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Abstracts of Papers Submitted to the American Gastroenterological Association

Abstracts of Papers Submitted to the American Association for the Study of Liver Diseases

Student Research Abstracts



TRANSAMINASES ELEVATION DURING PREGNANCY.

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Introduction: The main causes of transaminases elevation beside pregnancy are : alcohol, drugs, hepatitis virus , steatosis and seldom auto-immune or metabolic diseases (hemochromatosis, Wilson disease, alpha-1 antitrypsin deficiency). The relative contribution of these factors during pregnancy are unknown. The main goals of this study were 1) to determine the incidence of alanine aminotransferase (ALAT) elevation during pregnancy, 2) to state the role played by hepatitis virus and auto-immune diseases in pregnant women with ALAT elevation.

Patients and methods : From December 91 to October 92, ALAT (BIOTROL[®]) was determined in 3525 patients who delivered in public or private maternity hospitals. The upper normal limit (N) was calculated from 800 pregnant women sample and was set as the mean plus two standard deviations of these 800 values . When the ALAT was superior to 1,5 N (N=35), the sera was tested for Ag Hbs (Pasteur, Abbott), IgM anti-HAV (Abbott), IgM anti-Hbc (Abbott), anti-HCV (Abbott) by ELISA ; IgM anti-CMV by immunocapture (Wellcome); antinuclear, antismooth muscle, antimitochondrial, anti liver kidney microsome (LKM) antibodies by indirect immunofluorescence. **Results :** ALAT was superior to 1,5 N in 92/3525 patients (2,6%). IgM anti-HAV, anti-Hbc, anti-CMV were negative in all patients. Ag Hbs and anti-HCV were positive in one and four patients respectively. Antiperinuclear, antismooth muscle, anti-LKM antibodies were positive each one (1/160) in a patient. **Conclusion :** This results show that in our population ALAT is elevated in a small proportion of pregnant women and that viral hepatitis and auto-immune diseases are seldom responsible for this elevation (nearly 10%). This study suggests that drugs and pregnancy related liver diseases are the main causes of ALAT elevation during pregnancy.

CONCOMITANT EXPOSURE TO ETHANOL AND COCAINE HAS AN ADDITIVE TO ETHANOL TOXIC EFFECT ON KUPFFER CELL AND ENDOTHELIAL CELL FUNCTIONS. E.R. Abril, C.S. Jolley, J. Nishida, R.S. McCuskey, D.L. Earnest. Depts. of Medicine & Anatomy, University of Arizona Health Sciences Center, Tucson, AZ 85724.

Both cocaine (COC) and ethanol (EtOH) cause liver toxicity; simultaneous abuse of cocaine and ethanol (COC-EtOH) is not uncommon and can produce liver injury at a dose-duration of exposure earlier than with either toxin alone. We previously reported that liver parenchymal cell (PC) injury in COC-EtOH treated mice was accompanied by in vivo alterations in Kupffer cell (KC) and endothelial cell (EC) morphology by electron microscopy (EM). The rat appeared resistant to PC injury after a similar exposure to COC-EtOH. We have now evaluated the possibility in rats that functional abnormalities in KC and EC may precede overt PC injury during COC-EtOH dosing. Male S/D rats were fed a Lieber-DeCarli diet ±EtOH (36% of calories) for up to 14 weeks; COC was dosed IP up to 40mg/kg/day. In vitro evaluation: KC were isolated by standard methods (>95% purity, >90% viability), cultured in Iscove's medium and the following parameters measured: ⁵¹Cr sheep erythrocyte phagocytosis (PHAG), mitochondrial MTT reductase and TNF release. KC, EC, and PC morphology was assessed by EM. In vivo evaluation: Uptake of IV latex beads by KC and EC was quantitated by high resolution in vivo microscopy. **RESULTS:** In vitro studies showed that EtOH alone stimulated PHAG, MTT metabolism and TNF release by cultured KC. COC alone caused variable suppression, while COC-EtOH treatment produced severe (p<.05) suppression of KC function. By EM, morphology of KC and EC, but not PC, was abnormal. In vivo assessment: Sinusoidal blood flow was normal with all toxin doses. In contrast, KC phagocytosis was suppressed, most severely by COC-EtOH, and there was appearance of EC endocytosis. These data show that COC-EtOH causes KC and EC abnormalities prior to overt PC injury and suggest a role for abnormal sinusoidal liver cell function in COC-EtOH liver disease. Supported by NIAAA grant #08037.

DISTRIBUTION OF LIPIDS, BILE ACIDS AND APICAL MEMBRANE ECTOENZYMES IN CHOLESTEROL CARRIERS IN HUMAN AND RAT BILE. L. Accatino, M.Pizarro, N.Solis and C.Koenig. Departamentos de Gastroenterología y de Biología Celular y Molecular, Facultades de Medicina y de Ciencias Biológicas, Pontificia Universidad Católica de Chile, Santiago, Chile.

The mechanisms of biliary lipid secretion are unknown. Cholesterol (Ch) is carried in bile in complex multilamellar phospholipid (PL) structures (lamellae), in unilamellar PL vesicles and in bile acids (BA) mixed micelles. Integral apical surface membrane proteins such as the phosphatidylinositol-glycan-anchored ectoenzymes alkaline phosphatase (AP) and 5'-nucleotidase (5'-N) and the transmembrane enzyme gamma-glutamyl transpeptidase (GGT) are normally secreted into bile. This study was undertaken to describe the relationships between biliary lipids and these enzymes and to understand the mechanism(s) involved in the secretory process. With this purpose, we studied the relative distribution of Ch, PL, BA and total proteins and AP, 5'-N and GGT activities, in different bile density fractions enriched in lamellae, vesicles or micelles, isolated by a rapid ultracentrifugation method in a bile-metrazamide gradient (Hepatology 12:130S,1990) from human T-tube hepatic bile (n=4) and bile from rats fed with 1% diosgenin for 6 days, which presented a 5-fold increase of biliary Ch output. Four gradient density fractions were obtained: 1 (mean d=1.0573), 2 (d=1.0821), 3 (d=1.0962) and 4 (d=1.1226). At electron microscopy, after negative staining, the low-density fraction 1 was composed by stacked parallel lamellae and also by 35-140 nm diameter unilamellar vesicles. The high-density fraction 4 was composed by 9-24 nm diameter particles, consistent with mixed-micelle size. Fractions 2 and 3 showed mixed characteristics. Most of Ch (70-95%) and PL (45-55%) was in fraction 1, which contained less than 7% of BA and proteins. In contrast, 35-55% of BA and proteins, 10-17% of PL, and 0-4% of Ch were present in fraction 4. Activities of AP (60-70%), 5'-N (60-85%) and GGT (55-85%) were concentrated in fraction 4. In fraction 1, AP activity represented 30% of total in humans but was undetectable in rats; the activity of 5'-N was 13% and 19% and that of GGT, 3% and 25%, respectively. These results indicate that a significant but variable proportion of apical membrane enzymes is associated with PL-Ch lamellae and vesicles, suggesting that these structures originate from the canalicular membrane. The important association of enzymes with the low Ch, BA-enriched fraction 4 is consistent with a role of BA in solubilizing proteins from the membrane or biliary Ch carriers in vivo. (Grant FONDECYT 739-92).

GUT EICOSANOIDS GENERATION, PAF ACTIVITY AND ENDOTHELIN-1 CONTENT IN PORTAL HYPERTENSIVE AND BILE DUCT LIGATED RATS Z. Ackerman, F. Karmeli, G. Amir, D. Rachmilewitz. Hadassah University Hospital, Jerusalem, Israel.

Rats with partial portal vein ligation (PVL) and complete bile duct ligation (BDL) have increased splanchnic blood flow to all layers in gut wall. However, the gut mucosa in these animal models exhibit an impaired resistance to damage by ulcerogenic agents. We determined mucosal gastric and colonic generation of vasoactive substances because they may have contributed to the susceptibility of GI mucosa to damage. Rats with PVL (n=7), BDL (n=6) and sham operated (S) (n=10) were studied. After 17 days rats were anesthetized with ketamine (90 mg/kg I.M.). Splenic pulp pressure (PP) was measured, stomach and colon were removed and mucosa was extracted for determination of PGE2, TxB2, LTB4, LTC4 and endothelin-1 (ET) by RIA (ng/g) and PAF activity (pg/10 mg) by platelet aggregation. PP was >13 mmHg in PVL and BDL and 6 mmHg in S rats. No macroscopic lesions were seen in any of the removed tissues. Gastric mucosal PGE2 generation was decreased by 35% in BDL rats. Colonic LTB4 generation, PAF activity and ET content were all significantly increased in BDL rats. Gastric and colonic LTC4 and TxB2 generation were similar in all treatment groups.

		Stomach	Colon
PGE2	S	66.4 ± 1.9	67.4 ± 1.9
	BDL	43.0 ± 3.5*	61.0 ± 9.7
LTB4	S	4.0 ± 0.5	4.5 ± 0.56
	BDL	3.6 ± 1.1	9.2 ± 0.8*
PAF	S	48.0 ± 2.0	45.0 ± 2.0
	BDL	56.0 ± 4.0	62.0 ± 9.7*
ET	S	0.51 ± 0.22	0.39 ± 0.12
	BDL	0.23 ± 0.06	1.21 ± 0.16*

* = significantly different from S rats, p<.05.

Conclusions: 1) Mucosal gastric generation of PGE2 was decreased in BDL rats. 2) Mucosal colonic generation of vasoactive mediators was increased. 3) The above changes may render the gastrointestinal mucosa in rats with experimental portal hypertension susceptible to the damage incurred by noxious agents.