

PTU-110 CIRCULATING BONE MARROW-DERIVED STEM CELLS AND STEM CELL FACTOR SERUM LEVEL IN CHRONIC HEPATITIS C: RELATION TO HEPATIC PROLIFERATION AND FIBROSIS

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Introduction Bone marrow-derived stem cells (BMSCs) are pluripotent cells that can be mobilised into circulation and recruited to sites of inflammation where they promote local tissue repair. Therefore, the present work was designed to study circulating BM-derived hematopoietic stem cells (HSCs) and mesenchymal stem cells (MSCs) and serum levels of stem cell factor (SCF), a stem cell mobilising factor, in patients with chronic hepatitis C (CHC) in relation to hepatic proliferation and fibrosis.

Methods Thirty treatment-naïve patients with CHC and 15 healthy subjects were included in the study. The BM-derived HSCs and MSCs cells in fresh blood samples were identified as CD34⁺CD45⁺CD117⁺ and CD34⁺CD45⁺CD106⁺ cells respectively using flow cytometric assay. Serum SCF levels were measured using an enzyme linked immunosorbent assay kit. Liver biopsies were examined to assess METAVIR histological activity grade and fibrosis stage and steatosis grade. Immunohistochemical staining of liver specimens was done using monoclonal antibodies against cytokeratin (CK)7 for detection of hepatic progenitor cells (HPCs), Ki-67 as proliferation marker and α -smooth muscle actin (α -SMA) for identification of activated hepatic stellate cells (HpSCs).

Results Patients with CHC showed significant increases in the percentages of HSCs and MSCs in peripheral blood and serum SCF levels compared with healthy subjects ($P < 0.05$). Numerous CK7⁺ HPCs were detected mostly lining primitive bile ducts or as individual positive cells in the portal tracts. Hepatic proliferative activity evidenced as nuclear positivity for Ki-67, was observed in proliferated ductal profiles in portal tracts and within hepatocytes and directly correlated with HPC expansion. Based on the percentages of BMSCs in peripheral blood, patients with CHC were distinguished into two types of patients: "mobilizers" and "non-mobilizers". BMSC mobilizers showed a significant increase in serum SCF levels and significant decreases in HPC expansion, hepatic proliferative activity, serum levels of aminotransferases, histological activity grade, fibrosis stage and α -SMA expression compared with BMSC non-mobilizers ($P < 0.01$).

Conclusion Chronic HCV infection is associated with mobilisation of BMSCs from the BM into the circulation in parallel with an increased production of SCF, particularly when HPC activation and hepatic proliferative activity are impaired. Although the mobilised BMSCs are not sufficient to bring about hepatic repopulation, they may play an important role in limiting hepatic necroinflammation and fibrosis in HCV-induced liver damage.

Disclosure of Interest None Declared

PTU-111 A PROSPECTIVE STUDY OF INTRAVENOUS PARACETAMOL PRESCRIBING AND ITS USE IN PATIENTS AT RISK OF IATROGENIC PARACETAMOL INDUCED HEPATOTOXICITY

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Introduction Intravenous (iv) paracetamol can cause severe hepatotoxicity and lead to death if inappropriately prescribed¹. It is

increasingly being used for post-operative pain and pyrexia². There is a lack of awareness that paracetamol should be prescribed by weight when used in certain higher risk groups^{1,2}; including those weighing less than 50kilos and in malnourished patients³. This study assessed iv paracetamol prescribing in patients at increased risk of hepatotoxicity.

Methods Drug charts and medical records from 5 wards (3 surgical and 2 medical including 1 gastroenterology ward) were assessed prospectively over 3 days. All patients prescribed paracetamol were identified; those receiving iv preparations were included. The age, sex and weight were recorded in conjunction with the dose, route and number of paracetamol doses received by each patient. Intravenous doses were identified by countersignatures on drug charts or where iv was the only route indicated. Medical records were reviewed for a history of alcohol excess, chronic liver disease, chronic kidney disease (CKD), eating disorders, and those taking CYP450 inducing medications.

Results 59 patients were receiving paracetamol via any route. The average age was 74.6 years old (range 32–86). 25 patients had received iv paracetamol with 12/25 (48%) receiving the drug only via the iv route. The mean number of consecutive doses was 4.44 (range 1–28). 3 patients had CKD, 3 patients were on the CYP450 inducer Rifampicin and 1 patient had an eating disorder and CKD. 2 patients receiving iv doses were under 50 kg, one of which had CKD. Of the 9 patients deemed to be at risk of iatrogenic paracetamol induced hepatotoxicity, 0% had paracetamol prescribed at the recommended reduced dose of 3g per day.

Conclusion This study demonstrates that intravenous paracetamol was not being prescribed appropriately. Intravenous paracetamol should be reduced in high risk groups to 3g per day (15mg/kg/24 hours). With 25–37% of all hospital inpatients being deemed at risk of malnourishment⁴ a large patient cohort is at risk of paracetamol induced liver injury. Assessment of nutritional status and improved awareness of higher risk patients is needed to avoid iatrogenic paracetamol induced hepatotoxicity through poor prescribing.

Disclosure of Interest None Declared

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PTU-112 RIFAXIMIN FOR HEPATIC ENCEPHALOPATHY IS COST EFFECTIVE AT REDUCING EMERGENCY HOSPITAL ADMISSION

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Introduction Overt Hepatic Encephalopathy (HE) frequently results in emergency admission to hospital. Treatment with the non-absorbable antibiotic rifaximin is effective at preventing recurrence of overt HE but there are concerns about the high cost of the drug. The aim of this study was to evaluate the cost-effectiveness of rifaximin at reducing emergency admission to hospital.

Methods All patients commenced on rifaximin for HE from 1st January to 31st December 2011 were identified from the records of the pharmacy department at Freeman Hospital. The number and length of emergency hospital admissions for the period 1 year prior to starting rifaximin was compared to 1 year after starting the drug. Cost effectiveness was calculated using the standard British National Formulary (BNF) tariff for rifaximin and the estimated cost per day for acute inpatient admission to the Newcastle upon Tyne Hospitals Trust.

Results 64 patients (75% male, 53% ALD) were identified, 40 (63%) were on concomitant lactulose. In 8 patients rifaximin was discontinued (5 after transplant and 3 when HE excluded). 23 (36%) patients died within 1 year (median survival 62 days (range 2–364) and 33 (52%) were alive at 1 year and remained on rifaximin. Mean MELD of survivors was significantly lower than non-survivors (13.0 vs. 19.0 $P < 0.05$) and scores predicted 28 day mortality (median MELD 29 (range 4–37)). Complete data were available for 25 of the survivors and showed a significant reduction in the number of emergency admissions from a mean of 2.8 to 1.7 admissions per patient per year with rifaximin ($P < 0.05$). Duration of inpatient admission decreased significantly from a mean of 30.2 to 9.8 bed days per patient per year ($P < 0.05$). Taking into account the cost of one year's treatment with rifaximin (£3,687GBP) the reduction in the number of emergency admissions represents an annual saving of £3,468GBP per patient.

Conclusion Treatment with rifaximin for secondary prevention of hepatic encephalopathy appears to be cost effective at reducing emergency admission to hospital.

Disclosure of Interest None Declared

PTU-113 RIFAXIMIN IN NON-ALCOHOLIC STEATOHEPATITIS: AN OPEN-LABEL PILOT STUDY

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Introduction Mounting evidence implicates gut microbial dysbiosis in the pathogenesis of non-alcoholic steatohepatitis (NASH) by mechanisms including caloric salvage, lipopolysaccharide production, upregulation of proinflammatory cytokines, increased insulin resistance and consequent increases in body mass and hepatic steatosis. Rifaximin is a minimally-absorbed, gut-selective antibiotic with bactericidal activity against a broad spectrum of gut microbes, making it an attractive candidate therapy. We aimed to study the effect of Rifaximin on markers of hepatic inflammation, hepatic steatosis, hepatic and peripheral insulin sensitivity.

Methods Patients with biopsy-proven NASH, elevated aminotransferase values and no hepatic comorbidities were included in this open-label, randomised, cross-over study, all receiving 6 weeks of Rifaximin 400mg twice daily, before or after one of two 6 week observation periods on standard therapy. The primary endpoint was change in alanine aminotransferase (ALT) values after Rifaximin therapy. Secondary endpoints were change in percentage hepatic lipid assessed by hepatic proton magnetic resonance spectroscopy and change in hepatic and peripheral insulin sensitivity assessed by the hyperinsulinaemic euglycaemic clamp. Patients also had anthropometrics, serum biochemistry and cytokine profiling at each timepoint. Stool and urine were collected for subsequent analysis.

Results 15 patients, 13 male, 2 female, mean (SD) age 48(9.5) years were included. 7 had diabetes on oral hypoglycaemic

medications and 8 did not have diabetes. After 6 weeks of therapy, there was no difference in ALT before, 69 (40)IU/L, and after, 71 (43)IU/L, treatment, $p = 0.7$. Hepatic lipid content was 23.3(12.8)% before and 26.5(15.9)% after Rifaximin, $p = 0.16$. Peripheral insulin sensitivity (Rd) was unchanged, 29.5 (6.5) to 29.4 (10.0) mmol/kg min, $p = 0.91$, hepatic insulin sensitivity (% suppression of endogenous glucose production) was unchanged (35.2(10.1)% to 31.2(13.2)%, $p = 0.35$). There were no significant differences in body mass index, waist and hip circumference, IL 1b, IL6, IL10, IL18, CD14, TNFa, Leptin, Resistin and Adiponectin values with treatment.

Conclusion Treatment with Rifaximin was not associated with changes in markers of hepatocellular damage, hepatic lipid content, cytokine profile or insulin sensitivity in patients with NASH.

Disclosure of Interest None Declared

PTU-114 SEROLOGICAL AUTOANTIBODIES IN HEALTH AND LIVER DISEASE IN A BLACK AFRICAN POPULATION

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Introduction Some pathologic autoantibodies are useful in the diagnosis of autoimmune liver diseases. There is dearth of literature on the prevalence and pattern of autoantibodies in black population of Africans with liver disease, and none from Nigeria. This study sought to determine the prevalence and pattern of autoantibodies among patients with liver diseases and apparently healthy individuals in Nigeria.

Methods The seroprevalence of antinuclear antibodies (ANA), antimitochondrial antibodies (AMA), anti-liver kidney microsomal antibodies (Anti-LKM-1), anti-soluble liver antigen/liver pancreas (Anti-SLA-LP), perinuclear anti-neutrophil cytoplasmic antibodies (pANCA), were analysed in patients with liver diseases and apparently health controls, using ELISA method. Appropriate statistical methods were used for Odds ratio, Pearson Chi square and students' t-test. Significant statistical difference was specified at $p < 0.05$.

Results One hundred and twenty six patients with liver diseases (91 (72.2%) males and 35 (27.8%) females) and 82 apparently normal control subjects (59 (72%) males and 23 (28%) females) were studied over a two year period. The patients consisted of HCC 77 (61.1%), liver cirrhosis 32 (25.4%), chronic hepatitis 10 (7.9%), acute viral hepatitis 4 (3.2%), alcoholic cirrhosis 1 (0.8%) and primary biliary cirrhosis 2 (1.6%).

The control group consisted of Eighty two (82) apparently normal individuals consisting of were recruited over the study period to serve as controls. Of the 126 cases and 82 controls analysed for autoantibodies, except for ANA (107 cases and 67 controls) for autoantibodies only AMA was found to be significantly higher among cases compared with controls. Antimitochondrial antibodies were present in 76 (60.3%) of the cases compared with 36 (43.9%) controls ($p < 0.05$), while ANA were present in 42 (39.3%) of cases compared with 27 (39.7%) controls ($p = 0.68$). Anti-soluble liver antigen (anti-SLA/LP) and pANCA were completely absent among cases and controls Table 2.

Chronic hepatitis had the highest frequency of AMA, being positive in 9 (90%) of the 10 cases, this was followed by HCC, 48(62.3%) of the 77 cases tested were positive for AMA.

Conclusion Serological autoantibodies were equally present in both liver diseases and in health, and would not be sufficient for the diagnosis of autoimmune liver disease in Africans. Therefore, other parameters have to be considered whenever there is a clinical suspicion of autoimmune liver disease among Nigerians.

Disclosure of Interest None Declared