Portal Hypertension and Systemic Hypotension. Assessment by 24-Hour Blood Pressure Monitoring in Cirrhosis

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Cirrhotic patients have disturbed systemic haemodynamics with reduced systemic vascular resistance and arterial blood pressure. However, arterial blood pressure has never been investigated in cirrhosis during daily activity and sleep.

Systolic (SP), diastolic (DP), and mean arterial blood pressure (MAP), and heart rate (HR) were measured by an automatic ambulant device for monitoring blood pressure in 35 patients with cirrhosis, and in 35 healthy matched controls.

During daytime (7:00 am to 22:00 pm), measurements were performed at the intervals of 15 min and during night time at intervals of 30 min. The average number of measurements were 126 in each patient and 84 in each control subject. During daytime SP, DP, and MAP were significantly lower compared with controls (median 118 vs 72; 70 vs 68; 86 vs 94 mmHg respectively, p < 0.005). During the night time, SP, DP and MAP were almost similar in the two groups (106 vs 110; 65 vs 67; 78 vs 82 mmHg respectively, NS). In contrast, HR was significantly higher in the patients during day time (86 vs 72 min⁻¹, p < 0.0001) as well as during night time (80 vs 64 min⁻¹, p < 0.0001). In both patients and controls, SP, DP MAP and HR were lower during night time (p < 0.0001), but the decrease was significantly lower in the patients: SP (7 vs 17 mm Hg, p < 0.0001), DP (7 vs 11 mm Hg, p < 0.01), MAP (7 vs 12 mm Hg, p < 0.005), and HR (6 vs 11 min⁻¹, p < 0.002). SP, DP and MAP were lower in patients with advanced disease (Child C patients) in 18 compared to those with less severe hepatic dysfunction (Child A and B patients) during day time as well as night time (p < 0.1). Furthermore, the systolic blood pressure correlated significantly with Child score (r = −0.47, p < 0.01), serum albumin (r = 0.41, p < 0.05), serum bilirubin (r = −0.43, p < 0.05), and prothrombin time (r = 0.50, p < 0.005). Heart rate correlated significantly with serum sodium (r = −0.36, p < 0.05).

In conclusion, our results show that cirrhotic patients have lower systemic blood pressure and higher HR during day time compared with controls but a diminished reduction in blood pressure during night time. This indicates a major defect in the regulation of blood pressure in cirrhotic patients.

A Randomised Control Trial Comparing the Effect of Somatostatin-14 and Octreotide on Intrahepatic Oesophageal Varical Pressure (IOVP) in Liver Cirrhosis

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Somatostatin (SMS)-14 and its synthetic long acting analogue octreotide have been used during the last years in the treatment of acute oesophageal variceal haemorrhage. It has been reported the effects of these two peptides on portal venous and intravascular pressure have been variable. The aim of the study was to examine the effect of intravenous bolus injection of somatostatin-14 and octreotide on intravesophageal variceal pressure (IOVP) in 31 cirrhotic patients (post hepatic:13, alcoholic:16, cryptogenic:1, PBC:1) with oesophageal varices (small 1, medium:14, large:16) without previous history of oesophageal variceal haemorrhage or prophylactic treatment for bleeding.

After premedication with midazolam, IOVP was carried out during oesophageography with a 25 G needle connected to a pressure transducer. The transducer was attached to an amplifier and the pressure values were recorded on a computerised system (Gastrosoft, Synectics inc, Sweden). When the oesophageal luminal pressure was measured the vain was punctured 5-7 cm above the gastrooesophageal junction and the IOVP was recorded. Subsequently a bolus injection of 250 μg somatostatin-14 (11 patients) or 100 μg octreotide (10 patients) was given within 15 sec. On ten occasions 2 ml 0.9% NaCl were administered as placebo. Continuous recording of IOVP was achieved for an mean period of 5.2 min (range 3.8-9 min) after the drug administration. IOVP was calculated as the difference between intravesophageal and oesophageal luminal pressures. A small dose of 5% ethanamine oleate (if required) was given at the end of the procedure.

Results: For the SMS-14 group the IOVP before somatostatin infusion ranged from 16 to 40 mmHg (mean 24.18 ± 7.54 sd) and the administration of the drug was followed by a significant reduction of the pressure (mean 20.45 ± 3.35, p < 0.05). In contrast the obtained values of IOVP before and after the administration of the octreotide or the saline were not significantly different (octreotide group: from 23.9 ± 6.87 to 22.6 ± 3.32 mmHg, placebo group: from 22.1 ± 3.2 to 21.4 ± 3.16 mmHg).

Conclusion: Our findings indicate that bolus SMS-14 but not octreotide infusion reduces the IOVP in cirrhotics.

Surgical Procedures in Bleeding Esophagogastric Varices When Sclerotherapy Fails – A Strategy and Prospective Study

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In a 10-year period (Jan. 1, 1982–Jan. 1, 1992) 692 patients were admitted to the HEINZ-KALK-Hospital with bleeding esophageal varices. All patients were first treated with endoscopic sclerotherapy. 14 patients exsanguinated during the first 2 hours of admission or refused treatment. In 313 CHILD-PUGH C-patients longterm injection sclerotherapy was performed; 26 of them needed an emergency disconnection because of uncontrollable or early recurrent hemorrhage, and five an emergency narrow lumen mesocaval interposition shunt (NLMS). In the remaining 367 patients (182 CHILD-PUGH A and 185 B) endoscopic sclerotherapy (ES) was successful in 194. In 173 patients, with at least two rebleedings despite longterm sclerotherapy, specific selection criteria were used to assess suitability for shunt operation. This group was analysed prospectively. 85 patients refused shunt operation or did not fulfill selection criteria; in this group ES was continued. 88 patients were shunted: 54 NLMS, 32 distal splenorenal shunts (DSRS), 1 portacaval, and 1 proximal splenorenal LINTON-shunt were performed. The continued sclerotherapy and shunt groups were comparable concerning number, demographic characteristic, etiology, severity and history of liver cirrhosis. There was no significant difference of mortality at 30 days (5 vs 7%). Both groups were followed up to 1st of January 1993. Survival probability in the ES-group was 78% and in the shunt group 73%; this difference is statistically significant in favour of shunt operation (p < 0.01). Thus shunt procedures, performed in CHILD-PUGH A and B-patients who fail sclerotherapy and using specific selection criteria, are today the best treatment for bleeding esophageal varices resistant to longterm endoscopic sclerotherapy. Furthermore NLMS is a good alternative to DSRS if this is technically impossible or haemodynamically not advisable.

Prospective, Randomized, Double-Blind Trial Comparing the Endoscopic Injection of Ethanolamine vs Polidocanol in the Treatment of Bleeding Peptic Ulcer

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Endoscopic injection of sclerosant and/or vasoactive substances is considered an useful therapeutic approach of bleeding peptic ulcer. However, the relative value of most sclerobants is largely unknown. The aim of this study was to compare the efficacy of two different schedules of endoscopic sclerotherapy, namely epinephrine plus 5% ethanolamine olate (EE) vs epinephrine plus 2% polidocanol (EP), in the treatment of peptic ulcer, either actively bleeding (AB) or with stigmata of recent haemorrhage (SRH). Between April 91 and November-93, emergency endoscopy was performed in 1,183 patients with upper gastrointestinal bleeding. 241 patients (151 males, 90 females; mean age 64.1 ± 17.05) presented with either AB or with SRH. Peptic ulcers were stratified according to the bleeding pattern, AB (98 cases) or visible vessel/centinel clot (143 cases) and prospectively assigned to receive either EE or EP in a randomized, double-blind fashion. Data were analyzed according to intention to treat.

The hemostatic efficacy in the whole series, as defined by the ability to arrest actively bleeding lesions and/or to prevent rebleeding during hospitalization, was obtained in 76.5%, whereas the need of surgery and mortality were 16.6% and 14.8% respectively. Endoscopic sclerosis could not be done in 40 patients because of different reasons. There were no significant differences between EE and EP groups with respect to the common clinical and biological variables. EP performed significantly better than EE in hemostatic efficacy (p = 0.023), rebleeding rate (p = 0.039), transfusional requirements (p = 0.032) and mortality (p = 0.0038) in the AB group but not in patients presenting with SRH. The hemostatic efficacy of EP was higher than that of EE (odds ratio = 3.26; conf interval = 1.25-8.61).

The endoscopic injection of epinephrine+2% polidocanol compares favourably with respect to epinephrine+5% ethanolamine in arresting actively bleeding peptic ulcers.

Sclerotherapy versus Sclerotherapy and Propranolol in the Prevention of Rebleeding from Oesophageal Varices: A Randomized Study

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This trial was carried out to assess the value of propranolol for the prevention of recurrent variceal bleeding when combined with long-term endoscopic sclerotherapy.
Two-hundred patients (161 male, 39 female, age range 20–68 years) with portal hypertension mainly due to schistosomal periperipheral fibrosis and portal hypertensive cirrhosis presented with the first attack of haematemesis and/or melena which was endoscopically proven to be due to ruptured oesophageal varices were included.

After initial control of bleeding, patients were randomized into 2 groups: group 1 treated with endoscopic sclerotherapy alone and group 2 treated with sclerotherapy plus propranolol. They were followed for 2 years, group 2 had less rebleeding (14.3% vs 38.6% in group 1), lower variceal obliteration after obliteration (17% Vs 34% in group 1), longer period between variceal obliteration and recurrence (36 weeks Vs 21 weeks in group 1); but no change in mortality (12% in both groups).

Propranolol was well tolerated when given in a dose that reduces the resting pulse by about 25%. The mean initial daily dose was 90 mg and the mean maintenance dose 30 mg.

We concluded that patients treated with sclerotherapy should be given propranolol for the long-term management.

113 Courses and Predictors for Rebleeding in Patients with Peptic Ulcers and Nonbleeding Visible Vessels, A Prospective Observation

Detailed characterization of nonbleeding visible vessels (NBV) in terms of color, size evolution and time of rebleeding is important to the natural history of these lesions. Between March 1991 and September 1992, we prospectively observed 147 patients with 152 NBV in the ulcer bases. The color and size (measured with an endoscopic meter, Olympus M2-4K) of NBV were observed endoscopically every day for 3 days and then every other day until rebleeding or flattening of visible vessels occurred. Rebleeding happened in 63 (42.9%) patients. Of them, 61 (96.8%) rebled within 72 hours. Flattening of vV occurred in 84 (57.1%) patients. Of them, 82 (97.6%) had flattening of vV within 72 hours. Rebleeding rate increased with increasing vessel size (1 mm: 24/73, 2 mm: 15/35, 3 mm: 15/28, 4 mm: 6/10, 5 mm: 2/3, 6 mm: 2/2, 7 mm: 1/1, r = 0.97, p < 0.001). The rebleeding rate was highest in the white color vV (15/28, 53.6%) followed by red color (29/63, 46%), pink color (2/5, 40%), black color (13/33, 39%), dark red color (6/20, 30%), brown color (0/2), and gray color (8/1, 9%) (p < 0.05). The color evolutions of the vV were multifarious. With multivariate analysis, coffee ground fluid or blood retention in the stomach, and ulcer size 2.0 cm were independent predictors for rebleeding.

Conclusions: The majority of rebleeding or flattening of NBV occurred within 72 hours. Patients with NBV and independent predictors for rebleeding may need early aggressive management.

114 Small Bowel Angiodysplasia: A Possible Cause of Gastrointestinal Bleeding of Obscure Origin
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Gastrointestinal (GI) bleeding of obscure origin is still a problematic entity and some type enteroscopy has been advocated as the most suitable diagnostic method. The procedure, however, is time consuming and its effectiveness is limited by the lack of tip deflection and therapeutic channel. Aim of the study was to evaluate the diagnostic yield of push type enteroscopy which unlike some type method is quick and has interventional capability. Patients and Methods: Push type enteroscopy was performed using either an Olympus GIF 10 LY fiberscope or a GIF 100 videocenteroscope in 22 patients with GI bleeding of obscure origin (negative oesophagogastroduodenoscopy and total colonoscopy, normal coagulation parameters) with onset as melena (n = 15) or repeated finding of occult blood (n = 7). Results: The depth of insertion beyond the ligament of Treitz was 30–120 cm (median 70). The mean duration of the procedure was 15–20 minutes. The source of bleeding was identified in 10/22 (45%) patients all with angiodysplasia located in the jejunum (7 cases), in the third portion of the duodenum (1 case) and in both sites (2 cases). Angiodysplasias were diffuse in 7 cases and isolated in 3 cases. One of the isolated jejunal lesions, that was bleeding when discovered, was successfully electrocauterized. The remaining patients had medical treatment (estrogen/progestrone, octreotide). Conclusions: Angiodysplasias were identified as the cause of bleeding in 45% of our patients. This percentage is similar to that reported for the sonde type method, that does not consent the exploitation of the entire ileum. It can thus be surmised that it is not necessary to explore the entire small bowel to diagnose the cause of GI bleeding of obscure origin, and that identification of a single lesion is often enough for diagnostic purposes. Push type enteroscopy is useful as a first step towards diagnosis when total colonoscopy and oesophagogastroduodenoscopy are negative, followed by small bowel contrast enema, arteriography, sonde-type enteroscopy and intraoperative endoscopy in the event of failure.

115 Upper Gastrointestinal Bleeders Show Abnormal Bleeding Time Response to Aspirin Use
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Gastrointestinal bleeding is associated with NSAID use, especially ASA, in over 80% of cases (Gastro 1992; 103: 862), but the mechanisms of this association are poorly understood. To look for a possible mechanism whereby ASA might promote GI bleeding, 55 patients (58.8 ± 13.5; 79% males) with previous ASA-related-upper gastrointestinal (UGI) bleeding and 32 controls (45.1 ± 15; 60% males) with no history of bleeding were given 300 mg of ASA. In each person sequential ivy skin bleeding time (BT) and ASA and its metabolites in blood determined by HPLC were measured. Platelet aggregation, von Willebrand factor, VIII Ag, PT, PTT, and coagulation studies were also performed. Previous ASA/NSAIDs use was ruled out by measuring either platelet cyclooxygenase activity or platelet aggregation. Results: The mean (± SD) baseline BT was 2.85 ± 1.4 min in controls vs 2.8 ± 1.2 min in bleeders. In both groups ASA increased significantly BT to 2 and 4 hours after ASA use with the peak being at 2 h, and remaining constant until 6 h. As a group patients with ASA-related-UGI bleeding had a more prolonged BT than controls (Δ 2.5 ± 1.4 vs 1.8 ± 1.4 at 2 h; p < 0.001). A greater proportion of hyperresponders, defined as Δ BT > 3 mm of 2SD of controls (Δ > 4 mm), were found in bleeders (25% Vs 12%) than in controls (3.8%, 1/26; p < 0.05) and bleeders older than 60 (3.5%, 1/28; p < 0.01). BT in hyperresponders with a history of UGI bleeding related to occasional ASA use was higher than those with chronic use (Δ 7.8 ± 2.4 vs 4.8 ± 0.6; p < 0.01). Also peaks of ASA and salicylic acid in blood were different (p < 0.05) in hyperresponders than non-hyperresponder (ASA 1.2 ± 1 vs 0.5 ± 0.4 µg/ml; Salc. acid = 7.1 ± 3.9 vs 10 ± 4.1). No specific intraplatelet defects or any other abnormalities were found in any group. Conclusions: (1) A significant proportion of patients with history of ASA-related UGI bleeding presents an exaggerated bleeding time response to ASA use. (2) This defect is not due to intrinsic and specific platelet defects and might be related to age and a different ASA metabolism.

116 Efficiency of Endoscopic Injection and Laser Techniques in Peptic Ulcer Hemorrhage - Results in a Series of 795 Patients
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Introduction: Acute ulcer bleeding is also today a life threatening complica- tion of chronic ulcer disease. Every acute upper gastrointestinal bleeding has to be examined endoscopically at once. With endoscopy it is possible to de- termine the bleeding localisation and – if possible – the causes. Usually one succeeds with the today possibilities of endoscopic hemostasis in the initial and definitive treatment of the bleeding source.

Methods: Between 07/91 and 08/93 in 795 out of 10.143 gastroduodenos-copies in 791 patients (female 40.4%, male 59.6%, 19–92 years, mean 49 years) an emergency endoscopy was performed. In 511 endoscopies (455 patients, 64.3%) the cause was a bleeding ulcer (99.3%). Four patients (0.6%) had an emergency operation because an endoscopic hemostasis was not possible. In 511 endoscopies (455 patients, 64.3%) the cause was a bleeding of a gastric ulcer, in 284 (256 patients, 35.7%) of a duodenal ulcer. The intensity of bleeding at the beginning of endoscopy was as follows: 335 with pulsatile bleeding vessel (42.2%), 249 with active oozing bleeding (31.3%) and 211 with non active bleeding or with blood clot on the ulcer (28.5%). Endoscopic hemostasis was performed by laser or injection therapy (fibrin glue).

Results: In 580 out of 584 patients with an active bleeding an initial hemostasis was possible with endoscopy (99.3%). Four patients (0.6%) had an emergency operation because an endoscopic hemostasis was not possible. Further 20 patients (2.8%) had a recurrent bleeding. Surgical ther- apy was performed in 10 cases as ulcer excision or ligation of the bleed- ing vessel, in 14 cases as resective methods. From the 687 patients who were treated only endoscopically, 2 (0.3%) died in the follow-up of recurrent bleeding. In both cases there were advanced cancers so that we renunci- ated of aggressive therapeutic procedures. Of the surgical treated patients (n = 24) 6 died (25.0%) in the early postoperative follow-up. A definite endo- scopic hemostasis in active bleeding was possible in 560 out of 584 patients (96.9%).

Conclusions: The therapy of acute ulcer bleeding can be performed in nearly all cases by an aggressive endoscopic management initially (99.3%) and definitively (95.1%). Only a low percentage of the patients need in acute ulcer bleeding a surgical intervention. The prognosis of those patients de- pends mainly on the severity of accompanying illness.