Intravascular oesophageal variceal pressure (IOVP) assessed by endoscopic fine needle puncture under basal conditions, Valsalva’s manoeuvre and after glyceryltrinitrate application

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SUMMARY A simple and safe procedure providing sensitive and reproducible direct measurement of intravascular oesophageal variceal pressure (IOVP) during routine oesophagoscopy is described. The method requires only commercially available equipment. First results were obtained in 16 patients with oesophageal varices caused by liver cirrhosis (Child’s A) can be summarised as follows: (1) intravascular oesophageal variceal pressure was nearly identical in different varices of the single patient. (2) Varices grade III exhibited a significantly higher intravascular oesophageal variceal pressure than varices grade II (22±2.5 vs 15.7±0.6 mmHg, p<0.05). (3) After Valsalva’s manoeuvre there was a remarkable increase in intravascular variceal pressure by 13.6±1.0 mmHg irrespective of the variceal size. The high intravascular oesophageal variceal pressure values observed in grade III varices during the rise of the intraabdominal pressure may indicate an important risk factor for variceal haemorrhage. (4) Glyceryltrinitrate (1-2 mg sprayed onto the tongues of 14 patients) very effectively lowered the intravascular oesophageal variceal pressure from 22.8±2.0 to 12.0±0.4 mmHg in grade III varices, and from 16.3±0.4 to 10.0±0.4 mmHg in grade II varices (p<0.005 in both groups). We conclude that this method provides a suitable tool to study the effect of drugs with presumed influence on the oesophageal variceal pressure and that the impressive effect of glyceryltrinitrate in lowering intravascular oesophageal variceal pressure warrants further study on the effect of longer acting nitrates on intravascular oesophageal variceal pressure, and the rebleeding rate after oesophageal variceal haemorrhage.

Endoscopic sclerotherapy is accepted as an effective therapeutic procedure in acute oesophageal variceal bleeding.1-3 The possible complications of sclerotherapy such as disturbed oesophageal motility and the risk of stenosis,4-6 however, limit the prophylactic use of the procedure despite good long-term results.2-4

B-receptor blocking drugs have been recently described as effective in lowering the rebleeding rate of oesophageal varices presumably by reducing the pressure in the oesophageal varices.6-8 Nevertheless this presumed effect on the variceal pressure could not be shown owing to the lack of appropriate technique. Furthermore, clinical studies failed to confirm any beneficial effect of B-blockers in portal hypertension.9 10

Glyceryltrinitrate is another drug that has been considered to reduce portal pressure because of its dilatating effect on blood vessels. Some recent studies, however, yielded conflicting results concerning the effect of GTN on the variceal pressure,1-14 again mainly because of the lack of a method providing exact determination of the variceal pressure.

We, therefore, developed a simple and safe technique for direct assessment of the intravascular oesophageal variceal pressure during routine oesophagoscopy. The following report describes
the procedure and discusses its possible clinical relevance. Using this technique, we were able to show that glyceryl trinitrate significantly lowers the intravascular oesophageal variceal pressure.

Methods

Patients

Sixteen patients (11 men, five women, mean age 54±3-0 years) with oesophageal varices caused by histologically proven cirrhosis classified as Child’s A were included. All patients had recently bled from oesophageal varices, but not during the last three days before examination. Systolic arterial blood pressure exceeded 100 mmHg in all patients. Four patients were on treatment with spironolactone (50 mg/day).

Informed written consent was obtained from all patients. They underwent oesophagoscopy after intravenous application of 10 mg diazepam using a flexible endoscope (Olympus GIF-Q). The size of the variceal columns was subjectively graded by an experienced endoscopist according to the classification described by Paquet.3 Grade II (n=6) was applied for prominent, spontaneously visible varices, and grade III (n=10) for large variceal columns.

Manometric examination

For assessment of the intravascular oesophageal variceal pressure a commercially available sclerosing probe with a thin distal needle (diameter 0-71 mm, Olympus, Tokyo, Japan) was passed through the channel of the endoscope and the variceal columns were punctured 10 cm proximal to the cardia. The capillary lumen of the probe was perfused by the hydraulic perfusion pump according to Arndorfer15 with a constant perfusion volume of 0-2 ml sterile saline (0-9%) per minute. The perfused probe was attached to a Statham element (Beckman R 427 G). Pressure values were recorded using a Beckman R 511 A writer (Beckman, River Road, Ill., USA) on a paper running 1 mm/sec.

Each examination started with the registration of the oesophageal pressure at rest by positioning the needle free in the oesophageal lumen. Then the varices were punctured and the intravascular pressure was recorded. After removal of the needle from the variceal lumen the tip of the endoscope was routinely positioned into the stomach for three minutes providing a slight compression of the site of the puncture. Intravascular oesophageal variceal pressure was calculated taking the pressure in the oesophageal lumen as zero reference (Fig. 1). Values are expressed as X±SEM. For statistical analysis the exact Wilcoxon-Mann-Whitney test was used.

Protocol of the study

1 In 14 out of the 16 patients three different variceal columns were punctured. The intravascular oesophageal variceal pressure values obtained were compared for evaluating the intraindividual pressure variation in different varices. (2) In these 14 patients the effect of the intra-abdominal pressure rise on the intravascular oesophageal variceal pressure was examined, too. For this purpose oesophageal pressure (zero reference) and intravascular oesophageal pressure was examined before and during Valsalva’s manoeuvre. (3) In all 16 patients the effect of glyceryl trinitrate on the intravascular oesophageal variceal pressure was studied. After recording the intravascular oesophageal variceal pressure 1-2 mg glyceryl trinitrate (Nitro-Lingualspray, Pohl-Boskamp, Hohenlockstedt, W-Germany) was sprayed to the tongues of the patients. Three minutes later intravascular oesophageal variceal pressure was measured again.

Results

In all patients the original tracing consisted of a small spike obtained during the fine needle penetration of the variceal wall followed by a plateau reflecting the intravascular oesophageal variceal pressure and another spike due to retraction of the needle. A paravasal position of the needle was immediately visible by a sharp increase in pressure recorded due to the minimal compliant capillary perfusion system used. In this way the
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correct position of the needle could be indentified without any difficulties.

In some patients the same variceal column was punctured at different distances between 1 and 12 cm from the cardia. There were no differences in the pressure values obtained. Therefore we chose to carry out the puncture at 10 cm above the cardia in all the patients.

In the oesophageal lumen as well as in the variceal lumen respiratory pressure alterations amounting to approximately 4 mmHg (Fig. 1) were recorded. The pressure obtained intraindividually in each of the three different varices were nearly identical varying between 19-0±2-0 and 19-7±2-1 mmHg (Fig. 2). Individual pressure values ranged from 12-28 and even 44 mmHg in one single patient (Fig. 3). The basal intravascular oesophageal variceal pressure (Fig. 4) in varices grade II amounted to 15-7±0-64 mmHg and in varices grade III to 22-7±2-45 mmHg (p<0.05).

After Valsalva's manoeuvre there was a significant increase (p<0.001) in intravascular oesophageal variceal pressure which was nearly identical in both groups (13-6±0-8 and 13-5±1-4 mmHg respectively, Fig 4). Thus during Valsalva's manoeuvre, too, varices grade III exhibited a significantly higher pressure than varices grade II (37-3±1-4 vs 31-0±1-5 mmHg, p<0.05).

The application of glyceryltrinitrate (Fig. 5) reduced the intravascular oesophageal variceal pressure from (20.4±2.0 to 11.1±0.9 mmHg, p<0.005) irrespective of the initial variceal diameter (10.0±0.4 vs 16.3±0.4 mmHg in grade II

Fig. 2 Intravascular oesophageal variceal pressure obtained in each of three variceal columns (varix '1', '2', '3') of one single patient. Values obtained in one patient are connected.

Fig. 3 Intravascular oesophageal variceal pressure elevation caused by Valsalva's manoeuvre. The resting pressure (RP) and the pressure during Valsalva manoeuvre (VP) obtained in each patient is connected.

Fig. 4 Intravascular oesophageal variceal pressure in varices grade II and III under basal conditions (15-7±0-6/22-7±2-4 mmHg), Valsalva's manoeuvre (31-0±1-5/37-3±1-4 mmHg). The relative pressure elevation (∆IOPV) shows no difference (13-6±0-8/13-5±1-5 mmHg).
and 12.0±0.4 vs 22.8±2.0 mmHg in grade III varices).

Though at least three variceal punctures were undertaken on each patient only minute amounts of blood were delivered from the site of the puncture. Although only two patients underwent sclerosing therapy after intravascular pressure recording neither further haemorrhage nor other complications due to the diagnostic puncture occurred in any of the patients.

**Discussion**

The described procedure for direct determination of the intravascular oesophageal variceal pressure proved to be a safe and simple method. The fact that the pressure within any visible varix of one patient reliably reflects the individual intravascular oesophageal variceal pressure allows the procedure to be performed in a short period of time. Thus the discomfort for the patient hardly exceeds that of a routine oesophagoscopy. The strength of the procedure lies in the fact that it can be easily undertaken by any investigator familiar with the endoscopic techniques and that the technical equipment required is easily available and presumably already present in most community hospitals.

Other methods for indirect estimation of the variceal pressure such as measurement of the wedged hepatic and the portal pressure are risky for the patient and presumably not sufficient for exact determination of the variceal pressure itself.16–19 The indirect endoscopic manometry of oesophageal varices using a pneumatic pressure sensor fixed at the tip of a special endoscope20 21 recently aided by the inflation of a balloon proximal to the pressure sensor22 requires expensive, not commercially available equipment, and the results of this method may depend on the compliance of the variceal wall tissue. A further endoscopic procedure reported by McCormack23 permits detection of the blood flow in the varices, but does not obtain intravascular pressure. In contrast, our data outline the sensitivity, reproducibility and last but not least the safety of the procedure described in the paper. Furthermore, the data obtained by this procedure are apparently of clinical relevance. The finding that following intra-abdominal pressure rise (Valsalva's manoeuvre) in patients with large varices the mean pressure in the variceal lumen rises by approximately 70% and reaches the remarkable height of nearly 40 mmHg draws attention to the possible role of intra-abdominal pressure rise (ascites, coughing, defaecation) as major risk factor for acute oesophageal haemorrhage. In large varices intravascular oesophageal variceal pressure was significantly higher than in medium size varices. This was true for the basal values as well as for Valsalva's conditions. This finding corresponds with clinical experience reported by Paquet,3 Rose,4 and other authors19 20 indicating an increased risk of variceal...
haemorrhage in large oesophageal varices. If intravascular pressure in oesophageal varices is the leading factor in the cause of possible haemorrhage, our finding that individual pressure values are nearly identical in all varices of a given patient outlines the need to treat all visible varices when undertaking endoscopic sclerotherapy, and not only the one that has actually bled.

The measurement of intravascular oesophageal variceal pressure also provides a most reliable tool for examining the effect of drugs on the variceal pressure. In this study glyceryltrinitrate was shown to lower the intravascular oesophageal variceal pressure to approximately 50% of baseline values. In contrast, earlier studies dealing with the effect of glyceryltrinitrate on portal hypertension yielded conflicting results which might at least in part be explained by the different methods used. Because of the short half life time of approximately five minutes in plasma the reported effects of glyceryltrinitrate are transient and therapeutic applicability certainly depends on maintenance of appropriate drug levels. We, therefore, used intravenous infusion of glyceryltrinitrate (5 mg/h) in two patients and were able to control their severe bleeding from varices just below the cardia in the presence of oesophageal varices grade III and pronounced gastric varices, after the application of a Linton-Nachlas tube was not effective. In these patients intravascular oesophageal variceal pressure dropped from 24 and 22 mmHg to 4 and 8 mmHg respectively under intravenous glyceryltrinitrate treatment.

These preliminary results warrant further studies including a greater number of patients to define the exact role of glyceryltrinitrate in the treatment of acute variceal haemorrhage. Furthermore, the impressive effect of glyceryltrinitrate by lowering intravascular oesophageal variceal pressure as shown in our study should induce evaluation of the possible effect of longer acting nitrates on intravascular oesophageal variceal pressure and on the recurrence rate of variceal haemorrhage.

References


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