POSTER ABSTRACTS

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MORPHOLOGICAL FINDINGS ON RAT HEPATOCYTES IN ACUTE ALCOHOLIC INTOXICATION AND AFTER *TROFOPAR* TREATMENT

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Objective: The allyl alcohol (AIIyA) induced liver damage is characterized by membrane destruction and cell necrosis. Considering the Romanian liverprotecting drug *Trofopar'* as a natural structure isolated from the cell membranes, we proposed to determine the ultrastructural changes on rat hepatocytes in acute AIIyA intoxication and after *Trofopar'* treatment.
Methods: We investigated 4 groups (10 animals/group) of male Sprague-Dawley rats, weighing *150* g: 1st-control group, IInd - *Trofopar"* treated, IIIrd - intoxicated with AllyA 1% by stomach tube 0.5 ml/lOOg.b.w., daily, for 3 days, IVth- intoxicated with AllyA and then treated with *Trofopar'* s.c. 7mg/100g.b.w. at 0,6,24 and 36 hours. After sacrification (48 hrs after the treatment start), liver samples were fixed in 3% glutaraldehyde sol., dehydrated and included in Vestopal W. Thin sections (60µm) were cut, contrasted and examined at the electron microscope BS 500 TESLA.
Results: Alcoholic intoxicated cells showed: increase of the smooth endoplasmic reticulum, decrease ofglycogen content, vacuolization of the mitochondria matrix, lipid accumulation, perisinusoidal and interhepatocitar collagen proliferation and destruction of the liver parenchyma structure. The *Trofopar'* treatment determined:
mobilization of the lipids from the hepatocytes, cell ultrastructure recovering, disappearance of autophagolisosomal cell damage, increase of glycogen and biomembranes synthesis.
Conclusion: The acute alcoholic intoxication with AllyA induces severe ultrastructural changes of the hepatocytes. The *Trofopar"* treatment determines a very good restoration of the hepatocytes structures and functions.

Serum leptin concentration and leptin receptor levels in patients with fatty liver

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OBJECTIVE: Leptin, peptide hormone synthesized in adiposities, acts as a signal molecule, which takes part in regulation of body weight, fat mass and energy homeostasis via interaction with specific receptors. Liver tissue is one of organs with proved leptin receptors.
SUBJECTS: The aim of this study was examination of leptin (L) and leptin receptor (LR) levels in blood of patients with fatty liver.

METHODOLOGY: We investigated 14 patients (4 women,10 men, average age 43.2 yr with liver steatosis, diagnosed on ultrasound/histology. Diabetes mellitus in 50%, alcohol overconsumption in 29%. Serum concentrations of L and LR were assayed by ELISA method. Other laboratory examinations included analysis of lipids, blood glucose, liver enzymes, body mass index (BMI), percent body fat by bioelectrical impedance analysis (BIA).

RESULTS: Average levels: L 10.22 ng/mL, LR 48.59 U/mL, BMI 28.6, LPILR 0.30, LPIBMI 0.34, body fat 28% cholesterol 5.68 mmol/L (increased in 64%), triglycerides 2.59 mmol/L (increased in 22%). Increased values: transaminases 79%, bilirubin 15%, alkaline phosphatase 7%.
CONCLUSIONS: Leptin level in human body is result of many physiological interactions. On the other hand also many pathological conditions can influence this values. That is why interpretation of results is not unambiguous. Basal L level was increased in 71%, decreased in 22%. LR level increased in 43%, decreased in 43%, obesity was present in 79% according to BMI, in 50% according to BIA. Possible trends are suggested, but further studies on broader group of patients are needed. The study was supported by the grant GA- MZI8-3.

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Causes of non-alcoholic steatohepatitis in **2** five year prospective study.

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Aim of study: To establish the etiology of non-alcoholic steato hepatitis (NASH) in a randomized group of 100 individuals.

Material and method: 100 liver biopsies showing steatosis were studied after excluding alcoholic liver disease (by anamnesis, Michigan Alcoholism Screening Test, elevation of GGT, perivenular and perisinusoidal fibrosis. The etiology of steatosis was established based on medical records, drug history, physical exam, blood sugar, cholesterol, triglicerides, ASAT, ALAT, copper, ceruloplasmin, viral markers, other histological findings.

Results: The prevalence of NASH was 8% of all liver biopsies; 85% were individuals in the 5th or 6th decade; 60% were females. Obesity was the main etiology (75%), in 65% associated with dislipidemia and in 38% with diabetes; 10% had no-obese diabetes, 8% chronic viral C hepatitis, 4% chronic viral B hepatitis, 2% ulcerative colitis, 1% Wilson disease. All subjects had macrovesicular steatosis. Particular histological aspects were described in chronic hepatitis (portal and periportal inflammation and necrosis), in ulcerative colitis (periductal fibrosis) and in Wilson disease (Mallory bodies and positive copper stain).

Conclusion: NASH is infrequent (8% from all biopsies); it appears mainly in 50-60 year old women; obesity and associated diseases like dislipidemia and diabetes represent the main etiology (75%), followed by non-obese diabetes, chronic hepatitis, especially C, ulcerative colitis and Wilson disease.

TREATMENT OF ACUTE ALCOHOLIC HEPATITIS WITH GLUCOCORTICOSTEROIDS-PROGNOSTIC FACTORS

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Introduction. Acute alcoholic hepatitis(AAH) has an high mortality rate and any treatment that could reduce this rate is to be considered. The aim of our prospective study was to investigate the survival rate at one year after starting a treatment with corticosteroids (Prednisolone).

Material & methods. We studied 2 groups of patients with AAH, one group A of 50 patients (21F,29M with a mean age of43.6+/- 12.3 years) treated with 4Omg Prednisolone I-day and a second group B of subjects with AAH (21F,29M with a mean age of 46.2+/- 14.5 years) treated with placebo.

Both groups were evaluated one year after for survival rate . Meanwhile we performed a regression analysis in order to identify other possible prognostic factors(age, sex, alcohol consumption, hepatic steatosis or fibrosis on biopsy, hepatic transaminases).

Results. The survival rate at one year in the first batch with treatment with Prednisolone was 62%. In the second group of patients treated with placebo the survival rate was of 49% $p<0.05$, Student t test).

Conclusions. We conclude that the treatment with Prednisolone in acute alcoholic hepatitis improves the one year survival rate, in association with other possible prognostic factors ,independent from the treatment.

In vitro Zinc Modulation of Leukocytic Phagocytosis in Peripheral Blood of Chronic Alcoholic Hepatitis

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In our study we have investigated *in vitro* effects of *Zincor* (100 mg $ZnSO_4$ and 10 mg prednisone tablet) and *Unizinc* (KVP GmbH - 400 mg zinc and 100 mg aspartat/tablet) solutions with physiological sera, on leukocytes phagocytosis in the venous blood of 14 Chronic Alcoholic Hepatitis (CAH) patients and in 10 healthy people of about the same age, as controls. The phagocytic capacity of leukocytes was performed by the Latex Phagocytic Index (LPI%) and NBT tests. All testes were performed in basal conditions and after 30 mm. preincubation with 0.1 solutions of *Zincor* and *Unizinc,* separately used. The results indicated in the blood of normal persons, a decrease of phagocytic tests after preincubation with *Zincor* (NTB. 7.82±.75%, LPI: 51.61±1.26%) and an insignificant decrease after *Unizinc* preincubation (NBT: 7.89±1.12%, LPI:55.18±1.32%) than those in basal conditions (NBT: 9.25±2.21%, LPI: 59.92±1.22%). Both *Zincor* ~T: 6.97±1.21%, LPI: 47±1.33%) and *Unizinc* (NBT: 8.9±3.78%, LPI: 52.03±1.01%) induced an increase of phagocytic tests in peripheral blood of CAH patients than those in basal conditions (NBT: 6.48±2.35%, LPI: 45.4±1.25%). The results suggest that zinc is effective in CAH treatment as a support of phagocytic capacity, which is decrease by ethanol misuse, as well as an antioxidant.

Key words: zinc, NBT, LPI, leukocytic phagocytosis, chronic alcoholic hepatitis.

IN VITRO OXII)ATIV STRESS MODULATION IN LIVER ALCOHOLIC STEATOSIS

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In our study we investigated the oxidative balance determining Superoxide dismutase (SOD) and Glutathion (GSH) levels in 12 patients diagnosed with liver alcoholic steatosis (LAS) and 5 normal peoples, about the same age, as controls. SOD and OSH levels were performed in 30 mm. preincubated blood samples (2 ml) with vitamin E (0.2 ml) and in basal conditions, without vitamin E. SOD and GSH were determinate by rephractometrical method using the NBT (nitroblue tetrasolium) for SOD and DTNB (dithiobis nitrobensoic acid), for OSH. The results indicated higher levels of SOD (7.514±1.323) and OSH (584.45±65.01) in peripheral blood of LAS patients than that in the controls: SOD (5.592±0.794) and GSH *(537.14±26.52).* After the preincubation with vitamin E, the results indicated an increase in SOD (16.02±1.92) and GSH (1108±50.73) levels than that in basal conditions, as well as than in preincubated with vitamin E samples of controls:

SOD (9.238±2.163) and GSH (876.23±30.56). These results suggest that in LAS patients the oxidative stress is more intense than in healthy people of same age, that probably interfere in liver injuries, and vitamin E in this proportion is an effective free radicals scavenger in the peripheral blood of these patients.
Key words: liver alcoholic steatosis, oxidative stress, SOD, GSH, vitamin E.

HIALURONIC ACID IN LIVER STEATOSIS

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Hialuronic acid (HA) is postulated to be a noninvasive marker of liver fibrosis. It plays a structural role in the connective tissue matrix (proteoglikan) and participates in various cell to cell interactions.

The aim of the study was to evaluate HA concentrations in correlation with liver morphology and along with classical biochemical parameters of liver function in fatty liver disease, associated with alcohol abuse and chronic hepatitis **C.**

The study group consisted of 37 persons: 8 with chronic hepatitis C with liver steatosis, 8 patients with chronic hepatitis C without liver steatosis, 8 patients with fatty liver associated with alcohol abuse and 13 healthy volunteers as controls. In all 24 patients liver biopsy was performed. The HA serum concentrations were measured with enzyme-linked protein binding assay (Chugai Co., Japan). Obese and overweight patients were not included.

Results: hialuronic acid concentrations were significantly higher among patients with liver steatosis associated with chronic C hepatitis (95,5 ng/mL ± 40,3) as well as alcohol abuse related (102,4 ng/mL ±*56,6)* than in controls (56,9 ng/mL ± 17,8) and than in chronic hepatitis C patients without steatosis *(36,5* ng/mL ± 13,0). Among chronic hepatitis C patients steatosis was associated with older age (49 vs 25), higher stading grade (3 vs 1) and more active inflammation, according to Bianchi scoring (1997). Hialuronic acid concentrations correlated with OPT

activity in both groups of chronic hepatitis patients with and without steatosis (p<0,00l). The HA concentration in alcohol abusers group and chronic hepatitis C patients differed insignificantly.

Hialuronic acid may be a complementary parameter in diagnosis of liver steatosis.

Toxicity of acetaldehyde and ethanol in SK-Hep cells and amelioration by UDCA and TUDCA

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Ethanol and its highly toxic metabolite, acetaldehyde, induces a series of adverse cellular effects. Time- and concentration-dependency of ethanol-induced cytotoxicity on hepatocytes seems to be well investigated. In contrast little is known about the product of ethanol metabolism acetaldehyde. Therefore, the aim of this study was to investigate the ethanol and acetaldehyde induced cytotoxicity and the possible protective effects of UDCA and TUDCA.

Methods: The human hepatic tumor cell line SK-Hep has an manifold higher alcohol dehydrogenase (ADR) activity compared to HepG2. Cells were incubated for 24h at 37^0C in ot-MEM medium in the presence of increasing ethanol concentrations (0-100 mM; the physiological dosage in a heavy drinker) and acetaldehyde (concentrations 0-2.5 mM) with and without the bile acids UDCA, TUDCA (0-200 MM), respectively. Hepatotoxicity was assessed by the metabolic activity of the mitochondrial electron transport chain which was determined by means of the WST-1 reduction test. Activity of lactate dehydrogenase (LDH) served as an indicator of leakiness of the cell plasma membrane. All experiments were repeated 6-fold. Morphological appearance of the cells was determined microscopically.

Results: Metabolic activity of SK-Hep cells after 24 h incubation with ot-MEM medium was set to 100 % and was used as control. Addition of 3.5 mM acetaldehyde decreased metabolic activity by 37 % (p<0.002). Simultaneous incubation of I .5mM acetaldehyde with 100 MM UDCA yielded a decrease of 23 % (p<0.002) of the control activity and lead to an improvement by 14 % (p< ***0.05).*** When 100 MM TUDCA was used instead of UDCA metabolic activity decreased by 30 % (versus control p<0.002, versus 1.5 mM acetaldehyde p< *0.05).* 100 mM ethanol showed similar though more moderate changes. Simultaneous incubation of 1.5 mM acetaldehyde and 100 MM UDCA decreased leakiness by 52 % p<0.0S) whereas 100 µM TUDCA instead decreased leakiness by *58* %. 100 mM ethanol induced similar though lesser differences. Investigation of the efficacy of 1 h preincubation with UDCA or TUDCA followed by 24 h simultaneous incubation with 1.5 mM acetaldehyde revealed in all experiments a worsening of plasma membrane integrity compared to controls. Cells incubated with 1.5-2.5 mM acetaldehyde appeared morphologically rounded off, whereas simultaneous incubation with acetaldehyde and 25 MM UDCA showed spreading cells which were attached to the surface (normal finding).

Conclusion: Simultaneous incubation of ADH-containing SK-Hep cells with 1.5 mM acetaldehyde and 10-100 MM UDCA resulted in considerably improved cell viability as shown by metabolic activity, stability of cell membranes, and cellular morphology. TUDCA showed similar though lesser effects. Similar protective effects of bile acids were seen when cells were incubated with ethanol.

SERUM IgA ELEVATION IN NASH: CORRELATION TO HISTOLOGIC DISEASE SEVERITY

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NASH shares histologic features with alcoholic steatohepatitis (ASH) including sinusoidal IgA deposition (Liver 1988;8:281-6) and epidemiologic features with cryptogenic cirrhosis. We previously noted a slightly lower IgG:IgA ratio in both cryptogenic cirrhosis (3.6 ± 1.7) and NASH (4.7 ± 2.4) compared to chronic hepatitis C with cirrhosis (5.2 1 2.6) and PBC with cirrhosis (5.6 ± 2.3) (Hepatology 1999;29:664-9). **Aim:** To further study elevation of serum IgA in NASH, we examined levels of IgA and IgG in NASH patients with various stages of fibrosis. **Methods**: 84 patients (age 50112, 52 (62%) female with histologic NASH and quantitative immunoglobulins were studied. The patients were divided into 4 groups based on abnormalities of either IgG (normal 694-1618 mg/dl) or IgA (68-378 mg/dl) or both or neither. **Results**: 10 patients (12%) had elevation of both IgG and I~ (mean = 20101329 IgG and 788 ± 292 I~), 21(25%) had isolated elevation of IgA (570 1 210), and 51(60%) had normal IgG ~l07 1 234) and normal IgA (226 ± 79). Only two patients, both with mild histologic disease, had isolated elevation of IgG and thus were not further analyzed. In the other 3 groups, more advanced histologic disease (stage 3 or 4) was seen in 80% of those with abnormal IgA and IgG, 67% of those with isolated IgA elevation, and 33% of those with normal IgG and IgA ~--0.0l). The IgG:IgA ratio was 2.91 1.2, 2.610.7, and 5.4 ± 2 in each of the groups respectively (p<0.01) **Conclusions**: Isolated elevation of serum IgA is seen in 25% of NASH patients. Those with a disproportionate elevation of I~ frequently have more advanced liver disease. Elevated IgA could result from free radical injury in steatohepatitis regardless of underlying etiology.

Influence of bile acids on activities of isolated alcohol dehydrogenase
(ADH) and aldehyde dehydrogenase (ALDH) related to effects on
membrane order of SK-Hep cells in presence of ethanol

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Treatment of SK-Hep cells with ethanol or acetaldehyde resulted in a decrease of metabolic activities and an increase of membrane permeability. Ursodeoxycholic acid (UDCA) prevented cell damage caused by ethanol and its metabolite. The present study was performed to find out whether the protective effects of bile acids were caused by a direct influence on ADH or ALDH thus preventing, e.g., the formation of the highly toxic acetaldehyde, or by a stabilization of SK-Hep cell membranes.

Methods: Activities of isolated ADH and ALDH were determined according to Kato et al. (1). Incubation was carried out with 0.7 U/ml enzyme, 10 mmol/L NAD in 100 mM glycine/ NaOH buffer, pH 9 for 5 min at 37^0C. Subsequently 0-20 mM ethanol or 0-500 µM acetaldehyde were added. UDCA and CDCA were added in concentrations of 0.01-1 mM. Enzymatic reaction was followed between 120 s and 180 s at A_{340}: Activity [U/I] = $A_{120\sim}$-$A_1s_{0\sim}$/60s * DF ($A_{120\sim}$, absorption after 120s or 18Os, DF= dilution factor (705.46)) Electron Parametic Resonance Spectroscopy (EPR): Membrane order was determined using the spin label 5-doxyl-stearic-acid (5-DSA). 50 µl SKHep cell suspension (10 cells, after 24h incubation in PBS buffer pH 7.4 and at 37^0C with 0-20 mM ethanol, 100 µM UDCA or CDCA) was incubated with 100 µM 5-DSA for I mm at 25 ^{0}C. Thereafter measurements were carried out with a Bruker ESP 300 EPR instrument. Calculation of order parameter 5 was done according to Zimmer et al. (2): S -A_{11}/2-(A_1+C)1 A_{11}/2 + (Ai+C), C=1 .4-0.053 *(A_{11}/2-$A_1$12).*

Results: After incubation with 0-20 mM ethanol activity of ADH increased 2.7 fold from 42 U/I ***(2.5*** mM ethanol) to 112 U/I ($p<0.02$, n=8). Incubation with acetaldehyde decreased ADH activity. There was no influence of UDCA and CDCA on ADH activities. Results with isolated ALDH resembled the results found with ADH: In presence of 0.5 mM acetaldehyde, ALDH activity increased to values of 90 U/I $p<0.05$, n=8). Again there was no influence of UDCA. CDCA showed decreasing AILDH activities at higher concentrations.
Incubation with UDCA or CDCA alone did not change membrane order of s= 0.709 (control) in SK-Hep cells. 100 mM ethanol decreased the order parameter to s=0.702 ($p<0.01$, n=6).
The combination of 100 mM ethanol and 0.1 mM CDCA decreased the order further to 0.679 ***(p<0.05,*** n--6, compared to 100 mM ethanol). In contrast simultaneous incubation of 100 mM ethanol and 0.1 mM UDCA resulted in an increase of order (s= 0.711, $p<0.01$, n=6) above the values of controls.

Conclusions: UDCA and CDCA did not directly influence activities of isolated ADH or ALDH. UDCA prevented the decrease of the order of SK-Hep cell membranes in the presence of ethanol. Therefore, the protective effect of UDCA is rather to be seen at the cell membranes than in decreasing the synthesis of the highly toxic acetaldehyde.

NON-ALCOHOLIC STEATOHEPATITIS: EFFECT OF SHORT-TERM THERAPY WITH URSODEOXYCHOLIC ACID

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Non-alcoholic steatohepatitis NASH), because of its prevalence, frequent subclinical course, possible progression to liver cirrhosis, and yet missing of 'standard' treatment options, poses a challenge for contemporary clinician and researcher.
Aim of the study: To study effects of therapy with ursodeoxycholic acid (UDCA) upon the clinical course, blood biochemistry parameters and prospective serum markers of liver fibrosis in patients with NASH.
Methods: Series of 17 patients (4 women and 13 men) with NASH, diagnosed by clinical/laboratory investigation, ultrasonography, and/or liver biopsy, was studied prior to, and during the therapy with UDCA (given as Ursofalk® cps, DrFalk Pharma, Germany; dosage 3 x 250 mg/day; duration 6 months). Of the series, 9 patients were obese (inc. I diabetic of type II). Hyperlipoproteinemia was present in 15 of 17 patients. Following laboratory investigations were done prior to, and on 1st $_3$3rd, and $_6$6th month of the therapy with UDCA: FW, blood counts, prothrombin time (Quick); serum biochemistry: aminotransferases (ALT, AST), alkaline phosphatase (ALP), 7-glutamyl-transpeptidase (GMT), bilirubin, albumin, total cholesterol, triglycerides, HDL - cholesterol; serum markers of liver fibrosis: metalloproteinase-1 (MMP-1), tissue inhibitor of metalloproteinase- 1 (TIMP-l), N-terminal propeptide of procollagen III (PIIINP). Abdominal ultrasonography (with semiquantitative evaluation of liver ,,steatosis") was performed prior to, and on $_3$rd, and $_6$tb month of treatment.

Results: Afler the 6-month therapy with UDCA, the amelioration of ultrasonography findings, improvement of serum biochemistry (ALT, AST, ALP and GMT), and decrease of serum concentrations of PIIINP were observed in most of the patients. The changes were statistically significant for ALT, PIIINP and ultrasonography semiquantitative evaluation ~
0.05). There was no significant change of serum MMP-IITIMP-l concentrations after 6 months of UDCA treatment; in some patients an increase of MMP-1 concentrations after 1 month, together with a decrease or normalization of TIMP-l in serum after 1 and/or 3 months were noticed. Serum lipid parameters remained unchanged during the treatment. No significant weight reduction was observed during the study period. The therapy with UDCA was well tolerated, no adverse effects were recorded.
Conclusion: The short-term treatment with UDCA in patients with NASH has shown some effect on the biochemical activity of the disease. The risk of liver fibrosis development and its possible modulation by medical therapy should be further evaluated in well designed long-term clinical studies.

Alcoholic hepatitis complicated with type 1 hepatorenal syndrome successfully treated by albumin plasmaexpansion in combination with continual terplipressin infusion followed by hemodialysis.

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33-year old man with heavy alcohol consumption (>200 g daily) was admitted in ICU because of severe alcoholic hepatitis (bilirubin: 680,7 umo1/l, conjugated bilirubin: *589,6* umol/l, leucocytes: 89,0x10^{9}11). Diagnosis of type 1 hepatorenal syndrome was established (diuresis: 300 ml, creatinine: 283 umol/l, urea: 15,7 µmol/l). Continual terlipressin infusion (1 mg daily) in combination with plasmaexpansion (albumin 20 g and fresh frozen plasma daily) and corticosteroid therapy (initially methylprednisolone 250 mg daily for 7 days, later prednisone) was started. Because of infectivity therapy schedule (diuresis: 150 ml, natriuresis: 46 mmo1/l, urea: 60,4 mmol/l, creatinine: 817 µmol/l), at $_{9th}$ therapy day we started hemodialysis treatment in combination with previous therapy. After kidney function improvement this treatment was stopped at $_{31}$th therapy day (diuresis: 1150 ml, urea: 19,5 mmol/l, creatinine: 151 µmol/l), but activity of alcoholic hepatitis still persisted (bilirubin: 301,2 umol/l, leucocytes: *64,3x10^{9}11).* Corticosteroid and UDCA therapy continued and at $_{126}$th day of therapy patient had improved liver function (bilirubin: 21,5 umol/l), kidney function (urea: 9,2 mmol/l, creatinine: 134 µmol/l) and leucocytes: 9,5x10/l.

CHANGES IN GALLBLADDER MOTILITY IN THREE-DIMENSIONAL ULTRASOUND ESTIMATION

IN ALCOHOL DEPENDENT MALE PATIENTS DURING ABSTINENCE PERIOD.

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Alcohol, as myorelaxant may affect the digestive tract motility. Gallbladder motility may influence an intestinal lipids absorption, what can be among other things a pathophysiologic factor of liver steatosis, diarrhea after alcohol abuse period and changes in plasma lipids level to alcohol abstinence period related. The aim of this study was to determine gallbladder motility in alcohol dependent patients during abstinence period. **METHODS**: Sonographic gallbladder volume on an empty stomach and one hour alter fatty meal (0,5g of the butter per one kilogram of the body mass with two bread slices) was determined in 31 alcohol dependent male patients, who drank alcohol not later than 3 weeks before examination performance and after 4 weeks of abstinence period. As a control group we examined the 13 males, who denied alcohol consumption for last 3 weeks**. RESULTS**: Alcohol dependent patients had similar gallbladder fasting (25,6i8,7 vs. 30,OjlO,9m1) and postprandial (12,1i5 2 vs 12 7+6,9m1) volumes as control group. After 4 weeks of alcohol abstinence in alcohol dependent patients the gallbladder volumes didn't change significantly. No significant correlation was found between gallbladder volumes and contractions and alcohol dependence severity score (Short Alcohol Dependence Data, Michigan Alcoholism Screening Test), quantity of alcohol drinking for 90 days before the study start, smoking and age of patients. Age of alcohol dependence onset correlated (Spearman's rank correlation) with fasting gallbladder volume in the first examination (R= 0,41, p<0,04) and time of alcohol dependence duration correlated with fasting (R= -0,45, p<0,03) and postprandial (R= -0,54, p<0,007) gallbladder volume**. CONCLUSION**: We didn't find the influence of chronic alcohol abuse on gallbladder volume and contraction.

HEPATIC STEATOSIS AND Altered VERY LOW DENSITY LIPOPROTEIN (VLDL) FORMATION IN APOLIPOPROTEIN (APO) E3-LEIDEN TRANSGENIC MICE

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ApoE-deficiency leads to hepatic steatosis and impaired VLDL-triglyceride production in mice. A mutant apoE isoform, apoE3-Leiden, is associated with a dominantly inherited form of dyslipoproteinemia in humans. Aim of this study was to evaluate the effects of APOE*3 Leiden expression on hepatic lipid content, VLDL formation and liver morphology, by comparing mouse strains with different expression of the APOE*3~Leiden transgene. Immunogold-labeling revealed the presence of the mutant protein on sinusoidal membranes, in multivesicular bodies and in peroxisomes, a distribution pattern similar to that of endogenous apoE in rodents. Nascent VLDL particles associated with Golgi were also labeled. Hepatic triglyceride content was increased to maximally 233% of control values, depending on hepatic APOE*3 expression. Hepatic VLDL-triglyceride secretion was impaired (-20%) in high-expressing transgenics with a concommitant increase from 1.6 to 8.1 of the apoB48/apoBlOO ratio in newly formed VLDL. Hepatocytes of high-expressing transgenics contained characteristic inclusions (2Otam) containing ApoE3-Leiden.. In conclusion, this study demonstrates that introduction of human apoE3-Leiden in mice, in addition to reported effects on lipolysis and lipoprotein clearance, leads to hepatic deposition of the mutant protein, development of fatty liver and altered VLDL production. The latter findings are consistent with a role of apoE in the regulation of hepatocytic lipid metabolism.

ASSESSMENT OF GLUCOSE TOLERANCE, INSULIN AND C-PEPTIDE IN PATIENTS WITH CHRONIC LIVER DISEASES.

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Several abnormalities of glucose metabolism have been described in liver cirrhosis:. Although insulin is degraded primarily by the liver, C-peptide is not degraded significantly by the liver. Simultaneous measurement of insulin and C-peptide levels, therefore, may clarify the relative contribution of pancreatic secretion and hepatic breakdown to the hyperinsulinism of cirrhosis. We have investigated insulin (I RI) and C-peptide (C-P) levels of peripheral blood before oral glucose loads (75 g) and in 30, 60, 90 and 120. mm. after glucose loads. Fasting blood glucose (GLUC) levels of patients with liver cirrhosis (Ci) were significantly different from values in normal subjects (C), but were in the normal range for both groups. Patients with Ci showed mild or moderate GLUC intolerance after oral GLUC loads. The peak of GLUC levels in patients occurred later than in C. Fasting IRI levels were significantly higher in patients with Ci compared with C. IRI levels were also significantly higher during the oral OGTT test in patient with Ci in all points. Fasting C-P levels were also significantly elevated in patients with Ci compared with C. Fasting C-P/I RI ratio (molar ratio) was decreased significantly in Ci compared with C. The area under the glucose tolerance curve was significantly larger in Ci, than in the C. There was a significant correlation between fasting IRI levels and fasting C-P. levels in Ci. ($r=0,77$, $p< 0,01$). C-pep.IIRI ratio significantly correlated with prealbumin (~0,72, $p< 0,05$). Ratio of sums of 5 C-PI sums of IRI values at 0, 30, 60, 90,120 mm. OGTT significantly correlated with prealbumin and transferrin ($r=0,61$, $p< 0,05$ and r 0,73, $p< 0,05$). Peripheral IRI and C-P levels will be useful to assess the relative contribution of increased pancreatic secretion and decreased hepatic degradation of insulin to the hyperinsulinism of Ci. Peripheral resistance to the action of insulin and/or a reduced effect of insulin on hepatic gluconeogenesis may explain elevated fasting IRI and C-peptide levels in Ci.

STEATOHEPATITIS AS A RARE CAUSE OF INCREASED SERUM TRANSAMINASES ACTIVITY IN CHILDREN

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Steatohepatitis of unknown etiology (idiopathic steatohepatitis - IS, nonalcoholic steatohepatitis - NASH) is a rare ailment in childhood. The main diagnostic criteria are: liver steatosis (mainly macrovesicular) with concomitant inflammatory infiltration with/without fibrosis or cirrhosis in histopathological examination of liver biopunctate and lack of serological markers of hepatotropic viruses infection or excessive alcohol intake.

The aim of the study was to present the medical history of 3 boys (2, 3 and 4-year-old) with diagnosed steatohepatitis. The physical examination of 2 younger patients revealed weight and height impairment and hepatomegaly in all of them. In additional tests no deviations of the normal condition were observed but for increased serum transaminases activity in all boys and hypectriglyceridemia in older one.

In differential diagnosis, infectious diseases of the liver (infection with HAV, HBV, HCV, CMV, HSV, Giardia lamblia, Toxoplasma gondii), metabolic disorders (cystic fibrosis, Wilson's disease, galactosemia, fructosemia, tyrosynemia, alpha-l-antitrypsin deficiency), coeliac disease and autoaggressive disorders of the liver were excluded in those children.

In histopathological examination of biopunctates of the liver in light microscopy dominated mainly macrovesicular steatosis of liver parenchyma cells including necrosis. We also found the presence of inflammatory infiltration in portal-biliary space which consisted mostly of lymphocytic cells as well as fibrosis.

Ultrastructural examination also revealed changes characteristic to steatohepatitis.

In the treatment preparations of UDCA and EPL were applied which effected in decrease of transaminases activity in blood serum of these boys.