

($p=0.0013$) suggesting a compensatory anti-inflammatory response syndrome.

Conclusion HE relapse post-lactulose withdrawal is associated with derangements in bioenergetics, amino-acid, lipid and gut microbial metabolism as well as depression of the inflammatory response.

P23 ABSTRACT WITHDRAWN

P24 CYTOKINE BIOMARKER PROFILING IN ACETAMINOPHEN-INDUCED ACUTE LIVER FAILURE: IMPORTANCE OF MONOCYTE CHEMOTACTIC PROTEIN-1 IN PROGNOSIS AND HEPATIC ENCEPHALOPATHY

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Introduction Inflammatory cytokines have recently been described as reflecting severity of liver injury, grade of encephalopathy and prognosis in acute liver failure (ALF). The role of monocyte chemotactic protein-1 and peripheral monocyte count has not been well studied.

Method 35 consecutive patients admitted to our institution with a diagnosis of acetaminophen induced ALF were studied for the effect of a biomarker profile of inflammatory cytokines (IL-4, IL-6, IL-10, MCP-1, TNF- α , IFN- γ) levels at admission on grade of hepatic encephalopathy (HE) and prognosis. Modified King's College Criteria (KCC) was used in deciding whether to perform ELT. Assessment of HE and prognostic markers was investigated using logistic regression and receiver operating characteristic (ROC) curve analysis.

Results MCP-1 levels were significantly correlated with standard markers of severity of liver injury (INR: $R=0.737$, $p<0.001$; lactate: $R=0.772$, $p<0.001$; AST: $R=0.545$, $p<0.001$) and with IL-6 ($R=0.576$, $p=0.003$) and IL-10 ($R=0.679$, $p<0.001$). MCP-1 levels were significantly reduced in spontaneous survivors (1149 (range 168–12 998) compared to patients who died/underwent orthotopic liver transplantation (OLT) (7925 (1694–30 625), $p<0.001$, Mann–Whitney U test. The area under the ROC curve (AUROC) for MCP-1 and prediction of poor outcome was 0.88 (95% CI 0.68 to 0.97, $p<0.001$). There was no significant difference in performance of MCP-1 compared with IL-4 (AUROC 0.80 (0.59–0.93)) IL-6 (AUROC 0.83 (0.63–0.95)) or IL-10 (AUROC 0.84 (0.64–0.95)) $p>0.05$ for all; De Long method). MCP-1 performed better than peripheral monocyte count (AUROC 0.75 (0.57–0.85). TNF- α , TGF- β 1 and IFN- γ levels did not predict outcome. IL-6 better predicted the development of severe (grade 3–4) HE (AUROC 0.91 (0.72–0.98) compared with MCP-1 (AUROC 0.71 (0.49–0.87), $p=0.087$ (De Long method)).

Conclusion MCP-1 has similar behaviour to IL-4, IL-6 and IL-10 in outcome prediction in acetaminophen induced acute liver failure and better reflects poor prognosis than peripheral monocyte count. IL-6 may better reflect the severity of HE suggesting different roles for interleukins and MCP-1 in the pathogenesis of the inflammatory milieu in ALF.

P25 QUANTITATIVE COMPARISON OF MICROBUBBLE ULTRASOUND TECHNIQUES FOR THE ASSESSMENT OF HEPATIC FIBROSIS IN CHRONIC HEPATITIS C

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Introduction There is increasing interest in the development of imaging-based non-invasive markers for the assessment of chronic

liver disease severity. Contrast enhanced ultrasound uses microbubbles as kinetic tracers to assess liver disease severity by exploiting the intra- and extra-hepatic haemodynamic changes accompanying fibrosis and cirrhosis. Transit times of a peripherally administered microbubble bolus are reduced with increasing disease severity. Transit times have previously been calculated to include intra- and extra- hepatic components (the hepatic vein transit time, HVTT) or just the intra-hepatic component (hepatic transit time, HTT), but diagnostic accuracy has not been compared directly.

Aim The aims of this study were: 1. to compare the diagnostic accuracy of HVTT and HTT in gauging the severity of chronic hepatitis C (CHC) and 2. to assess the inter- and intra-observer reliability of the microbubble technique.

Method 75 patients with biopsy-proven CHC were studied, staged using the Ishak system. Recordings of Doppler US scans performed using the microbubble contrast agent SonoVueTM, were retrospectively analysed by two independent observers, blinded to clinical data, to determine the HVTT, defined as the time taken for the microbubble to travel from the antecubital vein to the hepatic vein, and the HTT, defined as the difference between the hepatic vein arrival time and the hepatic artery arrival time. Each patient had two recordings (with separate microbubble injections) at a 10 min interval. Diagnostic accuracy was assessed using the area under the receiver operator characteristic (AUROC) curve. Inter- and intra-observer reliability and inter-injection reliability were assessed using the intraclass correlation coefficient (ICC).

Results 35 patients had mild fibrosis (stage 0–2), 23 had moderate-to-severe fibrosis (stage 3–4) and 17 had cirrhosis (stage 5–6). The diagnostic accuracy (95% CI) of HTT and HVTT for the diagnosis of cirrhosis (stage >4) were 0.78 (0.64–0.92) and 0.71 (0.55–0.86). Diagnostic accuracy (95% CI) of HTT and HVTT for the diagnosis of fibrosis stage >2 were 0.75 (0.65–0.86) and 0.71 (0.59–0.83). Inter-observer reliability (95% CI) for HTT and HVTT were 0.92 (0.87–0.95) and 0.94 (0.91–0.97). Intra-observer reliability for HTT and HVTT were 0.98 (0.97–0.99) and 0.99 (0.98–0.99); inter-recording reliability were 0.97 (0.96–0.98) and 0.97 (0.95–0.98) respectively.

Conclusion HTT is more accurate than HVTT for the diagnosis of cirrhosis and moderate-to-severe fibrosis, while the reliability both of repeated recordings and of operators' assessment of recordings was very high. HTT reflects the intra-hepatic haemodynamic changes seen in more advanced chronic liver disease accounting for shorter transit times.

P26 HEPATOCELLULAR CARCINOMA SURVEILLANCE IN PATIENTS WITH ESTABLISHED CIRRHOSIS: THE BIRMINGHAM EXPERIENCE

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Introduction HCC causes approximately 1500 deaths per year in the UK and 95% of patients these have known established cirrhosis. Surveillance programme for patients with cirrhosis using six monthly α -fetoprotein (AFP) monitoring and ultrasound scanning (USS) is therefore recommended to ensure early identification of HCC at a stage when curative treatment is still possible. HCC identified by surveillance rather than incidental or symptomatic diagnosis results in better outcome and increased survival.

Aim Here we show the results of an audit of HCC surveillance at the Liver Transplantation Unit in Queen Elizabeth Hospital Birmingham against the British Society of Gastroenterology guidelines.

Method We identified consecutive 271 patients who had undergone HCC surveillance between January 2007 and January 2009. We divided the patients into high risk (hepatitis B, hepatitis C, men with alcoholic liver disease or PBC and haemochromatosis) and low risk groups. We collected their demographic data, surveillance results, treatment details and outcome.

Results Mean duration of follow-up was 22 months (range 1 to 32). 156/272 (57%) patients belonged to high risk group. Ten patients (4%) ceased surveillance as they underwent liver transplantation with indication other than HCC. Eight patients (3%) died during surveillance, unrelated to HCC and one patient was found to have pancreatic carcinoma on ultrasound done for HCC surveillance. 18 (6%) were found to have HCC, of whom (72%) were in the high risk group. Number of HCC present varied from 1 (72%), 2 (22%) and 3 HCC in just 1 (6%). Two patients (11%) were detected by abnormal AFP alone with further imaging confirming the diagnosis. Both of these were unsuitable for curative treatment. Majority (44%) were picked up on surveillance USS demonstrating abnormality then confirmed with further imaging. Fifty-six percent of patients with HCC underwent attempted curative treatment (liver transplantation 28%, resection 6% and radiofrequency ablation 22%); 23% received controlling treatment (TACE 6%, ethanol injection 17%) and 22% were referred for palliation.

Conclusion Our results show that a large proportion of HCC were detected in high risk group and 56% of these patients underwent curative treatment for HCC. A significant proportion (23%) also underwent other definitive treatment. There was a significant burden of HCC in the group conventionally classified as low risk group for HCC (18% of total HCC we identified in our series). 22% of our total identified HCC cases were not suitable for treatment other than palliation despite being on recommended surveillance and this may be improved by modifying surveillance interval or better definition of the high risk group. With this study we recommend present surveillance guidelines to be followed in all patients with cirrhosis, however, there may be scope for further improvement in outcome for cirrhosis patients developing HCC by modification of surveillance protocol in selected patients and also by modification of risk groups.

P27 NEUTROPHIL DYSFUNCTION: THE MISSING LINK BETWEEN AMMONIA, INFECTION AND HEPATIC ENCEPHALOPATHY?

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Introduction Neutrophil phagocytic dysfunction is associated with increased risk of infection and mortality in patients with cirrhosis. The p38-mitogen-activated protein kinase (MAPK) signalling pathway is a critical step in neutrophil activation and is modulated by chemokines, ammonia and endotoxaemia.

Aim This longitudinal study aims to characterise the relationship between neutrophil function and volume, plasma cytokine profile and ammonia, in order to assess neutrophil function as a biomarker of susceptibility to infection and contributor to the development of hepatic encephalopathy (HE) in cirrhosis.

Method Neutrophils were isolated at baseline, following the development of HE, and post-LT, from a cohort of 75 patients with cirrhosis and controls during an 18-month follow-up period. Phagocytosis was analysed by flow cytometry using FITC-labelled *E. coli* and oxidative burst (OB) was determined by the percentage of neutrophils producing reactive oxygen species (ROS) at rest and after stimulation with opsonised *E. coli*. Neutrophil volume was measured using flow cytometry and transmission electron microscopy. Clinical data, blood biochemistry, arterial ammonia and

microbial cultures were collected prospectively. Analysis of stimulated neutrophil intracellular cytokine production, plasma cytokine profile and neutrophil basal levels of phosphorylated P38-MAPK were performed.

Results At baseline patients had a median age of 54 (44–62), 31% were female, 43% were on antibiotics. Median MELD score was 17 (12–22). During follow-up nine patients developed overt grade 2–4 HE, 12 patients underwent LT and nine died. Neutrophil phagocytic capacity was significantly impaired in patients with advanced cirrhosis ($p=0.001$) and was associated with a 20% increase in neutrophil volume. In those who underwent uncomplicated LT, neutrophil phagocytic capacity improved by 15% within 72 h. Phagocytic impairment correlated with increasing plasma concentrations of CRP*, ammonia*, IgC*, proinflammatory cytokines TNF*, IL-6* and the anti-inflammatory cytokine IL-10* (* $p<0.05$, ** $p<0.01$). Resting neutrophil production of ROS as a measure of neutrophil activation was significantly increased in patients with cirrhosis with further elevation following the development of HE.

Conclusion Phagocytic dysfunction is universal in patients with cirrhosis and is related in part to the development of ammonia-induced neutrophil swelling, which is reversible following LT. Increasing levels of endotoxin and/or ammonia leading to neutrophil activation via the p38-MAPK pathway and resultant generation of ROS may prove the link between neutrophils, ammonia and infection in the development of HE in cirrhosis.

P28 OPTIMISING THE ANALYSIS OF THE ELECTROENCEPHALOGRAM IN HEPATIC ENCEPHALOPATHY

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Introduction Hepatic encephalopathy (HE) is the commonest complication of cirrhosis. It has a detrimental effect on quality of life and on survival. Nevertheless, there is no recognised gold standard for its diagnosis. The only objective diagnostic technique, which does not require patient co-operation, is the electroencephalogram (EEG). The current assessment of the EEG is based on measures of the mean dominant frequency (MDF) and the percentage θ ($\theta\%$) power from spectral analysis. However, this represents a fairly simplistic approach to analysis of complex shifting wave forms.

Aim To optimise the analysis of the EEG to provide more reliable criteria for the diagnosis of hepatic encephalopathy and the grading of its severity.

Method The patient population comprised 169 individuals (108 men, 61 women; mean (range) age, 55 (26–80) yr) with biopsy-proven cirrhosis, classified on the basis of clinical (Conn *et al*, 1977) and psychometric performance (PHES; Weissenborn *et al*, 2001), as neuropsychiatrically unimpaired ($n=85$), or as having minimal ($n=21$) or overt ($n=63$) HE. The reference population comprised 48 healthy individuals (25 men, 23 women; mean (range) age, 39 (22–58) yr). Standard 21-lead, eyes-closed EEG recordings were obtained in all subjects. EEGs were visually inspected and spectral analysis undertaken on a standard P3–P4 derivation (Amodio *et al*, 1999) and a SEDACA component (Montagnese *et al*, 2007). In addition, a measure of the stability of the posterior rhythm, F-mean, was obtained using a novel computational technique. A subset of 74 patients underwent a mean of 3 (2–9) repeat assessments over time. Performance of the variables was assessed using ROC analysis.

Results Four variables had good performance characteristics.

All four variables correlated significantly with the PHES scores ($p<0.05$). Significant changes in F-Mean ($p<0.05$), α -P3P4 and