P64 CENTRAL NERVOUS SYSTEM INVOLVEMENT IN PATIENTS WITH CHRONIC HEPATITIS C VIRUS INFECTION AND MINIMAL LIVER DISEASE

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[1]E Williams, [2]M Heeren, [3]C D Jackson, [2]H Pflugrad, [2]J Krause, [2]L M Weber, [2]K Wiessenborn, [1]M Y Morgan. *[1]Centre for Hepatology, UCL Medical School; [2]Department of Neurology, Medizinische Hochschule Hannover, Germany; [3]Department of Neurophysiology, Royal Free Hampstead NHS Trust, London, UK*

Introduction Individuals with chronic HCV infection are frequently fatigued and have difficulties with tasks of complex attention, visual scanning and psychomotor speed, even in the absence of significant liver injury. However, the objectivity of these findings has been questioned. Observed alterations in neurometabolite concentrations on cerebral ^{1}H-MRS further supports evidence of CNS involvement. These changes in cognition and ^{1}H-MRS seem to persist despite successful anti-viral therapy but this has not been studied systematically. No information is currently available on possible EEG changes in this population which, if present, might provide an easily available objective marker of CNS involvement.

Aim The aim of this study was to characterise the EEG in HCV-infected patients with minimal liver injury in relation to treatment status and treatment responses.

Method The study population comprised 114 HCV-infected individuals (75 women: 39 men) of mean (range) age 52.0 (25–75) years with little or no liver disease; the majority of patients had been infected by contaminated blood or blood products; none was misusing alcohol nor on treatment with interferon or psychoactive medication at the time of the study. All patients underwent formal assessment of fatigue, depression and anxiety and extensive psychometric testing. EEGs were recorded on the same day as the neuropsychometric assessment; reference data were obtained from 137 age/gender-matched healthy controls. The EEG was defined as *'fast'* if the relative β power was >30% on the P3-P4 derivation.

Results The prevalence of fast EEG activity was significantly greater in the patients than controls 43% vs 15% ($p<0.0001$). Significant correlations were observed between the presence of fast EEG activity and impairments in specific psychometric tests but not with fatigue, depression or anxiety. These abnormalities were observed independently of HCV-RNA levels and treatment status (Abstract P64 table 1):

Abstract P64 Table 1

	Untreated (%)		Treated (%)	
Variable	RNA negative (n=9)	RNA positive (n=55)	RNA negative (n=11)	RNA positive (n=39)
Fatigue	78	56	73	72
Depression	67	22	36	26
Anxiety	67	33	36	36
Fast EEG	33	42	36	49

Conclusion Patients with HCV infection with little or no evidence of liver injury show impaired cognitive function and an excess of fast EEG activity independent of fatigue, depression and anxiety. These findings hold true even if the patients have cleared the virus, either spontaneously or following anti-viral treatment. These results could be indicative of an effect of cerebral HCV-quasispecies similar to that suggested in HIV-associated dementia.

P65 ORAL ANTI-VIRAL THERAPY SHAPING THE INDICATIONS FOR HEPATITIS B LIVER TRANSPLANTATION OVER 2 DECADES

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[1 2]Y Htun Oo, [1 2]B Gunson, [1 2]D J Mutimer. *[1]Centre for Liver Research & NIHR BRU, University of Birmingham, Birmingham, UK; [2]Liver and Hepatobiliary Unit, Queen Elizabeth Hospital, Birmingham, Birmingham, UK*

Introduction Hepatitis B virus (HBV) infection is a major cause of liver disease. Nearly 350 million worldwide have chronic infection and around 600 000 persons die each year from consequences of HBV. Liver transplantation (LT) is an excellent treatment for HBV-related cirrhosis and hepatocellular carcinoma (HCC). Oral-antiviral therapy is effective in suppressing HBV replication. Before the introduction of oral anti-viral therapy the indications for LT were mainly fulminant liver failure (FHF) and hepatic decompensation. However, with availability of effective oral antiviral medication, there has been a change in the indication for LT in HBV infected patients, and the largest proportion has well compensated cirrhosis with HCC.

Aim To analyse the indication and outcome of LT for HBV patients in our unit over 24 years.

Method Retrospective database analysis of HBV related LT from 1986 to 2010. Indications, demographics, viral load, co-infection, oral anti-viral therapy, and outcome were examined.

Results 121 patients with HBV were transplanted. 18 recipients were female, average age at time of transplant was 50. 36 were Asian, 8 were of African descent. Lamivudine prophylaxis for viral load suppression was usually used for those who were transplanted after year 1993 and median viral load pre-LT for this patient group was 10^3 (range 10^2–10^6) copies/ml. 58/121 had LT between 2000 and 2010, and 63 before 2000. 12.6% (8/63) had LT for FHF before year 2000, and only 7%(4/58) since 2000 ($p=0.2$). 14 (22%) transplanted pre-2000 and 31 (54%) post-2000 had HCC ($p<0.001$). Median pre-LT bilirubin was 57 mmol/l (pre-2000) vs 31 (post-2000) ($p=0.003$) and median pre-LT INR was 1.7 (pre-2000) vs 1.2 ($p<0.001$) but pre-LT creatinine was not significant between two groups. Three patients had regraft (1=HAT; 1=PNF; 1=recurrence). There were 9 deaths related to recurrent HBV in patients transplanted pre-2000 and 1 death in patients transplanted post 2000. There are three recurrent HCC pre 2000 and five recurrent HCC post-2000. The difference in survival between the two groups approaches statistical significance ($p=0.13$). 69 patients are alive, eight patients are followed abroad. All patients were treated with Lamivudine post-LT. Since 2000, Lamivudine was used in combination with Adefovir for 11 patients and Tenofovir for three patients pre-LT to suppress viral replication. One patient was on Entecavir pre-LT.

Conclusion There is a change in the indication for LT in HBV patients since the introduction of oral antiviral therapy. An increasing proportion has well compensated liver disease with HCC as the indication for LT.

P66 LOW PRE-TREATMENT PLASMA HBSAG LEVEL AND ITS DECLINE DURING ADD-ON INTERFERON TREATMENT PREDICT RESPONSE TO COMBINED LAMIVUDINE/INTERFERON THERAPY IN TOLERANT CHILDREN WITH INFANCY-ACQUIRED CHRONIC HEPATITIS B

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I Carey, M Horner, M Bruce, S Bansal, D Vergani, G Mieli-Vergani. *[1]Institute of Liver Studies, King's College Hospital NHS Foundation Trust*

Introduction Changes in HBsAg plasma levels during antiviral therapy with pegylated interferon (IFN) predict response in adults

with chronic hepatitis B (CH-B). Whether pre-treatment HBsAg plasma levels correlate with liver relaxed circular (RC) HBV DNA and covalently closed circular (ccc) DNA is controversial. To date, no information is available on HBsAg plasma level behaviour and response to treatment prediction in tolerant patients with infancy-acquired CH-B treated with lamivudine (LAM) and IFN.

Aim To investigate whether HBsAg plasma levels predict response to LAM + IFN treatment in tolerant children with infancy-acquired CH-B, and to determine their association with plasma HBV DNA levels during treatment and with pre-treatment liver RC HBV DNA and cccDNA.

Method Patients: 23 children (8 males, median age 10.2 yrs) with infancy-acquired CH-B (all HBeAg positive), treated for 52 weeks [lead-in LAM (3 mg/kg/d) for 9 weeks; LAM plus IFN-α (5 MU/m^2 TIW) from week 9 for 44 weeks], were divided according to treatment response: 5 responders (R = anti-HBs seroconversion) and 18 non-responders (NR).

Methods: Plasma HBsAg and HBV DNA levels were measured before (treatment week 0, TW0), during (TW9, TW28, TW52) and after (follow-up week, FUW24) therapy by Abbott ARCHTECT_ assay and real-time TaqMan PCR [both $\log_{10}$ IU/ml]. Baseline liver RC HBV DNA and cccDNA was quantified by real-time TaqMan PCR [copies/ng genomic DNA]. Results are presented as median.

Results Baseline HBsAg levels were lower in R than NR (4.36 vs 4.74, p=0.02), but similar in R and NR at the end of LAM lead-in therapy (TW9) (4.34 vs 4.66, p=0.1). During IFN add-on therapy, at TW28 (2.34 vs 4.33) and TW52 (0 vs 4.08) levels were markedly lower in R than NR, the difference persisting at FUW24 (0 vs 4.51) (p<0.01 for all). Plasma HBV DNA levels were similar at baseline in R and NR (8.94 vs 8.98), but decreased significantly in R compared to NR at TW9 (4.91 vs 5.48), TW28 (3.42 vs 4.39), TW52 (1.57 vs 4.07) and FUW24 (0.27 vs 7.75) (p<0.01 for all). There was a strong positive correlation between plasma HBsAg and HBV DNA levels at TW28 (r=0.6, p<0.01) and TW52 (r=0.64, p<0.01). Baseline liver RC HBV DNA (43 800 vs 52 300 copies/ng genomic DNA) and cccDNA (41 vs 49 copies/ng genomic DNA) were similar in R and NR, with no correlation between liver RC HBV DNA or cccDNA and baseline HBsAg.

Conclusion Lower baseline HBsAg plasma levels and a sharp decrease of plasma HBV DNA levels at TW9 (LAM lead-in) followed by declining plasma HBsAg levels from TW28 (IFN add-on) heralds HBsAg clearance and response to treatment in tolerant children with CH-B.

P67 SWITCH TO OTHER NUCLEOS(T)IDE ANALOGUES THERAPY IN CHRONIC HEPATITIS B COHORT ON LONG-TERM DE-NOVO COMBINATION THERAPY WITH LAMIVUDINE PLUS ADEFOVIR: EFFICACY AND SAFETY

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I Carey, A Mendes, D Joshi, M Bruce, S Knighton, A Scalori, S Hughes, M Al-Freah, A Suddle, P M Harrison, [1]K Agarwal. *[1]Institute of Liver Studies, King's College Hospital NHS Foundation Trust*

Introduction Long-term de-novo combination therapy with lamivudine (LAM) 100 mg/d + adefovir (ADV) 10 mg/d is highly efficient, with no/minimal drug resistance and good safety profile. Tenofovir (TDF) 245 mg/d or entecavir (ETV) 0.5 mg/d are highly efficacious antivirals with high resistance barrier and provide alternative to LAM + ADV combination therapy.

Aim We aimed to investigate the virological and serological responses and renal/bone safety after switch from LAM + ADV to other antiviral drugs.

Method Patients: Nucleos(t)ide analogues naive 192 CHB patients (78% males, median age 40 y, 35% HBeAg+, 34% cirrhosis) were treated with de-novo LAM+ADV at a single-centre practice (median 36 months). 149 patients from this cohort were switched to other nucleos(t)ide analogues therapy: 101 (68%) to TDF monotherapy, 28 (19%) to TDF plus emctritabine, 14 (9%) patients to ETV monotherapy and 6 (4%) patients to other antivirals. Median duration of therapy after switch was 14 months. Reasons for the switch were following: 33 patients slow-response/non-response, 14 had drug-related renal impairment, 5 due to pregnancy, 2 after liver transplantation and 95 patients were switched for other reasons.

Methods Number of patients achieved HBeAg seroconversion and complete virological response (CR) (HBV DNA<12 IU/ml) was compared (LAM+ADV vs. switch). Differences between serum levels of HBV DNA, creatinine and phosphate and estimated glomerular filtration rates (eGFR) were assessed at each time-point and compared between groups and with baseline. HBV genotypic resistance was tested in all patients with suboptimal response by direct sequencing.

Results Baseline HBV DNA was significantly higher in LAM+ADV vs switch group (median $\log_{10}$ 4.6 vs 0.89 IU/ml, p<0.01), there was higher proportion of responses after switch than at time of switch and when compared to LAM+ADV (switch baseline 76% vs m3 switch 91%, p=0.02 vs m3 LAM+ADV 48%, p<0.01). On LAM +ADV therapy 14 patients achieved HBeAg and 3 patients HBsAg seroconversion and additional 3 patients and 1 patient seroconverted HBeAg and HBsAg after switch. No viral mutations associated with drug resistance were detected in LAM+ADV and after switch. There were no significant differences in serum creatinine or eGFR between groups at each time-point, but comparing to baseline there was significant decrease in eGFR from M18 onwards in LAM+ADV group (82.2 vs76.2 ml/s, p=0.04). The proportion of patients with eGFR <60 ml/s did not changed during LAM+ADV therapy and after switch. Serum phosphate levels [mmol/l] fell on therapy in LAM+ADV from M12 (M12: −0.04, M18: −0.06 and M24: −0.05) and remained unchanged after switch.

Conclusion Switch to other nucleos(t)ide analogues from long-term de-novo combination LAM+ADV therapy was efficient and was not associated with impact on renal/bone safety.

P68 IS IT WORTH TESTING UNSTABLE DRUG USERS FOR HEPATITIS C?

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B P Stephens. *Ninewells Hospital, Dundee*

Introduction Within the UK the main source of hepatitis C virus (HCV) infection is injecting drug use however, diagnosing HCV in chaotic drug users has often proved challenging, particularly if venous access is a problem.

Aim To evaluate the introduction of HCV dry blood spot testing (DBST) by staff working in addiction services and to determine if individuals who agreed to testing, returned for their results and accessed appropriate follow-up into either drug or HCV treatment.

Method The study was carried out over an 18-month period between 2009 and 2010. Testing for HCV was offered to individuals who accessed addiction services during this period. A follow-up appointment was issued for 2 weeks after testing. The numbers tested were monitored and data were collected on follow-up appointments attended.

Results During the study, 661 tests were carried out using the DBST method. 479 (72.5%) within needle exchange services and 182 (27.5%) from drug treatment services. 439 (66%) were male, and the age range was 18 to 51 years with a median age of 32 years. 608 (91.3%) individuals returned for the results of their test and 186 (28%) of the 661 tests were HCV antibody positive. Follow-up bloods were offered to all positive patients. Of the 147 (79%) who