P- 39 N-ACETYL CYSTEINE ATTENUATES ALTERATIONS GENERATED IN EXPERIMENTAL LIVER STEATOSIS INDUCED BY CHRONIC ALCOHOL CONSUMPTION PLUS A HYPERCALORIC DIET

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Introduction and Objectives: Metabolic disorders and alcohol consumption are the most common etiological agents in hepatic steatosis (HS). Metabolic alterations, oxidative stress, and inflammation are key mechanisms in the development of this disease. There is a few evidence that demonstrates the synergistic effects generated by both etiological agents. N-acetyl cysteine (NAC) is an antioxidant used clinically, whose efficacy in HS development induced by a hypercaloric diet plus alcohol consumption is unknown. This study aimed to evaluate NAC effects on oxidative stress, and metabolic alterations induced in HS generated by ethanol chronic consumption plus a hypercaloric diet in a mouse model.

Materials and Methods: Male mice (C57BL/6J, n=4) were divided into 3 groups. 1) Control, mice fed with a conventional diet and water ad libitum; 2) HF/OH, mice fed a hypercaloric diet, and 20% ethanol; 3) HF/OH+NAC, mice with the same treatments of HF/OH group, and NAC (300 mg/kg/day, p.o.). All treatments lasted 5 months. Serum biochemical markers were determined: AST, ALT, cholesterol, HDL, LDL, triglycerides, leptin, ghrelin, insulin, resistin, and GLP1; also, oxidative stress parameters such as MDA, and SOD, CAT and Nrf2 proteins expression were analyzed through colorimetric assays, and western blot. Finally, H&E staining was performed in liver samples.

Results: NAC prevents weight gain and metabolic alterations generated by concomitant consumption of a hypercaloric diet and alcohol; it also modulates changes in anorexigenic and orexigenic adipokines. On the other hand, NAC reduces the oxidative environment induced by both etiological agents and prevents tissue alterations in hepatic parenchyma.

Conclusions: NAC ameliorates alterations in processes related to establishment of HS induced by ethanol chronic consumption plus a hypercaloric diet. Its pharmacodynamic mechanisms go beyond its antioxidant capacity.

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P- 40 PENTOXIFYLLINE USE IN PATIENTS WITH ALCOHOL-ASSOCIATED HEPATITIS ADMITTED WITH ACUTE KIDNEY INJURY COULD DECREASE SURVIVAL: A GLOBAL STUDY

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Introduction and Objectives: Alcohol-associated hepatitis (AH) is a severe entity with a mortality of up to 30−50% at 1 month. Pentoxifylline combined with steroids has not demonstrated benefits in severe AH. Some studies have suggested that pentoxifylline may be beneficial in the subgroup of patients with acute kidney injury (AKI) and AH. However, there is no solid evidence of its benefit in mortality in this setting. This study aimed to determine the benefit of the use of pentoxifylline in patients with severe AH and AKI.

Materials and Methods: Global retrospective cohort study, including patients with severe AH and AKI at admission (2009 −2019). We used competing-risk models with liver transplantation as a competing risk to assess the potential effect of pentoxifylline.

Results: We included 655 patients with severe AH and AKI (30 centers from 10 countries). Median age was 48±11.6 years, 26.2% were females, and 52.5% were Caucasian. Around 68.7% of the patients had a prior history of cirrhosis, and 6.6% underwent liver transplantation. The MELD score on admission was 34 [15−74]. 43.2% of the patients used corticosteroids, while only 6.9% used pentoxifylline during hospitalization. In the univariate analysis, the variables independently associated with mortality were the female sex (sHR 0.740; 95%IC:0.577−0.948; p=0.018), MELD (sHR 1.034; 95%IC: 1.020 −1048; p<0.001), MELD 3.0 (sHR 1.034,95%IC:1.018−1.049, p<0.001), Maddrey's discriminant function (sHR 1.005, 95%IC:1.003 −1.008, p<0.001), serum albumin at admission (sHR 0.756; 95%IC:0.642−0.890; p=0.001), bilirubin at admission (sHR 1.011; 95%IC:1.003−1.019, p=0.006), serum creatinine (sHR 1.083; 95%IC:1.028−1.140, p=0.002) and pentoxifylline use (sHR 1.531, 95%IC:1.107−2.119; p=0.010)(Table). In the multivariate-adjusted model, the use of pentoxifylline was associated with increased mortality (sHR 1.620, 95%IC:1.190−2.204; p=0.002).

Conclusions: The use of pentoxifylline has no benefit in terms of mortality and could decrease survival in patients with AH and AKI.

Table.- Univariate and multivariate competing-risk analyses. Mortality is the primary event, and liver transplant is the competing risk.

	Univariate analysis			Multivariate analysis		
Variables	**sHR**	**95% CI**	**p-value**	**sHR**	**95% CI**	**p-value**
Age (years)	1.005	0.996–1.014	0.231	1.013	1.003–1.023	0.006
Sex (Female)	0.740	0.577–0.948	0.018	0.802	0.618–1.040	0.097
MELD	1.034	1.020–1048	< 0.001	1.043	1.021–1.065	< 0.001
MELD 3.0	1.034	1.018–1.049	< 0.001	-		
mDF	1.005	1.003–1.008	< 0.001	-		
Cirrhosis	1.100	0.821–1.473	0.522	-		
Corticosteroids use	1.051	0.845–1.308	0.650	1.058	0.842–1.329	0.628
Albumin at admission	0.756	0.642–0.890	0.001	-		
Bilirubin at admission	1.011	1.003–1.019	0.006	-		
Serum creatinine	1.083	1.028–1.140	0.002	0.973	0.892–1.329	0.628
Pentoxifylline use	1.531	1.107–2.119	0.010	1.620	1.190–2.204	0.002

sHR: Subdistribution Hazard ratio; mDF: Maddrey's discriminant function.

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P-41 IMPACT OF CHOLEMIC NEPHROSIS ON RENAL FAILURE IN CIRRHOTIC PATIENTS

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Introduction and Objectives: The development of acute kidney injury (AKI) in cirrhotic patients is of multifactorial origin, including urinary tract infections, diuretics, portal hypertension, shock, etc. Another important factor is cholemic nephrosis, which is considered when total bilirubin exceeds 20 mg/dl; this implies that bile pigments damage the distal tubule with deterioration of renal function, increasing morbidity and mortality. We aimed to evaluate the levels of hyperbilirubinemia in the development of AKI and its association with biomarkers of renal failure.

Materials and Methods: Retrospective and analytical study of a cohort of cirrhotic patients, to evaluate the development of AKI associated with bilirubin levels. Statistical analysis: A binary logistic regression model was performed considering bilirubin (greater than 20), NGAL (greater than 150), and cystatin (greater than 0.95) as associated factors. The significance of the model was considered with an alpha level of less than 0.05.

Results: 109 patients were included, 45 women 64 men, age 54.67 ± 11.6, Child-Pugh A: 2, B: 29, C: 78. The binary logistic model was significant W(1)=11.089, p=0.001. The OR for bilirubin was 4.37 (1.168-16.35, 95% CI P=.027), for NGAL OR 2.7 (1.08-6.71, 95% CI; p=.032) not significant, cystatin 0.64 (0.35-11.66, CI 95%; p=0.764).