perivascular and white adipose tissue, fibroblasts and platelets in the form of prochemerin. It has several active isoforms, which causes its pleiotropic effects, including prohypertensive action. A series of research has shown that chemerin has no effect on basal inflammatory status, but it promotes the production of nitric oxide and activates the PI3K-Akt-eNOS signaling pathway. The presence of endothelial dysfunction, which occurs in many cardiovascular diseases, increases the ability of chemerin to increase arterial tone, which causes the vasoconstrictor effect of this adipocytokine in the processes of vascular tone regulation and may contribute to the development of hypertension [2]. The main place of synthesis of nesfatin-1 is the hypothalamic nuclei. It is also synthesized in adipocytes, pancreatic beta cells, cells of gastric mucose and reproductive system. Nesfatin-1 is able to regulate carbohydrate metabolism. Recent data suggests that nesfatin-1 is involved in the pathogenesis of hypertension, which is potentially implemented through the central system of melanocortin and oxytocin, and also expresses vasoconstrictor effects by suppressing the synthesis of nitric oxide [3].

Aim: To study the relationship between serum levels of chemerin and nesfatin-1 and parameters of daily blood pressure monitoring (DBPM) in hypertensive patients depending on the presence and degree of obesity.

Materials and Methods. 82 patients with hypertension, aged 60 (55; 66) years, including 26 patients with overweight, 39 with obesity and 17 patients with normal body weight, underwent DBPM. The serum levels of chemerin and nesfatin-1 were determined by the immune enzyme method using Human Chemerin and Human Nesfatin-1 ELISA kits (Kono Biotech Co., Ltd., China). Statistical processing was performed using Mann-Whitney, Pearson criteria, K-mean cluster analysis. Quantitative attributes are presented as median (Me), upper (UQ) and lower (LQ) quartiles.

Results. Serum levels of chemerin and nesfatin-1 were significantly higher in patients with hypertension (p = 0.001) compared with healthy subjects. In order to detect the joint effect of the concentration of both cytokines on DBPM parameters, a cluster analysis was performed using the K-mean method; four non-intersecting clusters were obtained with a studying error p = 0.138. The inter-cluster analysis revealed statistically significant differences between clusters in the DBPM parameters that characterize the dynamics of changes of blood pressure in the morning, namely, the rate (HRSBP and SHPDBP) and the magnitude of the morning rise of BP (VRPDBP and VRPDBP), daytime systolic and diastolic variability of BP (VarSBP (D) and VarDBP (D)) and circadian rhythm of BP. The first cluster, where the high level of serum chemerin of 11.12 (8.2; 14.02) ng/ml was associated with high values of BMI (33.31 (30.47; 36.15) kg/m$^2$) was characterized by the most unfavorable type of distribution of circadian rhythms of BP, VarSBP and VarDBP. In contrast, the patients of the 3rd cluster with high serum levels of both cytokines: chemerin of 7.7 (6.52; 8.44) ng/ml, nesfatin-1 of 8.96 (8.55; 9.37) ng/ml, and low BMI (25.2 (23.1; 26.8) kg/m$^2$), had a predominant distribution of circadian blood pressure by dipper type, but high SHPSBP and SHPDNP. The most favorable in relation to the parameters of DBPM was the 2nd cluster with moderately low content of chemerin: 4.91 (4.42; 5.26) ng/ml and high level of nesfatin-1: 8.02 (7.67; 8.43) ng/ml. A significant direct correlation has been revealed between serum chemerin and the following parameters of DBPM: SHPSBP and SHRDBP: r = 0.35, p <0.05; VRPDBP and VRPDBP: r = 0.3, p <0.05; VarSBP and VarDBP: r = 0.34, p <0.05. There were no correlations between the parameters of DBPM and serum nesfatin-1.

Conclusions. Serum levels of chemerin and nesfatin-1 were significantly elevated in patients with hypertension. The relationship between serum chemerin and circadian rhythm, daytime variability of blood pressure and DBPM parameters that characterize the dynamics of morning changes of blood pressure was revealed. There was no convincing data on the effect of serum nesfatin-1 on DBPM indices.

References:


Key words: adipokines, metabolic syndrome, cardiovascular risk

Accepted for printing on 25 Sept 2018

DOI: 10.29256/v.02.02.2018.escbm22

MODIFIED PROTEINS IN BLOOD OF PATIENTS WITH DRUG-INDUCED NEPHROPATHY

Lee V.

Karaganda State Medical University, Kazakhstan

Nephropathy occurs when kidney-specific detoxification and excretion do not work properly due to the damage or destruction of kidney function by exogenous or endogenous toxicants. The kidney is a major site of organ damage caused by drug toxicity. Nephrotoxicity resulting from drug exposure has been estimated to contribute to 19–25% of all cases of acute kidney injury in critically ill patients [1]. Exposure to drugs often results in toxicity in kidney which represents the major control system maintaining homeostasis of body. Understanding the toxic mechanisms
for nephropathy provides useful information on the development of drugs with therapeutic benefits with reduced side effects. Mechanisms for drug-induced nephropathy include changes in glomerular hemodynamics, tubular cell toxicity, inflammation, crystal nephropathy, rhabdomyolysis, and thrombotic microangiopathy [2]. Biomarkers have been identified for the assessment of nephropathy. Although some of them fail to confer specificity and sensitivity The discovery and development of novel biomarkers that can diagnose kidney damage earlier and more accurately are needed for effective prevention of drug-induced nephrotoxicity [3]. The main purpose of our study was to investigate the oxidative modifications of proteins in blood plasma of patients with drug-induced nephropathies.

**Materials and Methods.** There were 75 patients divided into 2 groups depending on the type of the drug. The first group was represented by patients with psychotropic drug-induced nephropathy (amitriptyline in 75% cases); the second one – by patients with nephropathy caused by nonsteroidal anti-inflammatory drugs (NSAIDs – painkillers in 55% cases). The control group consisted of 22 healthy subjects. In blood plasma were detected reactive protein carbonyl derivatives (Levine et al, 1990), advanced oxidation protein products (AOPP) in serum (Witko-Sarsat et al, 1996).

**Results.** The reactive protein carbonyl derivatives level in blood plasma of the 1st group was lower in comparison with control one (p<0.05). AOPP concentration was the highest in serum of the 2nd group (p<0.05). Our results demonstrated that in blood of patients the patterns of oxidized proteins to be varied depending on the type of the drug group.

Naturally, a lot of questions arise concerning the mechanisms of protein modification and the possible regulation of this process. Thus, it remains unclear how to regulate the processes of “directed”, or “targeted” carbonylation of certain proteins by using NSAIDs or psychotropic drugs. It proves the need for further studies of metabolic disorders in the formation of different types drug-induced nephropathy.

**References:**

Accepted for printing on 25 Sept 2018

DO: 10.29256/v.02.02.2018.escbm23

**OVEREXPRESSION OF STAT4 IS A POSSIBLE DIAGNOSTIC MARKER OF EARLY STAGES OF MYCOSIS FUNGOIDES**

Grekova Е.V., Olisova О.У., Alekseeva E.A., Zaletayev D.V.

1 V.A. Rakhmanov Department of Skin and Veneral Diseases, I.M. Sechenov First State Medical University, 119991, Russian Federation;

2 Laboratory of medical genetics, Institute of molecular medicine, I.M. Sechenov First Moscow State Medical University, Russian Federation

Cutaneous T-Cell Lymphomas (CTCLs) include a clinical-pathologically heterogeneous group of non-Hodgkin lymphomas primarily developing and affecting the skin. Mycosis fungoides (MF) is the most common disease among the cutaneous T-cell lymphomas (85-90%). The accuracy of the diagnosis of MF, which is confirmed only by clinical, histological and immunohistochemical signs, is 50-75%. The aim of the study was to investigate genetic markers (FOXP3, STAT4, IL12B) for early diagnosis of mycosis fungoides.

**Materials and Methods.** A study involving 42 patients with MF and plaque parapsoriasis (PP) treated at the Dermatology Department of I.M. Sechenov First Moscow State Medical University and National Medical Hematology Research Center, was performed. The analysis of gene expression FOXP3, STAT4, IL12B was carried out by TaqMan Real time-PCR. The objects of the study were lesional skin samples of patients. A group with MF consisted of 29 patients, a group with PP consisted of 13 patients, a control group included 10 healthy volunteers.

**Results.** The study revealed that the level of STAT4 gene expression showed a significant (9 times) increase in the mRNA expression of STAT4 transcripts in patients with MF (166) compared with patients with PP (17.9; p<0.05) and 553 times - with healthy volunteers (0.3; p < 0.05).

There was also a statistically significant predominance of the level of mRNA expression of STAT4 transcripts in patients with spotted and plaque stages of MF (180; 318) compared with patients with PP (17.9; p<0.05) and healthy volunteers (0.3; p < 0.05), as well as a sharp decrease in patients with erythrodermic form of MF (7.19).

**Summary.** For early diagnosis of MF the level of expression of mRNA transcripts STAT4 is of great importance. Inclusion of STAT4 in the list of diagnostic features increases the accuracy of differential diagnosis of MF and PP from 59.1% to 81.8%.

**Key words: mycosis fungoides, early diagnosis, STAT4, FOXP3, molecular genetic method of diagnosis.**

Accepted for printing on 20 Sept 2018