

Furthermore, L-methionine, which is converted to AdoMet via methionine adenosyltransferase (MAT), but not D-methionine, regulated the proliferation of HSC. MAT2A was dominantly expressed in quiescent HSC, while MAT1A was in hepatocytes. Oral supplementation of L-cysteine and L-methionine attenuated TAA-induced liver fibrosis and reduced the expression of proteins for SM a-actin, PDGFRb and TGFbRII and mRNAs for collagen a1 (I) and TGFb-II in the liver tissues.

Conclusion: Supplementation of sulfur-containing amino acids may be important element to regulate the molecular activation, in particular proliferation, of HSC.

683 WILSON'S DISEASE: LONG TERM TREATMENT WITH ZINC SULPHATE

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A retrospective analysis was carried on Wilson disease's (WD) patients in order to describe the effectiveness and safety of therapy with Zinc Sulphate. We report our experience on 28 patients with WD over an 11 year period. The patients were followed at Padova Gastroenterology Unit. 19 males (67.9%). 53.6% with liver disease; 1 case of FHF; 39% with neuro/psychiatric disease; 13% diagnosed on the basis of the family history. Average age at presentation is 15.5 years (range 4-35): 13 years for hepatic presentation, 19 for neurologic one. We considered 2 treatment groups: 1) Zn as initial therapy: 10 patients. 70% improved; in 30% worsening; 2 cases with hepatic and neuropsychiatric involvement, added to non-compliance and HCV positivity in one case and one hepatic case with eight year delay diagnosis. All these patients underwent OLT. 2) DPCA as initial therapy in 18 patients: 35.2% of patients developed DPCA side effects, that disappeared with Zn; 28% cases of failure of improvement with DPCA (50% hepatic, 50% neurologic): with Zn therapy all were in improved conditions, but one hepato-neurologic case, who worsened until death; 21% patients switched from DPCA to less side effects Zn, but with any intolerance to DPCA; 11.6% on DPCA from the beginning improved and showed stable clinical conditions during a period of 1 and 9 years. 1 FHF after withdrawal of DPCA. Zn is safe and effective. DPCA is effective but its side effect may be severe. OLT is the end stage of treatment and it's effective.

684 NONALCOHOLIC-STEATOHEPATITIS (NASH) AND HEPATIC MITOCHONDRIAL BETA-OXIDATION.

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Background: Experimental data and studies with invasive methods suggest an increase of mitochondrial beta-oxidation as a source of oxidative stress in Nonalcoholic Steatohepatitis (NASH).

Aims & Methods: To evaluate the possibility of breath test with sodium-13C-octanoate to evaluate medium chain free fatty acid hepatic mitochondrial beta-oxidation. We studied 10 patients (8 male and 2 female; BMI 26.17 ± 2.40, range 22.05-29.01) with clinical and histological pictures fully compatible with a diagnosis of NASH and 20 healthy subjects matched for age, gender and BMI, as controls. Breath samples were collected before and every 15 minutes for 2 hours after ingestion of 100 mg of water-dissolved octanoic acid-1-13C, sodium salt, 99% atom isoenrichment (Isotec Inc., Miamisburg, OH). 13CO₂ enrichment in breath was analyzed by isotope ratio/mass spectrometry (Breathmat, Finnigan, USA). Results were expressed as cumulative percentage dose of 13CO₂ recovered at 120 minutes (%13C-OCT).

Results (mean±SD):

| | NASH | Healthy | P |
|--------------------|------------|------------|-------|
| BMI | 26.17±2.40 | 24.1±0.7 | n.s. |
| %13C=OCXT(120 min) | 33.66±4.67 | 26.50±3.17 | <0.05 |
| ALT (U/L) | 69.8±44.02 | 46±19.7 | n.s. |
| AST (U/L) | 39.16±6.4 | 29.5±5.1 | n.s. |
| gGt | 103±78.4 | 83±54.5 | n.s. |

Conclusion: Our results confirm, "in vivo", the enhanced beta-oxidation in the hepatocytes observed in vitro, pointing out the sodium 13C-octanoate breath test as a non-invasive tool for the in vivo assessment of liver beta-oxidation pathway.

685 DIETARY HABITS AND THEIR RELATIONS TO INSULIN SENSITIVITY IN NON-ALCOHOLIC STEATOHEPATITIS

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Background and Aims: The amount and type of dietary carbohydrate and fat may affect insulin sensitivity and hepatic disease in different conditions. Detailed data on alimentary habits of patients with NASH are sparse. We investigated the relation of diet to insulin sensitivity and liver disease in patients with non-alcoholic steatohepatitis (NASH) without type 2 diabetes, obesity or hyperlipidemia.

Methods: Twenty-five NASH patients (24 males, age 37 ±9 yr, BMI 25.6 ± 2.5 kg/m²) (mean ± SD) and 25 age-, BMI- and gender-matched healthy controls completed a 7-day daily alimentary record (data analyzed by the WinFood database) and an oral glucose tolerance test (OGTT). The whole body insulin sensitivity index (ISI) was calculated from the OGTT.

Results: Compared to controls NASH patients consumed more saturated fat (SFA: 13.7±3.1 vs. 10.0±2.1% kcal, p=0.000), total fat (39.1±4.8 vs. 31.1±5.2% kcal, p=0.000) and cholesterol (506±108 vs. 405±111 mg, p=0.002) and consumed less polyunsaturated fat (10.0±3.5 vs. 14.5±4.0% total fat, p=0.000), antioxidant C (84.3±43.1 vs. 144.2±63.1 mg, p=0.000) and E vitamin (5.4±1.9 vs. 8.7±2.9 mg, p=0.000). The ISI was significantly lower in NASH patients than in controls (3.38±1.61 vs. 7.07±1.50; p=0.000) and correlated with total energy intake (rs=-0.51; p=0.013) SFA (rs=-0.57) but not with BMI or waist circumference. ALT levels correlated with ISI (rs=-0.49), total energy intake (rs=0.58) SFA (rs=0.58) and dietary polyunsaturated-to-saturated fat ratio (rs=-0.50).

Conclusions: In conclusion, our NASH patients consume a diet richer in SFA and poorer in polyunsaturated fat and antioxidant C and E vitamin; the causal role of these dietary habits and the benefit of their correction need to be further assessed.

686 CASPASES, S-ADENOSYL METHIONINE AND ANTI-TUMOR NECROSIS FACTOR ALPHA SIGNALING FOR PROTECTION IN ETHANOL INDUCED APOPTOSIS IN NORMAL HUMAN HEPATOCYTES

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Ethanol (EtOH) induces apoptosis in liver cells.

Aims: 1-To assess the mechanism by which EtOH is signaling for apoptosis in normal human primary hepatocytes (NHPH). 2-To delineate the role of tumor necrosis factor alpha (TNFα) antibody (anti-TNFα), caspase-9 (CAPI9), caspase-3 (CAPI3) inhibitors and S-adenosyl-methionine (SAdMe) in cell protection against apoptosis.

Methods: NHPH were treated for 24 hours, either with 80 mM EtOH or 30 µg/mL TNFα. Apoptosis was assessed by ELISA, and by transmission electron microscopy. In a second set of experiments, prior to the same