

**МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ
БУКОВИНСЬКИЙ ДЕРЖАВНИЙ МЕДИЧНИЙ УНІВЕРСИТЕТ»**



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Slyvka N.O.

RENAL BLOOD FLOW AND LIVER INFLAMMATION IN THE HEPATORENAL SYNDROME

*Department of Patient Care and Higher Nursing Education
Bukovinian State Medical University*

Introduction. Hepatorenal syndrome (HRS) is a relatively common complication of cirrhosis and occurs in 39% of cirrhosis patients within five years since the diagnosis has been made. Generally accepted theory is that blood vessels of kidneys constrict because of the dilation of blood vessels in the visceral circulation, which is caused by factors of the liver disease. Histamine, prostaglandins, and nitrous oxide (NO) affects unstriated muscle structure of vessels, causing the dilation of blood vessels, which increases the blood flow and circulating leukocytes in it. But the role of inflammatory cytokines in the pathogenesis of hepatorenal syndrome is still under the study.

Objectives. The objective of the study was to analyze the impact of liver inflammation on the renal hemodynamic disorders in HRS.

Material and methods. We examined 90 patients in total: 30 – with alcoholic liver cirrhosis (ALC)+normal renal function (group 1); 30 ALC+renal failure, but without HRS criteria (group 2); and 30 ALC+HRS (group 3). We measured IL-6 and TNF- α levels in the blood serum by the kits of Immunoassay Cytoscreen (Biosource International, Camarillo, CA, USA), and NO level by Griess reaction. The index of interlobar arterial resistance (IARI) was estimated with the data of duplex dopplerography.

Results. The mean value of IARI in group 3 (0.76 ± 0.02) was statistically higher than in group 1 (0.64 ± 0.04) and group 2 (0.68 ± 0.01) ($p < 0.05$).

The numbers of NO were the highest in group 3 – 28.5 ± 3.2 mmol/L in comparison with 16.2 ± 2.5 mmol/L in group 1. There was no statistically significant differences between NO levels in groups 1 and 2 (17.6 ± 2.3 mmol/L) ($p > 0.05$).

TNF- α levels in the blood serum were significantly overstated in group 3 – 2.79 ± 0.68 pg/mL ($p < 0.05$) in comparison with 1.89 ± 0.34 pg/mL - in group 2 and 1.89 ± 0.34 pg/mL – in group 1.

Group 3 also revealed the high level of IL-6 – 15.35 ± 0.93 pg/mL ($p < 0.05$), while in group 1 and 2 it was 12.39 ± 1.07 pg/mL and 11.64 ± 1.32 pg/mL respectively.

Spearman's rank correlation analysis revealed the direct correlation between IARI and NO in the blood serum ($r=0.86$), IARI and levels of TNF- α in the blood serum ($r=0.73$), IARI and IL-6 in the blood serum ($r=0.67$) ($p < 0.05$).

Conclusions. Thus, this paper proves that proinflammatory cytokines, including TNF- α , IL-6 and NO, play a key role in the pathophysiology of HRS. The identification of serum levels of these cytokines, along with the routine biochemical and ultrasound examination, can help in early detection of renal hemodynamic disorders in patients with ALC even before renal dysfunction becomes clinically evident. It also makes the identification of a subgroup of ALC patients who have higher risks for HRS progression possible.

Sobko D.I.

ASSESSMENT OF INDICATORS OF MELATONIN AND GHRELIN CONCENTRATIONS IN THE BLOOD SERUM OF PATIENTS WITH ARTERIAL HYPERTENSION COMBINED WITH OSTEOARTHRITIS

*Department of Internal Medicine, Physical Rehabilitation and Sports Medicine
Bukovinian State Medical University*

Introduction. Diseases such as arterial hypertension (AH) and osteoarthritis (OA), which are common among the global population, are often combined. The combined course of these diseases is an important medical and social problem even in economically developed countries. In this regard, researchers are now paying considerable attention to the biochemical and molecular mechanisms underlying the development of hypertension and OA. Their efforts are aimed at identifying these diseases as early as possible and prescribing adequate complex therapy.

The aim of the study. To investigate the relationship between the peculiarity of the course of combined hypertension and OA and the concentration of ghrelin and melatonin in patients with these diseases.

Material and methods. According to the research program, 60 people in total of different ages and sexes, patients with hypertension and OA, were examined. The control group consisted of 10 practically healthy people.

Determination of the concentration of ghrelin in the blood serum of patients was carried out using the Human GHRL(ghrelin) ELISA Kit (Elabscience, the USA) immunoenzymatic method according to the instructions using a multichannel microspectrophotometer AutoPlex ELISA & CLIA Analyzer (92980) (Monobild, the USA).

The concentration of melatonin in the blood serum of patients was determined using a set of Melatonin ELISA reagents (IBL International, Germany) by immunoenzymatic method according to the instructions using a multichannel microspectrophotometer AutoPlex ELISA & CLIA Analyzer (92980) (Monobild, the USA)

The obtained data were processed by the methods of variational statistics using the Statistica 12.0 program.

Results. In accordance with the study plan, the levels of melatonin and ghrelin in fasting blood serum were determined in patients with combined pathology. Thus, in the subjects examined in the group with combined pathology, the average indicators of ghrelin levels were 1,7 times ($2,69 \pm 0,12$ ng/ml) lower than the similar indicator in the control group ($4,64 \pm 0,05$ ng/ml, $p < 0,05$), and melatonin – 2,6 times ($46,71 \pm 6,26$ pg/ml) compared to the same indicator in the control group ($125,43 \pm 8,13$ pg/ml, $p < 0,05$). The low levels of the investigated indicators in patients with combined hypertension and OA confirm our interest in them as markers for early diagnosis of the course and progression of these comorbid diseases. It should be noted that a direct correlation ($r = +0,59$, $p < 0,05$) of medium strength was established between the levels of melatonin and ghrelin in the studied patients with hypertension combined with OA. This relationship additionally confirms the importance of the above-mentioned indicators in the pathogenesis and course of combined hypertension and OA and requires further study. Considering all of the above, we consider it expedient to find out the relationship between the levels of ghrelin, melatonin and blood pressure indicators in patients with combined pathology. In the course of the study, it was established that in the group of patients with combined hypertension and OA, there was an inverse correlation ($r = -0,31$, $p < 0,05$) between indicators of average daily SBP and ghrelin concentration. An inverse correlation was also established between melatonin serum concentration indicators and average daily SBP data ($r = -0,49$, $p < 0,05$).

Conclusions. Indicators of ghrelin and melatonin concentrations can be recommended as "early" reliable prognostic markers of the development and progression of the mentioned comorbid pathologies.

Sydorchuk L.P.

**GUANINE NUCLEOTIDE-BINDING PROTEIN BETA-3 (GNB3, RS5443) AND
ENDOTHELIAL NITRIC OXIDE SYNTHASE (NOS3, RS2070744) GENES
POLYMORPHISM AS MARKERS OF OBESITY IN HYPERTENSIVE PATIENTS**

*Department of Family Medicine
Bukovinian State Medical University*

Introduction. More than 50% of patients with essential arterial hypertension (EAH) have additional cardiovascular risk factors, among which the most common are obesity, diabetes mellitus, metabolic syndrome, etc.

The aim of the study was to investigate polymorphic variants of the endothelial nitric oxide synthase (NOS3, rs2070744) and guanine nucleotide-binding protein beta-3 (GNB3, rs5443) genes as markers of obesity in EAH patients.

Material and methods. One hundred patients with EAH and target-organ damaging (2nd stage), moderate, high or very high cardiovascular risk were involved in the case-control study.