Somatostatin does not reduce oesophageal variceal pressure in liver cirrhotics

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SUMMARY Transmural oesophageal variceal pressure was determined by direct puncture of the varices in 27 patients with liver cirrhosis and oesophageal varices. Variceal pressure was not influenced three to six minutes after somatostatin bolus administration and slightly increased during somatostatin infusion. Thus, potential haemostatic benefits of somatostatin cannot be explained by pressure reductions in the varices.

Somatostatin has been reported as of potential benefit by some authors in the treatment of acute oesophageal variceal haemorrhage in liver cirrhosis, and this has been attributed to a portal venous pressure lowering effect of this drug. Other authors, however, were not able to confirm these findings. Results of placebo controlled clinical trials, assessing the effects of somatostatin in acute variceal bleeding are still lacking.

Measurement of oesophageal variceal pressure has only recently become a promising new approach to determine drug effects at the site of variceal rupture itself. It was the aim of the present study to examine whether somatostatin influences variceal pressure in patients with liver cirrhosis.

Methods

PATIENTS In 27 consecutive patients (23 men and four women, aged 59 (10) years) with alcoholic (n=20) or post-hepatic (n=7) liver cirrhosis, who were referred for sclerotherapy to the Endoscopy Unit of the Department of Medicine II, Klinikum Grosshadern, University of Munich. 33 measurements of variceal pressure were carried out. Seventeen belonged to Child’s group A, seven to B and three to group C. The patients had varices grade 2 to 4 according to Mannes et al. Ten patients had a history of previous gastrointestinal bleeding. The study was approved by the ethical committee of the medical faculty of the University of Munich and informed consent was obtained from all patients.

STUDY DESIGN In the first group of 15 consecutive patients somatostatin was administered and in a second group of 12 consecutive patients, saline was administered. If patients were studied twice (three patients in each group), drug administration was not repeated on the same day.

On seven occasions an iv bolus of 250 µg somatostatin 14 (Stilamin, Serono) dissolved in 2 ml 0-9% NaCl was injected within 30 seconds. On eight occasions 2 ml 0-9% NaCl were administered as a placebo. Transmural oesophageal variceal pressure was determined immediately before and 2.5–6.0 (4.3±1.5) minutes after bolus injection. Ten milligrams diazepam and 40 mg n-butyl-scopolamin were administered before the first measurement.

On 11 occasions an iv bolus of 250 µg somatostatin 14 was injected as described above followed by a somatostatin infusion (4-2 µg/min in 0-5 ml 0-9% NaCl/min). On seven occasions 2 ml 0-9% NaCl followed by a 0.5 ml 0-9% NaCl/min infusion were administered as a placebo. Transmural oesophageal variceal pressure was determined immediately before bolus injection and during—that is, 30 minutes after start of the infusion. Patients received 10 mg diazepam and 40 mg n-butyl-scopolamin before the measurements.

Heart rate and systemic blood pressure were assessed before and after bolus administration and at three minute intervals during infusion.
DETERMINATION OF VARICEAL PRESSURE

Determination of intravariceal oesophageal pressure was carried out before sclerotherapy via an endoscope (Olympus GIF K 2) by puncturing the varix with a sclerotherapy needle (od 0.7 mm) 5 cm above the gastrooesophageal junction. The needle was connected to a Teflon tube (od 1.5 mm) which was perfused with 0.6 ml/min H2O, using a low compliance capillary pump system (Mui Scientific, Canada) according to Staritz et al. The correct position of the needle in the vessel was identified by the typical respiration dependent pressure fluctuations (Fig. 1). Oesophageal luminal pressure was recorded simultaneously (Fig. 1) via a second Teflon tube of the same size attached to the outer surface of the endoscope and perfused as above. Calibrations were done before each session. Transmural variceal pressures were calculated as the difference between variceal and oesophageal luminal pressures (Fig. 1). Pressures were measured by electromechanical transducers and a Sensor Medics R 611 Dynograph recorder.

STATISTICAL ANALYSIS

Results are given as means (SD). Intraindividual pressures before and after drug administration were compared by Wilcoxon’s matched pairs signed-rank test. Pressure changes after somatostatin were compared with those after saline by the Mann-Whitney-Wilcoxon test. p-Values ≤0.05 (two-tailed) were considered statistically significant.

Results

Patients who received somatostatin were comparable with those who received saline with respect to sex, age, aetiology of liver cirrhosis, liver function, bleeding history, and variceal size.

After bolus injection of somatostatin mean transmural variceal pressure did not increase above basal values [18.3 (4.4) vs 19.4 (5.1) cm H2O before and after drug administration, Fig. 2A]. In controls, pressures were not influenced by bolus injection of saline [25.7 (7.7) vs 24.5 (8.1) cm H2O, Fig. 2B].

During infusion of somatostatin mean transmural variceal pressure was significantly (p=0.05) higher than before drug administration [18.9 (7.3) cm H2O vs 21.5 (7.4) cm H2O, Fig. 2C].

Fig. 1 Determination of transmural oesophageal variceal pressure. Upper curve: pressure recording via sclerotherapy needle (↓ needle punctures varix, ↑ needle is withdrawn from varix). Lower curve: continuous simultaneous recording of oesophageal luminal pressure via a second tube. 1) indicates 10 cm H2O, 2) indicates 10 seconds.

Fig. 2 Transmural variceal pressure before and after bolus administration of somatostatin (A) or saline (B) in individual patients.
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Fig. 3  **Transmural variceal pressure before administration of somatostatin (A) or saline (B) and during infusion of somatostatin (A) or saline (B) in individual patients.**

before drug administration, 21·7 (8·1) cm H₂O during infusion, Fig. 3A]. In contrast, pressures were not significantly influenced by saline infusion [27·0 (9·3) v 26·3 (9·1) cm H₂O, Fig. 3B].

The mean increase in pressure after somatostatin infusion (+14·8%) was significantly (p<0·02) different from the effect after saline infusion (−2·6%, Fig. 3).

In patients who received somatostatin there was no correlation between basal pressure and the pressure change induced by the drug (r = 0·2).

Table  **Systemic haemodynamics in patients who received somatostatin or saline**

<table>
<thead>
<tr>
<th></th>
<th>Arterial blood pressure</th>
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<tr>
<td></td>
<td>Systolic (mm Hg)</td>
<td>Diastolic (mm Hg)</td>
<td>Heart rate (min⁻¹)</td>
</tr>
<tr>
<td><strong>Bolus injection</strong></td>
<td></td>
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<tr>
<td>Somatostatin before</td>
<td>121 (18)</td>
<td>84 (10)</td>
<td>90 (26)</td>
</tr>
<tr>
<td>after</td>
<td>131 (12)</td>
<td>90 (13)</td>
<td>89 (26)</td>
</tr>
<tr>
<td>Saline before</td>
<td>120 (25)</td>
<td>76 (20)</td>
<td>100 (19)</td>
</tr>
<tr>
<td>after</td>
<td>124 (23)</td>
<td>78 (19)</td>
<td>94 (15)</td>
</tr>
<tr>
<td><strong>Infusion</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Somatostatin before</td>
<td>129 (20)</td>
<td>81 (17)</td>
<td>90 (22)</td>
</tr>
<tr>
<td>during</td>
<td>117 (19)</td>
<td>80 (16)</td>
<td>99 (19)</td>
</tr>
<tr>
<td>Saline before</td>
<td>133 (30)</td>
<td>71 (22)</td>
<td>97 (18)</td>
</tr>
<tr>
<td>during</td>
<td>131 (21)</td>
<td>78 (19)</td>
<td>92 (14)</td>
</tr>
</tbody>
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Blood pressure and heart rate were not significantly influenced by somatostatin (Table).

**Discussion**

The results of this study indicate that somatostatin 14 does not reduce transmural oesophageal variceal pressure at a commonly used dose to treat variceal bleeding. There was no change in pressure recorded 2·5–6·0 minutes after a somatostatin bolus injection and during somatostatin infusion the pressure was even slightly increased.

It has been assumed that the reduction of splanchnic blood flow caused by somatostatin leads to a reduction of raised portal venous pressure with a subsequent reduction of variceal pressure. Sonnenberg et al., however, did not find a decrease of portal venous pressure during a somatostatin infusion in patients with liver cirrhosis.

Bosch et al. have found that somatostatin decreases aygos venous blood flow. In the light of the present study these findings could be explained by postvariceal venous vasoconstriction and/or raised cardiopulmonary pressures. An increased variceal outflow resistance, could lead both to a decreased aygos flow and to increased variceal pressures, as found in the present study. To date, however, it is not known whether somatostatin influences the venous tone.

As other authors have reported a decrease in variceal pressure after application of somatostatin or its long acting analogue, it may be argued that our finding of an increased variceal pressure during somatostatin infusion was caused by introduction of the endoscope or by premedication. Variceal pressures remained unchanged, however, in the patients who received placebo under otherwise identical conditions. Such controls have not been described in the previous studies. In a pilot study (Kleber et al., unpublished observations) we found no evidence that n-butyl-scopolamin increases variceal pressure. Thus, the slight increase in variceal pressure observed after administration of somatostatin but not placebo cannot be explained by an effect of the premedication. Moreover, in the present study continuous recording of oesophageal luminal pressure was carried out simultaneously. Thus, transmural pressure gradients were recorded during the whole procedure of measurement (30–180 seconds) and influences of oesophageal luminal pressure changes caused by peristalsis or gas insufflation could be eliminated.

In summary, our results show that potential beneficial effects of somatostatin 14 in variceal haemostasis cannot be explained by pressure reduction in the varices.
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References


