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INFLAMMATORY SIGNALING AND RENAL BLOOD FLOW IN HEPATORENAL SYNDROME

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Background. Hepatorenal syndrome (HRS) is a relatively common complication of cirrhosis, occurring in 39% of cirrhotics within five years of their diagnosis. The predominant theory is that blood vessels in the kidney circulation are constricted because of the dilation of blood vessels in the splanchnic circulation, which is mediated by factors released by liver disease. But role of inflammatory cytokines in the pathogenesis of HRS is still under the study.

Objectives. The purpose of present study was to analyze the impact of liver inflammation to the renal hemodynamic disturbances in HRS.

Material and Methods. Totally we examined 90 patients : 30 alcoholic liver cirrhosis (ALC) + normal renal function (group 1); 30 ALC + renal failure, but without HRS criteria (group 2); 30 ALD + HRS (group 3). We measured serum IL-6 and TNF- α levels by Cytoscreen Immunoassay kits (BioSource International, Camarillo, CA, USA), and NO level by Griess reaction. The interlobar arterial resistance index (IARI) was estimated with duplex Doppler ultrasonography.

Results. The average value of IARI in group 3 (0.76 \pm 0.02) was statistically significantly higher than in group 1 (0.64 \pm 0.04) and group 2 (0.68 \pm 0.01) (p<0.05). NO levels where the highest in group 3 – 28.5 \pm 3.2 mmol/L, compared with 16.2 \pm 2.5 mmol/L in group 1. There was no statistically significant difference between NO levels in groups 1 and 2 (17.6 \pm 2.3 mmol/L) (p>0.05). TNF- α serum levels in group 3 where significantly increased – 2.79 \pm 0,68 pg/mL (p<0.05), compared with 1.89 \pm 0.34 pg/mL – in group 2 and 1.89 \pm 0.34 pg/mL – in group 1. Group 3 also demonstrated high rates of IL-6 – 15.35 \pm 0.93 pg/mL (p<0.05), when in group 1 and 2 it was 12.39 \pm 1.07 pg/mL and 11.64 \pm 1.32 pg/mL, correspondently. Spearman rank correlation analysis revealed direct correlation between IARI and NO serum levels (r=0.86), IARI and TNF- α serum levels (r=0.73), IARI and IL-6 serum levels (r=0.67) (p<0.05).

Conclusions: This paper brings evidence, suggesting that proinflammatory cytokines, including TNF- α , IL-6 and NO, play a pivotal role in the pathophysiology of HRS. Detection of serum levels of these cytokines, along with routine biochemical and ultrasound examination, might help to the early detection of renal hemodynamic disturbances in patients with ALC even before renal dysfunction becomes clinically evident. It also makes possible the identification of a subgroup of patients with ALC who are at higher risks for developing HRS.