

Commonest cause of death was cardiac related events (24%), followed by sepsis (23%) or liver related complications (14%). Disease duration prior to transplantation, initial presentation with autonomic rather than peripheral neuropathy, TTR mutation, and modified body mass index (mBMI) of <600, indicating poor nutritional status, were identified as significant factors influencing survival after LT ($p < 0.01$).

Conclusion Liver transplantation is rational and effective treatment for FAP with excellent long-term outcomes and 10-year survival >70%. Type of mutation, nutritional status, disease duration and degree of autonomic involvement are significant prognostic factors.

P73 PRELIMINARY RESULTS OF THE STUDY OF ACUTE LIVER TRANSPLANT (SALT): NSAID EXPOSURE AND RISK OF ACUTE LIVER FAILURE LEADING TO TRANSPLANTATION IN 7 EUROPEAN COUNTRIES

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Introduction The risk of acute liver failure (ALF) related to NSAIDs is still discussed and the European Medicines Agency requested a study investigating this. University Bordeaux Segalen conducted the study independently.

Aim To estimate the incidence rates of ALF leading to registration for liver transplantation (LT) in patients exposed to NSAIDs.

Method Multinational, multicentre, case-population study performed in France, Greece, Ireland, Italy, the Netherlands, Portugal, and the UK retrospectively evaluating a 3-year period (2005–2007) in adults. Data of ALF cases were sought through liver transplant registries and hospital records. Demographic and clinical data were collected for all ALF cases and drug use information was collected for the exposure window of 30 days prior to index date (ID, initial symptoms of liver disease). For ALF cases exposed to NSAIDs (ATC code M01A), rate per million treatment-years (tt-yrs) was calculated using sales data from IMS. Poisson CIs (95% CI) were estimated.

Results In the seven participating countries, 62 LT centres were identified and contacted, five were excluded (four paediatric, one oncology), and 50 actively contributed data before database lock. Among the 8824 patients identified from LT lists for the period 2005–2007, 500 were cases of ALF: 197 with identified clinical cause, 21 with incomplete or unavailable medical files, and 241 drug-exposed without identified clinical cause. Among the latter, 34 were exposed to at least one NSAID, 123 exposed to other drugs, and 84 were acute drug intoxications. Mean age of NSAID-exposed ALF cases was 43.8 years, 24 were female. Event rates per million treatment-years were 4.4 (95% CI 3.0 to 6.1) for all NSAIDs pooled, 5.6 (2.4 to 11.1) for nimesulide (8 cases), 5.8 (2.8 to 10.6) for ibuprofen (10 cases), 4.5 (1.5 to 10.4) for diclofenac (5 cases), and 4.7 (1.0 to 13.6) for ketoprofen (3 cases). 71 of the 157 non-intoxication cases had been exposed to paracetamol (9.8 per million treatment-years, 95% CI 7.7 to 12.4), and 83 of the 84 intoxications.

Conclusion In seven countries over 3 years only 34 NSAID-exposed ALF cases leading to registration for LT were identified with no

differences in incidence rates per million tt-yrs among the most used NSAIDs. Non-overdose paracetamol-associated liver failure was twice more common.

P74 HEPATOCYTE TRANSPLANTATION IN RATS WITH ACUTE LIVER FAILURE USING CELLS LABELLED WITH A CLINICAL GRADE MRI CONTRAST AGENT

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Introduction Hepatocyte transplantation is being evaluated as an alternative to orthotopic liver transplant. However, the fate of hepatocytes after transplantation is not well defined.

Aim The aims of the study were to: (1) investigate the possibility of labelling hepatocytes in vitro using superparamagnetic iron oxide nanoparticles (SPIOs), (2) determine the effects of labelling on cell viability and function, and (3) perform in vivo experiments on tracking labelled cells by MRI.

Method Human and rat hepatocytes were labelled in culture for 16 h with clinical SPIOs (12.5 µg Fe/ml) and protamine sulphate (3 µg/ml) as a transfection agent. Cellular iron uptake was determined using Prussian blue staining, and quantified by a ferrozine-based assay. Cell viability and function were assessed using LDH leakage, mitochondrial dehydrogenase activity, [¹⁴C]-leucine incorporation, albumin and urea assays. Effects of labelled cells on T2-weighted images were assessed in vitro using a 7-T MR scanner. Intrasplenic transplantation of 2×10⁷ male rat hepatocytes labelled with SPIOs (n=4) or non-labelled (n=4) was performed in female recipients 28–30 h after acute liver failure induction by intraperitoneal injection of D-galactosamine. Hepatocytes were also marked with the fluorescent dye CM-DiI. A control group (n=4) received medium injection only. T2*weighted gradient-echo images at 7-T MRI were acquired at day 7 post-acute liver failure induction. Transplanted cells were detected in the liver by PCR for the Y-chromosome (Sry-2 gene) and histological analysis.

Results Mean intracellular iron concentrations were 11.4±SE1.1 pg/cell in human and 8.6±0.3 pg/cell in rat hepatocytes. Cell viability and metabolic function were not significantly affected at these SPIO concentrations. In vitro MRI of SPIO-labelled cells (2000 cells/µl) induced a 50% change in T2 relaxivity compared to non-labelled cells. SPIOs were detected in rat liver as a decrease in the MRI signal intensity 6 days after transplantation in the three survivors. On histology most of the SPIO particles were located in Kupffer cells, indicating the loss of iron oxide particles from hepatocytes. In keeping with this, labelled cells could not be detected in the liver by the fluorescent dye or by PCR for Sry-2 gene.

Conclusion Optimum conditions to label human and rat hepatocytes with SPIOs were determined, which did not affect cell viability or metabolic function, and were sufficient for in vitro MRI detection. However, the clearance of hepatocytes after transplantation limits the value of MRI for assessing long-term hepatocyte engraftment.

P75 IMPAIRED CARDIORESPIRATORY RESERVE IN PRIMARY BILIARY CIRRHOSIS PATIENTS UNDERGOING LIVER TRANSPLANT ASSESSMENT

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Introduction It has been previously shown that PBC patients have bioenergetic abnormality in both peripheral and cardiac muscle. In