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METADOXINE IN ACUTE ALCOHOL INTOXICATION: A DOUBLE BLIND RANDOMIZED PLACEBO CONTROLLED STUDY

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Background. At present there are only preliminary clinical results on the efficacy of metadoxine (pyridoxol L-2-pyrrolidone-5-carboxylate) in acute alcohol intoxication. Aim of this study was to investigate the effectiveness of metadoxine in the management of patients affected by acute ethanol intoxication. Methods. A double-blind, randomized multicenter, placebo-controlled trial was carried out on 58 patients with acute ethanol intoxication. Patients were treated with a single dose of 900 mg i.v.metadoxine (n=29) or with placebo (n=29). Patients were clinically and biochemically evaluated at 0.5, 1, 2, 3, 6, 9, 12 hrs after treatment. Results. Treatment with metadoxine significantly decreased the half-life of ethanol in blood (from 6.70 ±1.84 to 5.41 ±1.99 hrs; p<0.013) showing a faster rate of ethanol elimination. The effects on ethanol half-life in blood were accompanied by a faster onset of recovery from intoxication, defined as the time of the transition of blood ethanol levels to the immediately lower range defined by intoxication categories (in g/L: 0 to 0.5 absent; 0.51 to 1.0 mild; 1.1 to 2.5 moderate; > 2.5 severe). Thus the median time to onset of recovery was 0.95 h with metadoxine and 2.34 h with placebo (p=0.013). The effects of treatment on blood alcohol levels were paralleled by a significant decrease in the rating of the toxic clinical symptoms (agitation, aggressive behaviour, mental impairment and jerky movements). At 1 hr the proportion of patients (15/29) showing a decrease in toxic score (>25% of maximum) was significantly higher (p<0.02) than in the placebo group (6/29). At 2 h the improvement of toxic symptoms (in per cent of maximum possible) was 68 ± 28 vs. 44 ± 27% in controls (p< 0.002). Conclusions. In patients with acute ethanol intoxication metadoxine accelerated the elimination of ethanol from blood, leading to faster recovery from intoxication, and improved the behavioural toxic symptoms. Metadoxine could be helpful in the management of acute ethanol intoxication.

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MELD (MODEL FOR END-STAGE LIVER DISEASE) IS MORE ACCURATE THAN MADDREY DISCRIMINANT FUNCTION IN ORDER TO PREDICT SURVIVAL OF PATIENTS WITH ALCOHOLIC HEPATITIS (AH).

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Introduction. Discriminant Function (DF) of Maddrey is up today the predictive score used in AH, even if it includes a non standardized variable (PT measured in seconds). New prognostic scores including liver and renal function need to be evaluated in AH, which severe form is caracterized by bad prognosis, multiorgan failure and no successfull therapy. Aims. We evaluated traditional prognostic scores (DF, CCLI, Chil-Pugh) and clinical/biochemical parameters in patients (pts) with diagnosis of AH admitted to our Unit from January 1997 to October 2001. Methods. We studied 30 consecutive pts with clinical diagnosis of AH [1]. Pts with HBV/HCV infection, HCC, bacterial infections at admission and obstructive jaundice were excluded. 11 patients with DF>32 underwent to corticosteroid treatment. Clinical and biochemical assessment at admission and after seven days was performed; comparison between pts died by 60 days from admission (Short-Term Mortality [S-T-M]) and survivors was then made. Results. 15 (50%) pts died (M/F= 2; average age ±SE= 53 ±3 yrs) and 15 survived (M/F= 2; 53 ±2 yrs). S-T-M rate in severe AH (DF>32) was 65%. Hepato-Renal Syndrome (HRS) was the first cause of death (47%). Liver cirrhosis was present in 83% of pts. DF at admission and after 7 days confirmed to be the best sensitive and predictive score, while plasmatic creatinine showed the highest specificity (100%). So we tried to apply MELD score, which includes creatinine value, to our group of pts. Multivariate analysis of all parameters and scores selected MELD as the only indipendent variable affecting S-T survival. Then we compared MELD and DF using ROC curves obtaining a c-statistic respectively of 0.911 ±0.056 and 0.867 ±0.064. Corticosteroid treatment was not selected as predictor of survival. Conclusions. Renal function impairment is a critical event in determining outcome of pts. with AH. MELD score, which has been validated only in chronic liver disease, seems to be the most valuable score in predicting survival also in our series of AH. If our data will be confirmed in larger series, MELD should be considered in order to identify patients suitable for more aggressive, specific treatment protocols.

[1] International Group, Lancet 1981 Mar 28: 707-11.

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SUSTAINED ALCOHOL ABSTINENCE IMPROVES BIOCHEMICAL PARAMETERS IN PATIENTS WITH CHRONIC ALCOHOLIC LIVER DISEASE.

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BACKGROUND: Long-term alcohol abuse is one of the most important cause of chronic liver damage. Prolonged abstinence is considered the basis of alcoholic liver disease treatment.
AIMS: To assess biochemical liver improvement after prolonged alcohol abstinence in comparison with continuous alcohol consumption.
PATIENTS AND METHODS: We analysed 102 patients with chronic alcoholic liver disease. Alcohol intake was more than 150-200 g/daily for at least 5 yrs. 51 pts (36 M and 15 F, mean age 52.8, range 27-78 yrs) initiated alcohol abstinence after diagnosis and maintained it for at least 12 months. A second group of 51 pts (37 M and 14 F, mean age 52.6 yrs, range 25-77 yrs) continued alcohol abuse. Serum parameters were verified after 12 months. Data were analysed by t test and chi-square test.
RESULTS: Significant decreases of mean AST level (41.8 ±4.0 vs 78.7 ±9.5 IU/L, p<0.0001), GGT (63.7 ±9.5 vs 147.2 ±32.2 IU/L, p<0.009), and total bilirubin (1.7 ±0.2 vs 2.4 ±0.4 mg/dL, p<0.008) were observed in abstinent patients. Unexpectedly, in drinking patients significant decreases were found for AST (87.0 ±11.9 vs 104.6 ±10.0 IU/L, p<0.04), GGT (305.6 ±58.1 vs 462.4 ±87.0 IU/L, p<0.005), and MCV (97.0 ±1.1 vs 99.7 ±1.3 fL, p<0.0004); significant increases were observed in serum albumin (3.8 ±0.1 vs 3 5 ±0.1 g/dL, p<0.0001), and platelet count (175,896 ±15,252.4 vs 128,188 ±10,983.6/mcL, p<0.0001)
The analysis of paired data for each patient showed a significantly higher rate of normalization for AST (16 vs 5 pts, p<0.02), GGT (14 vs 2 pts, p<0.004), total bilirubin (9 vs 3 pts, p<0.003), albumin (20 vs 2 pts, p<0.003), and platelet count (16 vs 6 pts, p<0.04) in abstinent vs drinkers. Moreover, this latter group of patients showed a significantly higher rate of worsening for AST (9 vs 1 pts, p<0.03), ALT (10 vs 2 pts, p<0.04), GGT (15 vs 2 pts, p<0.002), total bilirubin (12 vs 1 pts, p<0.004), MCV (15 vs 2 pts, p<0.002), albumin (10 vs 2 pts, p<0.04), and platelet count (9 vs 1 pts, p<0.03).
CONCLUSIONS: Our findings show that in chronic alcoholic liver disease sustained alcohol abstinence may lead to an improvement of biochemical parameters, whereas prolonged drinking may induce a worsening of laboratory parameters in some, but not all, patients with continuous drinking.

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NASH AND HOME PARENTERAL NUTRITION: HEPATIC SIDEROSIS A ROLE IN DISEASE PROGRESSION?

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Nonalcoholic steatohepatitis (NASH) is a significant form of chronic liver disease in adults and children. Pathology ranges from indolent to end-stage liver cirrhosis. Among the different condition and agents that cause NASH (drug-induced steato-hepatitis, severe insulin resistance, occupational hepatotoxicity, diabetes mellitus, obesity, hyperlipemia, rapid weight loss, jejunoileal bypass) total parenteral nutri-tion (TPN) needs to be mentioned specially in patients with short bowel syndrome.
While steatosis, hepatocyte ballooning degeneration, mild acute and chronic inflammation and perivenular, perisinusoidal collagen deposition are the specific histological criteria for the diagnosis, iron deposition is also reported in 15-55% of NASH biopsies reviewed. As in our previous report, concerning liver biopsies of 6 patients maintained with home TPN, we described NASH, siderosis and fibrosis in this study we investigate the cause of siderosis and the role of iron in the progression of liver disease.
In the same six patients (3M; 3F) who underwent liver biopsy because home TPN and abnormal liver function tests, we studied iron metabolism: serum transferrin saturation, iron and ferritin serum levels and oral intake of iron. Hepatic siderosis and fibrosis were respectively assessed semiquantitatilvely by iron staining with SCHIOT index and by stains for collagen using BRUNT score staging. TGF- β and CD4/CD8 were detected in liver biopsies while HFE genetic mutation was checked in serum. Correlation test was used to define the interrelationship among parameters.
Our results show that NASH occurred in 16.6% while fibrosis and siderosis respectively in 83 and 100% of patients treated with TPN. Normal values of serum iron and transferrin saturation levels and a raised serum of ferritin level were de-tected in patients. Oral intake of iron is obviously low in patients but significantly (r=0.9) correlate with SCIOT index.
SCIOT index is also significantly (r=0.96) cor-related with BRUNT score.
These data point out that: a) patients surviving because the use of TPN have a moderate risk for NASH and an high risk for fibrosis and siderosis; b) hepatic siderosis could be considered a marker of disease progression.