute variceal bleeding confirmed by endoscopy as the probable source of bleeding, data were available on all-cause mortality or control of bleeding, and follow-up was ≥ 48 hours. Studies of prevention of rebleeding were excluded.

## DATA EXTRACTION

Data were extracted on study quality and characteristics, dose and route of octreotide and other therapies, duration of therapy, follow-up, all-cause mortality, sustained control of bleeding during follow-up, and complications.

## MAIN RESULTS

13 study reports (1077 patients) met the inclusion criteria. Alternative therapies were placebo or no additional therapy (5 studies), vasopressin (3 studies), terlipressin with or without nitroglycerin (2 studies), sclerotherapy (2 studies), and balloon tamponade (1 study). Octreotide was not associated with a reduction in mortality for all studies (weighted relative risk [RR] 0.89, 95% CI 0.69 to 1.14) or compared with any other single therapy. Patients who received octreotide had a lower incidence of rebleeding than did those receiving any other therapy (Table), vasopressin or terlipressin (RR 0.58, CI 0.42 to 0.81), or placebo or no therapy (all patients received endoscopic therapy before randomization) (RR 0.46, CI 0.32 to 0.67). Overall results for complications were heterogeneous, precluding general conclusions. A subgroup analysis found that major complications were less common with octreotide than with vasopressin or terlipressin (RR 0.31, CI 0.11 to 0.87).

## CONCLUSION

Octreotide reduces rebleeding more than does vasopression or terlipressin in patients with upper gastrointestinal hemorrhage who have endoscopically confirmed esophageal varices as the probable cause of hemorrhage.

*Sources of funding: In part, American Digestive Health Foundation and National Institutes of Health.*

*For correspondence: Dr D.A. Corley, S-357, University of California at San Francisco, Box 0538, San Francisco, CA 94143-0538, USA. FAX 415-476-0659.*

**Octreotide for patients with upper gastrointestinal hemorrhage probably caused by esophageal varices (duration of studies up to 60 d)***

| Outcome | Weighted event rates | | RRR (95% CI) | NNT (CI) |
|---|---|---|---|---|
| | Octreotide | Any other therapy | | |
| Rebleeding | 19% | 32% | 37% (23 to 49) | 8 (5 to 16) |

*Abbreviations defined in Glossary.

## COMMENTARY

The meta-analysis by Corley and colleagues supports previous meta-analyses that suggest that octreotide, when added to endoscopic therapy or when compared with medical therapy or sclerotherapy, is beneficial and safe for esophageal variceal bleeding but does not decrease mortality (1). Assessment of meta-analyses requires careful examination of the clinical questions addressed and the studies included. No trial in this review studied the efficacy of octreotide alone compared with that of placebo alone.

A double-blind, placebo-controlled RCT of octreotide alone in patients with liver disease and upper GI bleeding showed no benefit in the overall study population or in those with variceal bleeding (2), but this study was published only in abstract form. Similarly, no benefit was seen in 2 of 3 double-blind, placebo-controlled RCTs of somatostatin alone (3). In apparent contradiction, RCTs indicate that the efficacy of octreotide is similar to endoscopic therapy, which is, in other studies, documented to be effective for variceal bleeding. Furthermore, octreotide plus endoscopic therapy improves control of bleeding more than does endoscopy alone.

Comparisons with other medical therapies suggest greater efficacy for octreotide. However, the suggestion that octreotide may be more effective than terlipressin is difficult to reconcile with results from RCTs comparing terlipressin with placebo or inactive treatment, which show that terlipressin improves mortality and control of bleeding (1). No other medical therapy has been shown to decrease mortality in acute variceal bleeding.

In summary, trials of highest methodologic quality fail to document that octreotide alone is better than placebo, although efficacy is suggested if octreotide is compared with other therapies or used with endoscopic therapy. Octreotide combined with endoscopy should be the medical therapy of choice for U.S. patients hospitalized with acute variceal bleeding. Outside the United States, such agents as terlipressin and somatostatin, if available, must also be included as appropriate options.

*Loren Laine, MD*
*University of Southern California School of Medicine*
*Los Angeles, California, USA*

***References***

1. **D'Amico G, Pagliaro L, Bosch J**. Pharmacological treatment of portal hypertension: an evidence-based approach. Sem Liver Dis. 1999;19:475-505.
2. **Burroughs A**. Double-blind RCT of 5 day octreotide versus placebo, associated with sclerotherapy for trial/failures. Hepatology. 1996;24:352A [Abstract].
3. **Gotzsche PC, Gjorup I, Bonnen H, et al**. Somatostatin v placebo in bleeding oesophageal varcies: randomised trial and meta-analysis. BMJ. 1995;301:1495-8.

  