# Portal hypertension

## OIII/1 1011

SEASONAL VARIATIONS IN ADMISSION FOR ACUTE VARICEAL HAEMORRHAGE AND RESPIRATORY TRACT INFECTION SUGGEST COUGHING MAY PRECIPITATE VARICEAL HAEMORRHAGE. +R Sutton, *EMI Williams, ++G Pellegrini, +S Tedman, +SA Jenkins, +R Shields
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Intravariceal pressure increases after a Valsalva manoeuvre, an effect that may also occur after coughing. To determine whether coughing may precipitate acute variceal haemorrhage, we have compared the seasonal variation in emergency admissions for bleeding oesophageal varices with that for respiratory tract infection.

Monthly figures for emergency admissions relating to acute variceal haemorrhage, all other acute gastrointestinal haemorrhages (ICD 578), all respiratory tract infections (ICD 465.9, 481-488, 519.8, 519.9) and all other emergency admissions were compiled for the Royal Liverpool University Hospital from 1982 to 1991 inclusive. Data relating to varices admissions were obtained from a prospective varices database compiled between 1980 and 1992, whereas all other data were obtained from the Regional Information Unit. Admissions for winter quarters (Oct-Mar) were compared to those for summer quarters (Apr-Sep).

Total admissions for all emergencies (winter vs summer: 78,253 vs 76,321) and all non-variceal-haemorrhage (687 vs 640) showed no significant seasonality, whereas admissions for acute variceal haemorrhage (118 vs 79; Chi square 6.4, 1 df, $p<0.02$) and respiratory tract infection (2,341 vs 1,630: Chi square 112.7, 1 df, $p<0.001$) showed similar predominance in winter months.

These results demonstrate a similar seasonality to admissions for acute variceal haemorrhage and respiratory tract infection, and implicate coughing as a factor that may precipitate acute variceal haemorrhage.

## OIII/3 1030

**TRANSJUGULAR INTRAHEPATIC PORTOSYSTEMIC SHUNTS (TIPS) BY USING THE STRECKER STENT IN THE TREATMENT FOR VARICEAL BLEEDING.**
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TIPS is an new developing technique with potential broad applications in the management of gastroesophageal varices (GEV) hemorrhage. The present study was aimed to asses the safety, efficacy and applicability of this procedure.
Thirty-two patients had an indication to place a TIPS but it was possible only in 29 (90.6%) of them; 8 (27.6%) had acute variceal bleeding refractary to endoscopic and pharmacologic management; the other 21 patients (72.4%) had frequent rebleeding (mean episodes 3±1.7) not controled by endoscopic sclerotherapy (12) or pharmacologic treatment (9); the shunt was performed during the first week after a 24-hours period free from hemorrhage. All patients had advanced cirrhosis (Child A=4, B=19, C=6). TIPS was created by a Strecker metallic endoprothesis dilated to a diameter of 11 mm. During the follow-up period we performed laboratory tests, upper-endoscopy, serial angiography and Doppler-ultrasounds at 1, 3, 6 and 12 months after the procedure. Shunt disfunction (SD) was defined when there was more than 50% reduction of the shunt lumen diameter, assesed by angiography during the follow-up, comparing the original stent diameter.
**RESULTS:** The portosystemic pressure gradient (PSPG) significantly decreased (22.4±5.7 vs 8.9±5.3; $p<0.0001$) after the procedure, with a mean reduction percentage of 62.2%. Four patients (13.8%) rebleeded during follow-up; the hemorrhage appeared at 3.75±1.55 (range 2.5-6) months after the technique. The percentage of patients free of hemorrhage reached 80% at 6 months. There were two deaths in the follow-up; one of them due to hepatic failure, during the first month and the second one from uncontrolable GEV bleeding. SD was found in 8 patients (27.6%); 4 of them showed GEV rebleeding in spite of angiographic and sonographic controls. Stenosis of hepatic vein was seen in 5 patients, non-thrombotic stent obstruction in 2, and shunt oclussion caused by neointimal proliferation in the last one. Angioplasty was needed in 4 from 8 (50%) who presented SD and the rest also needed a new prothesis. The cumulative percentage (Kaplan-Meier plot) of SD was 0.23 at 6 months. Eight patients between 12 whose stent ended at medial hepatic vein (66%) presented SD, although we did not find any SD when the vein was the right one (17 patients) $p<0.01$. Hepatic encephalopathy (HE) was analized in 20 patients; 3 patients developed "de novo" HE (15%), whose control was easy, except for one patient.
**CONCLUSIONS:** TIPS seems to be efficacious for controling gastroesophageal varices bleeding. SD is a frequent finding and has some anatomical related factors, so a close follow-up is needed. HE after the procedure develops in a minority of patients and is generally mild and manageable.

## OIII/2 966

NADOLOL DOES NOT IMPROVE THE RESULTS OF SCLEROTHERAPY IN PREVENTION OF VARICEAL REBLEEDING. C.Villanueva, J.Balanzó, F.J.Martinez, D.González, H.Toro, F.Vilardell. Department of Gastroenterology. Hospital Sant Pau. Barcelona. Spain.
Endoscopic variceal sclerotherapy (EVS) is a useful treatment in the secondary prevention of bleeding. However there is a high risk of rebleeding with EVS. The aim of this study was to assess whether nadolol could improve the results of EVS.
METHODS: During a two year period, 40 patients with their first hemorrhage from esophageal varices were randomized after the control of bleeding with emergency EVS, to receive long-term EVS either alone (n= 18) or plus nadolol (n= 22). Admission criteria to the trial were: age between 18 and 75 years, liver cirrhosis, Pugh's class A or B and the absence of hepatocarcinoma, portal thrombosis, severe associated diseases or contraindication for betablockers. EVS was performed by intravariceal injection of 5% etanolamine at days 0, 4, 10, 30 and then monthly until eradication of varices. Nadolol was administered during the whole follow-up in a dose to reduce resting pulse rate by 25% (mean final dose: 79+34 mg/d).
RESULTS: Both groups were well-matched for clinical and biological data. Follow-up was similar in both (10+7 months in EVS group vs 13+6 in EVS plus nadolol). There were no differences between the two groups when considering rebleeding (39% in EVS alone vs 55%), major rebleeding (27% vs 24%), transfusional requirements (mean by rebleeding: 4.6+3 vs 4.7+1, units), number of sessions of EVS to varical eradication (3.5+1.4 vs 3.4+1.4) or mortality (2 patients in each group).
CONCLUSIONS: In patients undergoing long-term EVS for prevention of variceal rebleeding, nadolol confers no additional benefit.

## OIII/4 216

**INTERIM REPORT OF A PROSPECTIVE RANDOMIZED CONTROLLED TRIAL OF TRANSJUGULAR INTRAHEPATIC PORTOSYSTEMIC SHUNT (TIPS) VERSUS SCLEROTHERAPY FOR PREVENTION OF RECURRENT VARICEAL HEMORRHAGE.** AJ Sanyal, AM Freedman, ML Shiffman, VA Luketic, PP Purdum, J Tisnado and P Cole. Medical College of Virginia, Richmond, Virginia, USA.
The relative efficacy and safety of TIPS vis-a-vis endoscopic sclerotherapy (EST) for prevention of recurrent variceal hemorrhage (VH) remains unknown. We report the current status of our trial of TIPS vs EST for VH. **METHODS:** Survivors of a documented esophageal variceal bleed were randmized to either TIPS (n=37) or EST (n= 31), 7 and 9 (mean) days after an acute bleed. ß blockers were stopped in all cases at entry (n=7). Patients with terminal cancer, pregnancy and portal vein thrombosis were excluded. TIPS patients received a single Schneider wall stent while EST patients underwent intravariceal EST using 12-20 cc of 5% Na morrhuate every 2-3 weeks until all varices were obliterated. All patients were followed clinically, with endoscopy and duplex sonograms at entry, day 7, month 1 and then at 3 month intervals. All TIPS patients also underwent angiography at 6 months. Liver functions (LFTs) including lidocaine metabolite formation (MEGX) were assessed every 1-2 months in all subjects. **RESULTS:** At entry, both groups were comparable. TIPS was successfully placed in 35/37 patients and mean portosystemic gradients decreased from 22 to 11 mm Hg ($p<0.0001$). The technical failures received EST. After a median follow-up of 250 days, no significant differences in rebleed rate (TIPS vs EST) (4:7) (defined by hemetemesis/melena) or deaths (5:3) were noted. Although the frequency of hospitalizations in EST patients were higher (25 vs 15), medical costs were not significantly different. TIPS complications included: capsule rupture (n=1), transient partial portal vein thrombosis (n=7), shunt thrombosis (n=3), fever (n=7), encephalopathy (n=9) and intravascular hemolysis (n=2). EST complications included: chest pain (n=8), fever (n=3), ulcers (n=6) and strictures (n=2). On endoscopy, following initial variceal disappearance (30/34), varices reappeared between 3-6 mths in 5 patients. On angiography, 13/17 TIPS patients had reappearance of varices due to shunt-stenosis which were, however, amenable to dilatation. Variceal obliteration has been achieved in 24/31 EST patients after a mean of 4 sessions. LFTs worsened in TIPS patients but were not significantly different from controls **CONCLUSIONS:** While the trial is still incomplete, these data suggest that both procedures are equally effective for VH. Both procedures are associated with their unique profile of morbidity. Varices frequently recur during long-term follow up after TIPS due to shunt-stenosis, and angiography is the only reliable method of detection.

## OIII/5 949

**ECHODOPPLER EXAMINATION OF THE PORTAL CIRCULATION AFTER TRANSJUGULAR INTRAHEPATIC PORTOSYSTEMIC SHUNT (TIPS): PRELIMINARY RESULTS.** A.De Santis, O. Riggio, M. Merli, R. Servi, T. Stati, P. Rossi and L. Capocaccia, Cattedre di II Gastroenterologia e di IV Radiologia, Università "La Sapienza", Rome, Italy.

TIPS is a radiological method for treating upper gastrointestinal (GI) bleeding in cirrhotic patients. TIPS has been shown to decrease the portosystemic gradient by about 40%. Nothing is know of the effects of TIPS on portal haemodynamics. **MATERIALS AND METHODS:** We examined 4 patients (1 male and 3 females), mean age 65.7 years (range 58-72). These underwent an urgent EGDS after an upper GI bleeding which revealed the site of bleeding in the esophageal varices. A Wallstent Stent was placed in each patient. A doppler examination was performed as soon as possible after bleeding and repeated at 48 hours and 7 days after TIPS. The maximum (VMax) and average (VMean) velocity of blood flow in the portal (PV), splenic (SV), superior mesenteric veins (SMV) and stent were measured. The longitudinal diameter of the right lobe of the liver and spleen was also measured. **RESULTS:** The stent mean diameter was 7.5 mm. The table shows Vmean in VP, SV, SMV and stent (cm/s),

| | Portal | Splenic | Sup. Mes. | Stent |
|---|---|---|---|---|
| Vmean basal | 18.1 | 26.1 | . | 85 |
| Vmean 48 h | 32.5 | 31.5 | 14.6 | 95.7 |
| Vmean 1 Week | 30.6 | 34 | 18 | 99.5 |

The VMax values, after 7 days, increased by 82.2% and 34% in the PV and SV, respectively. Simultaneously, the longitudinal diameter of the right lobe of the liver and spleen decreased 9% and 5.8%, respectively. In 3 cases, after 48 hours, a thrombosis of the left branch of the portal vein appeared. **CONCLUSIONS:** TIPS procedure causes a major increase in blood flow velocity in portal vessels. Blood mean velocity in the stent is similar to that in the arteries and Doppler spectrum profile is broad. TIPS causes a reduction in the liver and spleen diameters and a thrombosis of the intra-hepatic portal branch was observed in most cases.

## OIII/7 1012

**HYPOVOLAEMIA AND REPERFUSION IN PORTAL HYPERTENSION: EFFECTS OF SOMATOSTATIN, OCTREOTIDE AND VASOPRESSIN.** J. Yates, D.M. Nott, H. Kynaston, N. Davies, L. JinLai, D. Billington, R. Shields & S.A. Jenkins, Department of Surgery, Royal Liverpool University Hospital, Liverpool, U.K.

The majority of patients receiving vasoactive drugs to control variceal bleeding are hypovolaemic and in the process of being resuscitated during therapy. However, since there is a paucity of data on the effects of vasoactives on portal haemodynamics during hypovolaemia and reperfusion we have undertaken such a study in portal hypertensive rats.

Hypovolaemic, portal hypertensive rats (partial portal vein ligation) received infusions of somatostatin (0.4 μg/kg/h) octreotide (0.4 μg/kg/h) vasopressin (0.08 μU/g/h) or saline. Reperfusion was commenced 15 min after the start of drug administration. Portal pressure and arterial blood pressure were measured continuously and collateral blood flow (consecutive intrasplenic administration of $^{99}$Tc-methyl diphosphonate and $^{99}$Tc-albumin microspheres) at 5 min intervals throughout the study. Portal pressure was decreased and collateral blood flow increased following haemorrhage ($p < 0.001$ ANOVA). Administration of vasopressin during hypovolaemia had no effect on portal pressure but collateral blood flow was increased. In contrast portal pressure increased during infusions of somatostatin and octreotide whereas collateral blood flow was decreased ($p < 0.01$). During reperfusion collateral blood flow was increased in all rats except those receiving octreotide (76.7 ± 7.3 to 40.1 ± 9.2% $p < 0.01$). The efficacy of vasoactive drugs is related to their ability to reduce blood flow through the collateral circulation including the varices. The results of this study suggest that of the three vasoactives studied, only octreotide is capable of reducing collateral blood flow during haemorrhage and resuscitation.

## OIII/6 985

**ECHO-DOPPLER AS A SUITABLE NON-INVASIVE TECHNIQUE TO ASSESS RENAL HEMODYNAMIC CHANGES INDUCED BY OCTREOTIDE IN CIRRHOTIC PATIENTS** G. Antonica, C. Sabbà,, E. Berardi, P. Buonamico, D. Pugliese, G. Ferraioli,(*) O. Albano *Istituto di Clinica Medica I, University of Bari, Bari, Italy. and (*) Ospedale Civile di Scafati, Salerno, Italy.*

BACKGROUND Octreotide, a synthetic analogue of somatostatin, induces vasocostriction in splanchnic vessels of cirrhotic patients. Recently, a vasoconstrictive effect of somatostatin has also been described on renal circulation of cirrhotics (Gastroenterology 1992;103:1868-1874). Previous controlled studies have shown a good sensitivity of Echo-Doppler technique in detecting acute hemodynamic changes in splanchnic circulation due to vasoactive drugs. This study was designed to assess the acute hemodynamic effect of Octreotide on the renal arterial vascular bed in cirrhotic patients by Echo-Doppler technique.

PATIENTS AND METHODS Fifteen cirrhotic patients, 10 males and 5 females, mean age 63±3 yrs, Child-Turcotte class A n.2, B n.10 and C n.3, have been studied by an ATL UM8 duplex system after an overnight fast and 30 min after the administration of a single dose of Octreotide (100 mcg, s.c.). The right renal interlobar arteries have been studied at the renal ilum with an angle of insonification <60° using a coronal scan, by an operator unaware of the study design. Maximum blood flow velocity was measured from the maximum frequency shift,. and mean velocity (Vmean) was calculated by the formula Vmean=0.57xVmax. The pulsatility index (P.I.), which is independent from Doppler angle of insonification and correlates with vascular peripheral resistance, was calculated by the formula: P.I.=Vmax-Vmin/Vmean. In this operator blind study , five measurements were averaged at baseiine and five at 30 min' after Octreotide (coefficient of variation for Vmean 3%, for P.I. 6%).

RESULTS Values are reported as Mean±SD. A paired Student's t-test was used for comparisons between baseline and 30 min after Octreotide values.

| | Baseline | 30' after Octreotide | p values |
|---|---|---|---|
| Vmean (cm/sec) | 24.0 ± 8.6 | 18.5 ± 5.6 | <0.001 |
| P.I. (arbitr.Units) | 1.46±0.28 | 1.59±0.40 | <0.05 |

CONCLUSIONS These data indicate the capability of Echo-Doppler for non-invasively depicting hemodynamic changes acutely induced by vasoactive drugs in renal vascular bed. The reduction of Vmean and the increase in P.I. suggest that Octreotide increases renal vascular resistances in cirrhotic patients. Further studies are needed to assess the clinical meaning of this finding.

## OIII/8 260

**Plasma ANF in cirrhosis: Relation to plasma volume, regional and peripheral hemodynamics, arteriovenous "shunting" and neurohormonal response.** Fernández-Rodriguez CM, Andrade A, Zozaya JM, Quiroga J, Mallo R, Penas J, Rodriguez-Martinez D, Prieto J. Hospital Xeral,Vigo. Dep. Int. Medicine. Clinica Univ. de Navarra.

In liver cirrhosis, a decreased effective arterial central blood volume by peripheral arterial vasodilation has been claimed to initiate sodium and water retention. However, plasma ANF is an index of central vascular fullness and has been often reported to be risen in decompensated cirrhotic patients in which arteriolar vasodilation and arteriovenous shunting may decrease the resistance to venous return in a similar manner to that observed in experimental arteriovenous fistula, where a neurohormonal pattern of arterial underfilling and venous side overflow is seen.

**Aims:** To study whether plasma ANF is related to systemic and peripheral hemodynamic changes, peripheral arteriovenous shunting and neurohormonal response in a group of cirrhotic patients.

**Methods:** 8 healthy subjects and 24 cirrhotic patients (group I: 7 without ascites, group II: 9 with ascites and UNaV>10mEq/24h and group III: 8 with ascites and UNaV≤ 10 mEq/24h) were studied. Cardiac output and femoral hemodynamics were measured by pulsed-wave duplex-Doppler and systemic and femoral vascular resistances were obtained by standard formulas. Blood volume, neurohormonal mediators and the femoral arteriovenous difference of oxygen content (Ca-vO2), were also determined in all cases. Plasma ANF was determined by RIA with double antibody separation, without plasma pre-extraction.

**Results:** Cardiac output (CO), femoral blood flow (FBF) and blood volume (BV) were increased and systemic vascular resistance (SVR), femoral vascular resistance (FVR) and Ca-vO2 were reduced in group III as compared with groups I and control. Plasma ANF was 34.75±5 pg/mL in group I and 44.295.4, 67.89±8.8 and 84.125±10.76 pg/mL (M±EEM) in groups I, II and III respectively (ANOVA; $p<0.001$. Group III vs. I and control). Plasma ANF directly correlated with CO (r:0.616; $p<0.001$), BV (r:0.555;$p<0.001$) and FBF (r:0.537;p: 0.001) and inversely coprrelated with SVR (r:-0.455;$p<0.02$), FVR (-0.434;$p<0.02$) and Ca-vO2 (r:-0.516;$p<0.01$).

**Conclusions:** Our data support that the arterial vascular tree is underfilled in cirrhotic patients. On the other hand, the blood volume at the venous vascular compartment is expanded probably by a decrease to venous return by arteriolar vasodilation and arteriovenous shunting.

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