Terlipressin for acute esophageal variceal hemorrhage

George N Ioannou¹, Jenny Doust², Don C Rockey³

¹University of Washington, Gastroenterology, S-111-GI, Seattle, USA. ²Faculty of Health Sciences and Medicine, Bond University, Gold Coast, Australia. ³Department of Gastroenterology and Hepatology, Duke University Medical Center, Durham, USA

Contact address: George N Ioannou, University of Washington, Gastroenterology, S-111-GI, Veterans Affairs Puget Sound Health Care System, 1660 S. Columbian Way, Seattle, WA 98108, USA. georgei@medicine.washington.edu. (Editorial group: Cochrane Hepato-Biliary Group.)

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ABSTRACT

Background

Terlipressin (triglycyl lysine vasopressin) is a synthetic analogue of vasopressin, which has been used in the treatment of acute variceal haemorrhage. In contrast to vasopressin, terlipressin can be administered as intermittent injections instead of continuous intravenous infusion and it has a safer adverse reactions profile. However, its effectiveness remains uncertain.

Objectives

To determine if treatment with terlipressin improves outcome in acute oesophageal variceal haemorrhage and is safe.

Search strategy

Randomized clinical trials were identified by searching the following databases (November 1999): The Cochrane Hepato-Biliary Group Controlled Trials Register, The Cochrane Controlled Trials Register on The Cochrane Library (Issue 3, 1999), MEDLINE, EMBASE, Biosis, and Current Contents. The bibliographies of identified publications were checked. Experts in the field and the manufacturers of terlipressin were contacted. For the update of this review, no new randomised clinical trials were identified on any of the databases (October 2002).

Selection criteria

All randomised clinical trials, which compared terlipressin with: (a) placebo or no treatment, (b) balloon tamponade, (c) endoscopic treatment, (d) octreotide, (e) somatostatin and (f) vasopressin, in the setting of acute variceal haemorrhage.

Data collection and analysis

Eligibility, trial quality assessment and data extraction were done independently by two reviewers. The primary outcome measure was mortality. Secondary outcomes were failure of initial haemostasis, rebleeding, procedures required for uncontrolled bleeding or rebleeding, transfusion requirements and length of hospitalisation.

Main results

Twenty studies were identified for all the comparison groups, involving 1609 patients. There were seven studies (with 443 patients) comparing terlipressin to placebo, five of which were considered to be high quality studies based on the Jadad scale. The meta-analysis indicates that terlipressin was associated with a statistically significant reduction in all cause mortality compared to placebo (relative risk...
0.66, 95% confidence interval 0.49 to 0.88). Three studies (with 302 patients) were identified comparing terlipressin to somatostatin, two of which were high quality studies; only one high quality study (219 patients) comparing terlipressin to endoscopic treatment was identified. Within the limited power provided by these small numbers of patients, no statistically significant difference was demonstrated between terlipressin and either somatostatin or endoscopic treatment in any of the outcomes. For the remaining comparison groups (terlipressin versus balloon tamponade, terlipressin versus octreotide, and terlipressin versus vasopressin) only small, low quality studies were identified and no difference was demonstrated in any of the major outcomes. There was no significant difference between the terlipressin group and any of the comparison groups in the number of adverse events that caused death or withdrawal of medication.

Authors’ conclusions

On the basis of a 34% relative risk reduction in mortality, terlipressin should be considered to be effective in the treatment of acute variceal hemorrhage. Further, since no other vasoactive agent has been shown to reduce mortality in single studies or meta-analyses, terlipressin might be the vasoactive agent of choice in acute variceal bleeding.

**Plain Language Summary**

Terlipressin is a safe and effective treatment for bleeding from oesophageal varices which is a life threatening complication of cirrhosis of the liver

Esophageal varices are abnormal dilatations of veins in the lower part of the swallowing tube (oesophagus) that may develop in patients with chronic liver damage (cirrhosis). Bleeding from these varices is a life threatening complication with mortality between 20 and 50 per cent. Bleeding from varices may be treated with medications and/or with an endoscope which is a flexible tube with a camera at the end which allows direct visualization and treatment of bleeding varices. The reviewers evaluated the safety and effectiveness of a drug called terlipressin; they reported that terlipressin appears to be as safe as other treatments and that terlipressin may reduce the mortality from variceal bleeding as compared to placebo. The reviewers did not have sufficient data to decide whether terlipressin was better or worse than other available treatments such as other drugs (somatostatin, octreotide) or endoscopic treatment.