undergoing liver transplantation. Significant variations exist among liver transplant centres in the risk of post-transplant biliary disease that cannot be accounted for by differences in recipient, donor or graft characteristics.

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OP16 EVIDENCE FOR COMPARTMENTALISED ENDOTOXAEMIA AND ITS EFFECT ON NEUTROPHIL FUNCTION IN THE PORTAL CIRCULATION IN CIRRHOSIS

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Introduction Bacterial translocation and endotoxaemia are important in the pathogenesis of neutrophil dysfunction in cirrhosis. At present, it is not clear whether systemic endotoxaemia occurs as a consequence of a defect at the gut barrier interface or diminished hepatic function and associated portosystemic shunting.
Aim The aims of this study were (1) to quantify the degree of portal endotoxaemia and the contribution of the liver in the regulation of systemic endotoxin (ET) levels, (2) to determine intestinal production of cytokines and adhesion molecules and (3) to determine whether the portal and hepatic milieu modulates neutrophil function.
Method 12 patients with cirrhosis (54±3.2 yr, Pugh 10.2±1.0, eight male, four female) were studied prior to and 1-h after TIPSS insertion. Blood was sampled from the artery, hepatic vein (HV), portal vein (PV) and its tributaries. PV blood was sampled before insertion of the TIPSS. Endotoxin (ET) (LAL assay), LBP, BPI, IL-6, IL-10, TNFR55, TNFR75, sICAM and sELAM (using ELISA) were measured. Neutrophil respiratory burst and phagocytosis was measured using FACS in neutrophils derived from the HV and PV, prior to and following cross-incubation with PV and HV plasma, respectively.
Results TIPSS insertion resulted in a significant increase in arterial ET levels from 0.08±0.02 to 0.19±0.02 EU/ml (p=0.0001). Mean ET levels in the PV and HV pre-TIPSS insertion were 0.22±0.02 and 0.04±0.02 EU/ml respectively. Transintestinal (TI) and transhepatic (TH) ET fractional extraction (FE) rates were 2.7±0.7 and −0.5±0.06, respectively. HV neutrophil resting burst was significantly increased from 52±5.3 to 78±4.5% after incubation with PV plasma (p<0.0001). Conversely PV neutrophil resting burst was significantly reduced from 85±3.5 to 60±5.3% (p<0.0001) after incubation with HV plasma. Positive intestinal FE rates were observed most markedly with BPI, IL-6 and IL-10. Neutrophil phagocytosis was reduced post-TIPSS from 66±7.5 to 42±6.5% (p=0.0004) and resting burst increased from 62±5.6 to 87±2.8% (p=0.0001).
Conclusion This study provides direct evidence for portal endotoxaemia in cirrhosis. The data suggest that the liver is responsible for compartmentalising ET and associated neutrophil dysfunction within the portal circulation. Intestinal production of IL-6 and IL-10 was also demonstrated. TIPSS insertion disturbs this compartmentalisation and exposes the systemic circulation to portal endotoxaemia. Strategies to diminish portal endotoxaemia or enhance hepatic ET clearance capacity are important therapeutic targets to minimise neutrophil dysfunction in cirrhosis.

OP17 CLINICAL EFFECT OF ALBUMIN DIALYSIS IN PATIENTS WITH INTRACTABLE PRURITUS CORRELATES CLOSELY WITH CHANGES IN AUTOTAXIN ACTIVITY BUT NOT BILE SALT LEVELS

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Introduction About 5% of patients with severe cholestatic liver disease have intractable pruritus. Albumin dialysis is an effective treatment for these patients but the mechanism through which it reduces the severity of pruritus is not clear. Autotaxin (ATX) is a 125 kD protein which cleaves a choline group of lysophosphatidylcholine (LPC) thereby forming the biological active lysophosphatidic acid (LPA). Increased serum ATX activity has been described in patients with cholestatic pruritus (*Gastroenterology*, 2010; in press).
Aim The aim of the study was to determine the effect of albumin dialysis using molecular adsorbents recirculating system (MARS) on autotaxin activity and bile salts and their relationship to the severity of pruritus.
Method 15 patients (11F/4M, PBC 10, PSC 2, other 3) with severe pruritus that was resistant to medical therapy were treated in 31 sessions (each consisting of 3, 8-h treatments; median follow-up of 12.8 months) with MARS. The intensity and severity of itch was quantified using an itch severity scale (ISS) and the visual analogue scale (VAS) pre and post treatment and then weekly for up to 12 weeks. ATX activity was measured in diluted serum samples and albumin dialysate before and after MARS treatments using a fluorescence assay. ATX protein levels were determined by Western blotting. Bile salts were measured by LCMS.
Results MARS treatment was associated with immediate, significant and complete response (R) in 11 patients, two patients had a partial response (PR) and two patients had no response (NR). Median ATX activities were not different between responders and non-responders (R=216.5; NR=306.6). A mean reduction of ATX activity of 27.6±4.13% was seen in R, 10.7±10.3% in PR and 1.5±1.48% in NR. This change in ATX activity was directly correlated with the reduction in ISS (r2=0.59; p<0.005) and VAS (r^2=0.47; p<0.02). The change in serum ATX activity correlated closely with the change in serum ATX protein level (r^2=0.5; p<0.01). Expectedly, no ATX activity was measureable in the albumin dialysate. ATX levels returned to pre-treatment values with relapse of itching which occurred in all responders between 6 weeks and 4 months. No significant changes in serum bile salts were observed.
Conclusion Our study suggests an important role for ATX activity in modulating the severity of pruritus in cholestatic patients providing novel insights into the pathogenesis of itch in cholestatic disease. The reduction is not due to removal of circulating ATX into the dialysate suggesting that MARS treatment either reduces the production of ATX or enhances its hepatic clearance. Alternatively, or in addition, either a substrate or co-factor of ATX is extracted by the MARS system.

OP18 ABNORMAL LIVER HISTOLOGY IN PATIENTS TAKING METHOTREXATE CORRELATES POORLY WITH DOSAGE OR DURATION OF THERAPY AND REFLECTS ESTABLISHED RISK FACTORS FOR STEATOHEPATITIS

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Introduction Chronic liver injury has been described in patients taking low dose methotrexate (MTX) for psoriasis or rheumatological