POSTER PRESENTATIONS

ACUTE LIVER FAILURE

P01 A WELL REPRODUCIBLE PORCINE MODEL OF ACETAMINOPHEN INDUCED ACUTE LIVER FAILURE OFFERS DEFINED SURVIVAL TIMES

C. Thiel[1], K. Thiel[1], A. Etspueler[1], M. Morgalla[2], S. Rubitschek[1], S. Schmid[1], W. Steurer[1], A. Königsrainer[1], M. Schenk[1] [1]University Hospital Tuebingen, Tuebingen, Germany; [2]University Hospital Tuebingen, Tuebingen, Germany

Background and aims: Severe intoxication following acetaminophen overdose is the most common cause of acute liver failure in many western European and North American countries. A reproducible large animal model of acetaminophen intoxication has not been successfully evaluated previously.

Methods: Eight male pigs underwent an acetaminophen intoxication receiving an initial enteric bolus of 250 mg/kg body weight acetaminophen followed by acetaminophen plasma level (300–450 mg/L) adapted enteric maintenance dose of 1000–3000 mg/h to the onset of acute liver failure (prothrombin time value <30%). Vital and ventilation parameters were continuously recorded until death. Saline, hydroxyethylstarch, fresh frozen plasma and erythrocytes units were used for volume substitution, norepinephrine to prevent severe hypotension.

Results: All animals developed acute liver failure after a median of 24 (20–30) hours, which was confirmed by laboratory values, clinical course and histologic examinations. All animals died due to acute liver failure after further 21 (16–32) hours, precipitated by cerebral oedema.

Conclusions: Using an initial enteric acetaminophen bolus, followed by body weight adapted acetaminophen plasma level intoxication it was possible to establish a reproducible, clinically relevant porcine model which may be used for the investigation of novel therapeutic approaches in this life threatening condition.

P02 EFFECTS OF LARGE PORE HEMOFILTRATION IN A SWINE MODEL OF FULMINANT HEPATIC FAILURE

O. Detry[1,2], N. Janssen[1,2], J.-P. Cheramy-Bien[1,2], J.-O. Defraigne[1,2], P. Delanaye[3], B. Lambermont[3] [1]University of Liège, CHU Liège, Liège, Wallonia, Belgium; [2]University of Liège, CHU Liège, Liège, Wallonia, Belgium; [3]University of Liège, CHU Liège, Liège, Wallonie, Belgium

Introduction: Systemic inflammatory response might be involved in pathogenesis of brain oedema and intracranial hypertension complicating fulminant hepatic failure (FHF), by inducing an increase in cerebral blood flow and brain water content. We recently demonstrated in endotoxic shock models in the pig, that large-pore membrane hemofiltration (LPHF) with a 80 kDa cutoff may induce a significant IL-6 and IL-10 clearance and an improvement of hemodynamic stability and survival. In this study, we used the validated ischemic FHF model in the pig, to evaluate the effects of this 80 kDa LPHF on intracranial pressure (ICP) and cerebral blood flow (CBF) and on hemodynamic parameters, in relation with the clearance of proinflammatory cytokines and the blood liver tests.

Methods: Fifteen pigs were randomised in three groups: sham, FHF, and FHF + LPHF. FHF was performed by porto-caval anastomosis and hepatic artery and bile duct ligation. All pigs were monitored over the following 6 hours. In the FHF + LPHF group, LPHF was instituted for 4 hours, from Time 2–6 hours. Hemodynamics, CBF and ICP were continuously recorded. AST, aromatic amino acids, total bilirubin, glucose, lactate, IL-6, IL-10, TNFα, were collected before liver devascularisation (T0), and after two (T2) and 6 (T6) hours.

Results: The FHF groups developed blood characteristics of liver failure, without difference between FHF, and FHF + LPHF, two groups that developed intracranial hypertension. Despite a cytokine clearance, there was no significant difference in CBF and ICP between FHF and FHF + LPHF.

Conclusions: In this ischemic FHF pig model, LPHF with a 80 kDa cutoff did not improve liver tests, nor CBF or ICP.

P03 LIVER TRANSPLANTATION FOR ACUTE HEPATIC FAILURE DUE TO CHEMOTHERAPY-INDUCED HEPATITIS B VIRUS REACTIVATION IN LYMPHOMA PATIENTS

T. Noterdaeme[1], L. Longrée[2], C. Bataille[3], A. Deroover[1], A. Lamproye[4], J.J. Delwaide[4], Y. Beguin[5], H. Pierre[1], O. Detry[1] [1]CHU, Liège, Belgium; [2]CHC, Liège, Belgium; [3]CHR Huy, Huy, Belgium; [4]CHU, Liège, Belgium; [5]CHU, Liège, Belgium

Hepatitis B (HBV) reactivation induced by chemotherapy is a recent problem encountered in the management of malignant diseases. Chemotherapy-induced HBV reactivation may ultimately lead to terminal acute liver failure. Liver transplantation (LT) remains currently the only definitive treatment option for such cases, but is generally denied to patients suffering from malignancy. Herein, the authors describe two cases of cancer-free and HBV graft re-infection free survivals after LT performed for terminal liver failure due to HBV reactivation induced by chemotherapy for advanced stage lymphoma. These two cases, and some other reports in the literature, may suggest that patients suffering from hematologic malignancies and terminal liver disease should be considered for LT, if the prognosis of their hematologic malignancy is good.

P04 ACUTE LIVER FAILURE BY AMANITIN INTOXICATION: LIVER TRANSPLANTATION OR WAIT FOR SPONTANEOUS REGENERATION? EVALUATION OF PROGNOSTIC INDICATORS IN A PORCINE MODEL

C. Thiel[1], K. Thiel[1], K. Scheuermann[1], E. Hawerkamp[1], A. Diewold[1], W. Klingert[1], J. Lauber[1], M. Morgalla[2], A. Königsrainer[1], M. Schenk[1] [1]University Hospital Tuebingen, Tuebingen, Germany; [2]University Hospital Tuebingen, Tuebingen, Germany

Background: Acute liver failure caused by drug ingestion, viral hepatitis or poisoning is still associated with an extremely high mortality rate. Liver transplantation remains the life-saving therapy for all effected individuals, but shortage of donor organs remains the limiting factor. Aim of this study was to simulate the clinical course of α-amanitin intoxication in a pig model. Prognostic indicators for spontaneous liver regeneration were evaluated.

Methods: Seven male German landrace pigs received 5 mg (0.15 mg/kg body weight) ($n = 4$) α-amanitin intravenously or 10 mg (0.35 mg/kg body weight) ($n = 3$) intraportally. Pigs remained under deep general anesthesia until conclusion of the study protocol. Ventilation and vital parameters were recorded continuously, laboratory values including TNF-α as a potential regeneration marker were analysed every 8 hours, liver biopsies were taken every 24 hours.

Results: All pigs 100% (8/8) developed acute liver failure, which was defined by a prothrombin time below 30% within 40 ± 8 hours. All pigs receiving 10 mg amanitin died due to multi-organ failure. Pigs which received 5 mg amanitin survived poisoning. They recovered spontaneously after 50 ± 14 hours in acute liver failure and were euthanized after 112 hours, when prothrombin time returned to levels above 50%. Clinical, biochemical and histological signs of liver regeneration were recorded. Laboratory values started to recover 96 ± 7 hours after intoxication paralleled by clinical stabilisation. TNF-α levels in the regenerating animals were significantly higher starting from 48 hours after intoxication. First histological appearance for regeneration could be detected by Ki67 immunostaining 72 hours after intoxication in liver biopsies.

Conclusions: TNF-levels and liver biopsies were identified as the first indicators for spontaneous liver regeneration 48–72 hours after intoxication even long time before liver function biochemically and clinically impairs.

P05 MOLECULAR ADSORBENTS RECIRCULATING SYSTEM IN PATIENTS WITH LIVER FAILURE – EXPERIENCE OF A SINGLE ROMANIAN CENTRE

E. Rusu, M. Voiculescu, D. Zilisteanu, E. Mindrut, G. Ismail, S. Ioanitescu, M. Mihaila Carol Davila University of Medicine and Pharmacy, Bucharest, Romania

This is a retrospective, observational study regarding the experience of a single center in the application of the Molecular Adsorbents Recirculating System (MARS) albumin dialysis in patients with liver failure. From January 2002 until October 2010, we performed 58 MARS sessions, in 32 patients, with mean age 38.7 ± 19.1 years. The etiology of liver failure was: acute liver failure (ALF) in 10 patients, acute-on-chronic liver failure (AoCLF) in 12 patients, post – liver transplantation (LTx) in 8 patients, and post-hepatectomy in 2 patients. Before starting MARS, 10 patients presented multiorgan dysfunction, 6 patients required mechanical ventilation, 10 patients presented sepsis, 10 patients had renal impairment. In ALF group we noticed an improvement in bilirubin, creatinine and an increase in mean arterial pressure ($P < 0.05$). Of the 10 patients with ALF, 5 patients survived due to their own liver recovery. In AoCLF group, we obtain a significant decrease in bilirubin, creatinine, an increase of sodium and improvement of the MELD score ($P < 0.05$). Two patients survived, two patients were transplanted, and for the remaining patients the mean survival was 26.0 ± 33.3 days. In the post-LTx group, we noticed a significant improvement in bilirubin, creatinine, lactate, and sodium ($P < 0.05$). In this group, one patient was retransplanted, one patient is alive and the mean survival of the other 6 patients was 28.5 ± 39.8 days. MARS therapy was well tolerated and efficiently removed toxins. MARS seems to be a promising therapy for ALF, allowing the patient's own liver to recover or to gain time until transplantation. The timing of treatment initiation and proper patient selection is very important for clinical success. The unfavorable prognostic factors were multiple organ dysfunction and sepsis.