218 PREDICTION OF IRON OVERLOAD WITH A NEW MASS SPECTROMETRY METHOD FOR DETECTION OF HEPCIDIN IN PLASMA

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Hepcidin (Hep) has emerged as the primary regulator of iron homeostasis. Previous studies on assessing urinary levels of Hep are of limited availability. We have developed a new method for quantifying Hep in plasma by SELDI-TOF mass spectrometry, using the 25-AA peptide as reference standard.

Aims:

1. to assess the performance of this new method in different conditions of iron metabolism disorders;
2. to assess the diagnostic validity of non invasive serum markers in identifying iron overload.

Methods: The following groups of subjects were enrolled into the study: 1. type I hemochromatosis (HE)(n = 10), NAFLD (n = 17), chronic hepatitis C (n = 10), healthy controls – previously enrolled in a general population epidemiological study – with normal ultrasound, normal LFTs, alcohol assumption <20 g ethanol/day, and negative for C282 mutations (n = 155). The following parameters were assayed in each case: plasma Hep, C282Y and H63D mutations of the HFE gene by Taqman probes; serum iron, ferritin (SF), transferrin saturation (TfSat), transaminases, GGT, glucose, insulin, total cholesterol, HDL-cholesterol, LDL-cholesterol, triglycerides.
Results: Plasma Hep levels were significantly higher in HCV+ (26.3±7.2 nmol/L) pts compared to controls ($p < 0.05$), and were positively correlated with SF ($p < 0.001$). H63D heterozygous subjects revealed a pattern of iron overload (significantly higher serum iron, SF, TfSat, and lower Hep/SF ratio) compared to H63D wild type subjects. By analysing data with the Biomarker Pattern 5.0.2. Software, in order to identify the most significant discriminant markers between HE and controls, we obtained a four-terminal node algorithm which included as main splitters Hep/SF ratio, glucose and iron. These variables allowed a correct diagnosis of HE with a 100% sensitivity, 98.6% specificity and AUROC=0.993.
Conclusions: The new plasma Hep mass spectrometry method yields accurate measurements which reflect pathologic and genetic influences; simple non invasive markers (Hep/SF ratio, glucose and iron) can predict the presence of HE.
For Two Study Group

219 LIVER STIFFNESS MEASUREMENT: AN APPROPRIATE SCREENING METHOD TO DETECT LIVER FIBROSIS IN THE GENERAL POPULATION

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Aims and Background: Liver stiffness measurement (LSM) by transient elastography (TE, FibroScan) has been used to detect fibrosis in patients with various types of chronic liver diseases. Our aim was to assess LSM in an apparently healthy population above 45 years and to screen for liver fibrosis and cirrhosis in subjects showing elevated LSM values.
Method: 1358 subjects, randomly assigned for a free medical check-up in a Social Medical Center, were consecutively enrolled in the study. All subjects had a complete medical examination and laboratory tests in additiona to LSM performed the same day by a single operator. The following data were collected: declared alcohol intake, BMI, waist circumference, transaminases, GGT, platelets and mean globular volume, HDL and LDL cholesterol, triglycerides, fasting glucose and serological tests for HBV and HCV. Subjects with LSM values over 8kPa were referred to a liver center.
Results: 238 subjects were not considered for analysis because missing data (n = 23), unreliable LSM values (n = 107) or LSM failure (n = 108). Among the 1120 remaining subjects, 80 (7%) had LSM over 8.0 kPa and 8 (0.7%) had a LSM superior or equal to 14.6kPa. All patients with LSM over 8.0 kPa were referred to a hepatologist and 28 underwent liver biopsy. Cirrhosis was diagnosed in all patients with LSM ⩾14.6kPa (alcoholic n = 4, viral C n = 2, viral B n = 1, metabolic n = 1). Among the 72 subjects with LSM >8 and <14.6 kPa, 45 subjects were overweighted with a metabolic syndrome, 18 were alcoholic, 5 had a chronic hepatitis C and 4 a chronic hepatitis B. Liver fibrosis was observed in all biopsies performed in this group (n = 20), non-alcoholic steatohepatitis (NASH) being associated in 10 cases.
Conclusion: In a group of 1120 individuals reflecting a general population above 45 years, the prevalence of cirrhosis was at least 0.7%. With a threshold of 14.6kPa, the specificity and positive predictive value of LSM for the diagnosis of cirrhosis was 100%. Among the subjects displaying LSM values >8 kPa LSM was highly predictive of liver fibrosis, associated with NASH in 50% of the cases.

220 PREDICTIVE FACTORS OF TRANSPLANT FREE SURVIVAL IN PATIENTS WITH FULMINANT AND SUBFULMINANT HEPATIC FAILURE: RESULTS FROM A RANDOMIZED CONTROLLED MULTICENTER TRIAL

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In this prospective, controlled, randomized, 16 centers study, patient with fulminant or subfulminant hepatic failure were randomized, once they met the Clichy or King's College criteria for liver transplantation, either to a conventional treatment (CONV) or to MARS® combined to CONV. Stratification was added according to paracetamol etiology. We reviewed predictive factors of death and of transplant free survival in the current criteria while awaiting liver transplantation.
Results: From August 2004 till December 2007, 102 patients (49 CONV, 53 MARS; 57% females) with a mean age 40.4±13 years (extremes 18–70 years), were included in the Intent To Treat (ITT) analysis. The main etiology of ALF was due to paracetamol (38%, 19 CONV, 20 MARS). At inclusion, 32 patients were under mechanical ventilation (13 CONV, 19 MARS), grades of encephalopathy and mean values of ALAT:4455±4862 IU/L, total bilirubin:191±181 μmol/L, INR:8.3±4.1, factor V:17.8±10.8% and creatinine:210±175 μmol/L were not significantly different in both groups. There was a trend in improvement in the MARS group for the 6 month survival rate (84.9% vs 75.5%) and mainly in paracetamol group (85% vs 68.5%) but it did not reach statistical significance. Overall 68/102 patients were transplanted (82.5% in the non-paracetamol group and 41% in the paracetamol group; $p < 0.0001$) with a median delay listing-incision of 16.2 hours. Univariate analysis showed that at inclusion MELD score ⩾40 ($p = 0.02$), low mean Aortic Pressure ($p = 0.0003$), high neutrophil count ($p = 0.046$), low fibrinogen ($p = 0.05$), high creatinine ($p = 0.02$), high lactate ($p = 0.003$), low total proteins ($p = 0.01$), high LDH levels