changes in CCL2 expression and activation in the brain during encephalopathy derived from liver failure. 2) Investigate the role of microglial activation and recruitment in the pathogenesis of HE. Methods: Male C57Bl/6 mice were injected with 100 mg/kg of the hepatotoxin azoxymethane (AOM) to induce HE. Mice were monitored for signs of cognitive impairment and brains were collected and dissected prior to neurological symptoms, at the onset of minor and major ataxia, and at coma. In parallel, mice were then injected with 100mg/kg/day of CCR2 antagonist or CCR4 antagonist for three days prior to the injection of AOM. Tissue was collected at the time that coma was reached. Immunofluorescence, immunoblotting, and real time PCR was performed for CCL2, CCR2, and CCR4. Microglia activation was assessed by immunofluorescence against the microglia marker Iba1. Results: CCL2 mRNA expression is greatly increased prior to the onset of neurological decline in the cortex and remains elevated when compared to vehicle-treated controls. CCL2 protein was significantly elevated in the cortex but not the cerebellum as determined by immunoblotting. Immunofluorescence validated this effect and found localized immunoreactivity of CCL2 with the neuron marker NeuN. Correlated with elevated CCL2 expression was increased microglia activation as demonstrated by Iba1 immunoreactivity. Treatment with CCR2 and CCR4 antagonists, which inhibit CCL2 activity, reduced microglia activation and neurological decline of AOM mice. Conclusions: The data demonstrates that CCL2 is upregulated during HE and inhibiting its activity via CCR2 or CCR4 antagonists slows HE progression. This supports that during HE neurons may release CCL2 to recruit and activate microglia leading to pathological inflammation.

Mo1843

Parenteral Fish Oil Reverses Cholestasis in Parenteral Nutrition Associated Liver Disease

Ryan Spurrier, Christa N. Grant, Pui Yuk Yan, Tracy Grikscheit, Russell Merritt

Background: Parenteral nutrition (PN) with conventional intravenous lipid emulsion is often necessary in the treatment of children with short bowel syndrome. PN associated liver disease (PNALD) is a known complication of such therapy and can be fatal. Substitution of parenteral fish oil for conventional intravenous lipid emulsions has shown promise in the treatment of PNALD. Objective: This report describes the initial experience at this institution with parenteral fish oil as treatment of PNALD in pediatric patients. Design: The Institutional Review Board approved this study to evaluate parenteral fish oil as a substitution in parenteral nutrition for pediatric patients who developed PNALD while receiving standard PN with a soybean based lipid emulsion. Cholestasis was defined as serum direct bilirubin >2 mg/dL. Laboratory markers of liver dysfunction including platelet count, international normalized ratio (INR), and direct bilirubin were evaluated. We identified 28 subjects who completed a course of parenteral fish oil lasting at least three weeks. Results: The mean (range) age at enrollment was 126 (37-451) days. The mean (range) duration of parenteral fish oil therapy was 106 (25-344) days. Four deaths and one liver transplant occurred. Among the 24 surviving patients, direct bilirubin dropped by a mean of 4.4 mg/dL(from 5.1 to 0.8), (95% CI: 3.52 - 5.18). Platelet count and serum albumin did not change significantly, while INR actually trended up slightly (from 1.17 to 1.35. Cholestasis was reversed in 23 of 24 surviving patients demonstrating a final direct bilirubin ≤2.0 mg/dL. Among these responders, direct bilirubin fell by an average of 0.13 mg/dL/day. After a mean follow up time of 19.7 months only 26% of patients still required TPN compared to 54% at the completion of therapy. Conclusions: The results of this study support the potential role of parenteral fish oil for pediatric patients with PNALD. We observed resolution of cholestasis in more than 80% of subjects with PNALD after substitution of parenteral fish oil for conventional intravenous lipid.

Mo1844

Predicting Acute Liver Failure in Dengue Infection

Chamila Ranawaka, Madunil A. Niriella, Ravindu S. Kumarasena, Jesenthu K. Miththinda, Arjuna P. De Silva, Ranjan Premarathna, H. J. de Silva

Background: Dengue infections (DI) can range from being asymptomatic to severe illness. Unusual manifestations such as encephalitis, myocarditis, and acute liver failure (ALF) have been recognized. ALF is uncommon, but has a poor prognosis. The aim of this study was to identify predictors of ALF in DI. Methods: Serologically confirmed patients with DI who were admitted to hospital from January 2009 to March 2010 were included. Patients consisted of direct admissions as well as referrals, some with deranged liver functions. Data was obtained from patient records. Clinical details and serum biochemistry was evaluated for up to five days from onset of illness. ALF in DI was defined as evidence of coagulation abnormality [International normalised ratio (INR) ≥ 1.5], and any degree of mental alteration (encephalopathy) in a patient without pre-existing cirrhosis. Results: Out of 240 patients [57.7% male, 42.3% female; mean age 35.6 years (SD 15.4 years)], 164 had dengue with warning signs, 27 had dengue without warning signs and 49 had severe dengue. 15/49 severe dengue patients had profound shock. Abdominal pain, persistent nausea and vomiting (PNV), bleeding, hepatomegaly and ascites were present in 125, 92, 39, 129 and 28 cases respectively. Elevated aspartate aminotransferase (AST), serum bilirubin (SB), alkaline phosphatase (ALP) and gamma glutamyl transpeptide (GGT) were observed in 208, 20, 18 and 60 patients respectively. Of the 240 patients 41 had AST >1000 IU/ml (this included 4/15 with profound shock). 16/41 patients with AST >1000 IU/ml, including 4 with profound shock, developed ALF while none with AST<1000 IU/ml developed ALF. In patients with AST >1000 IU/ml, presence of 2 or 3 of elevated SB, elevated ALP or PNV predicted the development of ALF with 93.8% sensitivity, 98.7% specificity, 83.3% positive predictive value and 99% negative predictive value (Fisher's exact test). Conclusions: Dengue patients with AST<1000 IU/ml are not at risk of developing ALF. Patients with AST >1000 (regardless of presence or absence of profound shock), with 2 or 3 of elevated SB, elevated ALP or PNV seem to be at risk of developing ALF. These findings need to be validated in a larger cohort of patients.

Mo1845

The New Strategy of Autologous Hepatocyte Transplantation to Prevent From Liver Failure After Massive Hepatectomy

Sadahiko Kita, Takamichi Ishii, Takahiro Ochiya, Etsuro Hatano, Toshimi Kaido, Shinji Uemoto

Aims: Postoperative liver failure is one of the most critical complications of extensive hepatectomy for hepato-biliary cancer. Allo-hepatocyte transplantation has been considered as an attractive method for lethal post-hepatectomy liver failure, which could be an alternative to liver transplantation. However, this therapy needs graft hepatocytes from donors and immunosuppressive agents after transplantation. On the other hand, resected livers of patients with hepato-biliary cancers contain not only cancer cells but also large amount of normal hepatocytes. In this study, we aimed to utilize normal hepatocytes that existed in resected livers, and evaluate the effectiveness of autologous hepatocyte transplantation in animal models of post-hepatectomy liver failure. Method: Post-hepatectomy liver failure was induced by 90% hepatectomy in F344 wild-type rats. Graft hepatocytes were obtained from F344 transgenic rats carrying the enhanced green fluorescent protein (EGFP) gene, which helps to distinguish between graft hepatocytes and original residual hepatocytes. The isolated hepatocytes were transplanted into mesenteries of hepatectomized wild-type F344 rats. Approximately 20% of all isolated cells from a F344 EGFP rat liver were transplanted to each recipient. We evaluated the engraftment of the transplanted cells using trans-illuminator, their hepatic function at the implanted sites by immunohistology, and their effects on survivorship of extensive hepatectomized rats. To evaluate the function of transplanted hepatocytes, we transplanted normal hepatocytes into the mesenteries of Nagase analbumin rats (NARs), and measured the serum level of albumin. And, we examined whether transplanted liver cells stimulate regeneration of remnant liver by measuring remant liver/ body weight ratio. Result: The transplanted cells were successfully engrafted into recipients' mesenteries, which were confirmed by detecting green fluorescence and immunohistochemistry at 3 and 7 days after transplantation. At 7 days after transplantation, the survival rate of the hepatocyte transplantation group (69.2%) was significantly improved (p=0.00043) in comparison to that of the non-transplantation group (7.7%). And, the serum albumin level of the transplanted NARs continued to increase just after cell transplantation till 16 hours after transplantation, and then gradually decreased. Moreover, at 2 days after transplantation, the remnant liver/ body weight ratio in transplantation group was a little higher than that of the non-transplantation group. Conclusion: This study demonstrates the engraftments and liver functions of the transplanted hepatocytes, which could lead the improvement of the survivorship. Our results open the doors to the possibility of the autologous hepatocyte transplantation to prevent from post-operative liver failure

Mo1846

Bilirubin As a Predictor of Short Term Prognosis in End Stage-Patients With Chronic Liver Disease

Jorge A. López-Velázquez, Varenka J. Barbero-Becerra, Vicente Sánchez-Valle, Norberto C. Chavez-Tapia, Misael Uribe, Nahum Mendez-Sanchez

Background: Acute on chronic liver failure is characterized by a sudden deterioration of liver function due to liver injury itself or extrahepatic precipitating factors which lead to end-organ dysfunction. This condition shows a high incidence of short and medium term mortality about of 50-90%. Complex prognostic scores have been described to assess the prognosis of this lethal disease. Nevertheless, in order to find an accurate marker to predict outcome at end-stage cirrhotics, we proposed that bilirubin, a simple liver function marker which is widely used by prognostic scores in hepatology, might be a suitable marker to evaluate the outcome in acute on chronic liver failure patients. This could help to prioritize those patients in which liver transplantation is the only therapeutic choice. Aim: This study aimed to investigate the role of bilirubin in predicting short term prognosis in acute on chronic liver failure patients. Methods: We carried out a retrospective cohort study of patients with diagnosis of acute on chronic liver failure with at least 1 week follow-up during 7 years (2005-2012) in a University hospital (Medica Sur Clinic & Foundation). Demographic, clinical and biochemical variables (creatinine, international normalized ratio, sodium, conjugated and unconjugated bilirubin and albumin) were analized to draw the receiver-operating-characteristic-curves (ROC) at the first day hospital admission and the outcome patient at one week. Results: In a cohort of 66 patients, 32/34 (women/men), with an age average of 64 (range 25-87 years). Chronic liver failure was secondary to: Hepatitis C virus infection (n=20), criptogenic cirrhosis (n=27), alcoholic liver disease (n=16) and hepatocellular carcinoma (n=3). The majority of patients (59%) died within 1 week follow up. At the first day hospital admission, the AUCs data from conjugated bilirubin (0.757; 95%CI 0.636-0.877; P=0.000), unconjugated bilirubin (0.731; 95%CI 0.606-0.857; P=001) and total bilirubin (0.751; 95%CI 0.629-0.873; P=0.001) were significantly higher. Accordingly to the outcome patient AUCs values, conjugated bilirubin (0.821; 95%CI 0.719-0.924; P=0.000), unconjugated bilirubin (0.883; 95%CI 0.798-0.969; P=0.000), total bilirubin (0.875; 95%CI 0.787-0.962; P=0.000) were significantly higher (Figure) than the first day hospital admission values. Unconjugated bilirubin seems to be the most predictive outcome value in acute on chronic liver failure patients. Conclusions: Bilirubin could be a suitable marker in the prediction of short term prognosis in acute on chronic liver failure patients. High levels of unconjugated bilirubin may predict accurately the outcome of acute on chronic liver failure patients.