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ON THE STATE OF FUNCTIONAL ACTIVITY OF THE SYMPATHETIC-ADRENAL SYSTEM AND FREE RADICAL PROCESSES IN WOMEN OF FERTILE AGE WITH METABOLIC SYNDROME

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Abstract:

This article shows study the relationship between disorders of the functional state of the sympathetic-adrenal system (SAS) and the processes of lipid peroxidation in women of fertile age with metabolic syndrome.

INTRODUCTION. Combining in recent decades into clusters of risk factors for cardiovascular diseases (CVD) has shown that the mortality rate is largely influenced by factors: obesity, type 2 diabetes mellitus (DM), arterial hypertension (AH), insulin resistance (IR), hyperinsulinemia (GI) and hyperlipidemia. It is known that each of these factors included in the definition of "metabolic syndrome" increases the risk of heart disease. An increase in blood pressure (BP) on the background of obesity is often accompanied by an increase in the activity of the sympathetic nervous system [1,2,3,4,5]. hypertension often serves as one of the first clinical manifestations of MS.

Recent data indicate the widespread prevalence of obesity in women. Being a continuously progressive somatic disease, obesity contributes to the formation of a wide range of cardiovascular disorders. Attention is drawn to the high frequency of abdominal obesity [6,7,8,9].

The processes of lipid peroxidation (PLP) lead to the accumulation of oxidized low-density lipoproteins (LDLP), which entails a violation of microcirculation. From this point of view, the study of the processes of SEX in MS has become particularly interesting, since one of the main biochemical indicators of blood in this case is an increase in the level of biogenic amines in the blood. Recent studies indicate that in order to understand atherosclerosis, hypertension and coronary heart disease, diabetes mellitus (DM), it is necessary to study biogenic amines (adrenaline, norepinephrine, serotonin, etc.) and their precursors, metabolic products and enzymes involved in their metabolism [2, 9, 10, 11,12]. Often, the state of the sympathetic-adrenal system (SAS) was not studied in a complex: either only individual fractions of catecholamines (CA) were studied, or the content of CA and their decay products in MS patients. The study of the functional state of SAS by the level of excretion of all fractions of CA with a parallel study of the composition of SEX in women of fertile age with MS was not carried out.

OBJECTIVE: To study the relationship between disorders of the functional state of the sympathetic-adrenal system (SAS) and the processes of lipid peroxidation in women of fertile age with metabolic syndrome.

MATERIALS AND METHODS. 91 women aged 25-49 years were examined in the hospital, who were randomized into the following 3 groups: I (control) – healthy persons aged 25-40 years – 15 people; II – patients with arterial hypertension – 39 people aged 29-49 years; III group – patients with arterial hypertension in combination with MS -37 women in aged 26-49 years.

The following methods were used to diagnose MS:

1. The body mass index (BMI) was determined by the formula: weight (kg)/height (m)2. According to the WHO classification, body weight is considered excessive if the BMI exceeds 24.9.
2. Abdominal obesity was determined by measuring the waist circumference (WC) between the edge of the lower rib and the wing of the ilium. The physiological indicator was taken as: for women less than 80cm.
3. To determine metabolic disorders in patients, the level of total cholesterol (ChS), triglycerides, very low-density lipoproteins (VLDL), LDL, high-density lipoproteins (HDL), atherogenicity coefficient (lipid spectrum was determined biochemically by the Reflotron-Roche express analyzer), blood glucose (glucose oxidase method) were studied. The general clinical examination was carried out according to generally accepted programs (clinical analysis of blood, urine, ECG, X-ray examination of the chest organs, etc.).

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Determination of adrenaline (A), norepinephrine (NA), dopamine (DA) and DOPA in daily urine was performed by trioxyindole fluorimetric method modified by E.S. Matlina, Z.M. Kiseleva, I.E. Sofieva (1965). Determination of the content of conjugates of catecholamines (KA) in urine was performed according to the method described by T.I. Lukicheva, V.V. Menshikov, T.D. Bolshakova (1971). The blood KA level was determined by the ELISA method on the CatCombi ELISA apparatus. The sex products in the blood serum were determined by the method of B.V.Gavrilov et al. (1987), MAO in the blood – according to the method of A.I. Balakleevsky (1976).
The results of clinical studies were processed using the applied statistical processing programs of the Excel program, as well as by the method of variational statistics using the Student's t-criteria tables. The differences between the arithmetic averages were considered statistically significant at $p<0.05$.

RESULTS AND DISCUSSION. As can be seen from Table 1, the maximum level of total cholesterol, triglycerides, LDL is observed in group III, compared with the control and II groups. Compared with the control, the value of total cholesterol in patients with hypertension increased by 30.4%, and in women with MS - by 47.8%. The triglyceride content in group III exceeded the control value by 71%, in group II by 44.4%. The LDL level in group II exceeded the indicator of the control group by 53.8%, the LDL content in group III increased by 99.7% compared to the healthy group. HDL in groups II and III was reduced compared to the control. When comparing the first and second groups, the difference in blood glucose levels was 8.8%, and in groups I and III – 46.6%.

Table 1.
The content of lipids, glucose in blood serum in practically healthy patients with arterial hypertension and metabolic syndrome

Groups	Total CHS, mmol/l	Triglycerides, mmol/l	LDL, mmol/l	HDL, mmol/l	VLDL, mmol/l	Atherogenicity index units	Plasma glucose, mmol/l
I group	4,6±0,1	1,5±0,1	2,6±0,2	1,4±0,1	0,4±0,1	2,8±0,3	4,5±0,2
II group	6,0±0,2	1,8±0,2	4,0±0,2	1,2±0,3	0,5±0,2	4,0±0,2	4,9±0,2
III group	6,8±0,3	2,6±0,1	5,2±0,3	0,9±0,4	0,7±0,3	5,2±0,2	6,6±0,3
R1-2	R<0,001	R<0,05	R<0,001	R<0,05	R<0,05	R<0,01	R<0,05
R 1-3	R<0,001	R<0,001	R<0,001	R<0,05	R<0,05	R<0,001	R<0,001
R 2-3	R<0,05	R<0,001	R<0,01	R<0,05	R<0,05	R<0,001	R<0,01

Table 2 shows the average values of daily urinary excretion of KA in all examined groups. In the study, we noted a statistically significant increase in the excretion of A and NA in the daily urine of patients with hypertension and MS. Thus, the daily excretion of total A in patients with hypertension with healthy individuals increased by 43.9% ($P<0.001$), total by 39.2%. Excretion in the daily urine of all fractions of DA and DOPA in patients with hypertension is statistically significantly lower than the control level. The excretion of free, conjugated and total A and NA in MS patients was statistically significantly higher than in healthy patients. The difference in DOPA excretion in MS was 27.8% ($P<0.01$) (Table 2).
Table 3 shows the results of the study of A and NA in the blood of healthy women and patients with hypertension and MS. When analyzing the indicators, we noted a significant increase in the content of A and NA in patients compared to the control group. (Thus, the level of A in MS patients exceeded 3 times the indicator of healthy, and patients with hypertension by 1.5 times. The content of NA in the blood of MS patients was increased 2.7 times in the control group, and 1.4 times in comparison with the examined AH.) When analyzing the MDA data, we noted a statistically significant increase in the content in group III compared to group I by 102.7%, and the difference between groups I and II was 41.1%.
The MAO study showed a statistically significant decrease in its level in groups II and III ($P<0.001$)

Table 2.
Daily excretion of catecholamines in urine in practically healthy and patients with metabolic syndrome

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Groups	Catecholamines									
	A, mcg/day			NA, mcg/day			ДА, mcg/day			DOPA mcg/day
	Free.	con.	cum.	Free.	con.	cum.	Free.	con.	cum.	
I	4,5±0,1	3,7±0,2	8,2±0,2	8,9±0,2	9,2±0,1	18,1±0,2	79,2±6,2	182,6±5,8	461,8±6,4	47,3±0,8
II	6,0±0,1***	5,8±0,2***	11,8±0,2***	11,8±0,1***	12,3±0,1***	24,1±0,2***	159,8±5,1*	168,3±4,6^	328,1±8,6^	50,2±0,6*
III	9,2±0,3***	8,2±0,2***	17,4±0,2***	12,9±0,4***	12,2±0,3***	25,2±0,2***	165,2±4,4*	159,4±2,8^	324,6±9,4*	58,8±0,8**

Note. A – adrenaline, NA – norepinephrine, DA – dopamine, MAO – monoamine oxidase, Sv. – free, Con. – conjugated, Sum. – total. * - P<0.05; ** - P<0.01; *** - P<0.001; ^ - unreliable.

Table 3
The content of adrenaline and norepinephrine, MAO and MDA activity in the blood of practically healthy and patients with metabolic syndrome

Groups	**adrenaline**, nmol/l	Norepinephrine, nmol/l	**MDA** nmol/ml	MAO, un/ekc
I	0,76±0,2	2,68±0,2	3,4±0,3	0,08±0,002
II	1,9±0,1	5,9±0,1	4,8±0,2	0,054±0,0029
III	2,2±0,2	6,7±0,2	6,9±0,4	0,042±0,003
R-1-2	r<0,001	r<0,001	r<0,01	r<0,001
R-1-3	r<0,001	r<0,001	r<0,01	r<0,001
R-2-3	r<0,05	r<0,001	r<0,01	r<0,001

1. Thus, we found a statistically significant increase in the daily excretion of free and conjugated forms of KA (A, NA, DA) in MS patients. In the blood plasma of these patients, there was a significant and statistically significant increase in the content of cholesterol, lipoproteins, CA and POL products, and MAO was also reduced.
2. Thus, the results of the conducted studies have shown that in MS, the activation of CAC occurs, expressed by an increase in the content of A and NA in the blood and urinary excretion of KA (A, NA, YES, their precursor DOPA). A further increase in the tension of the activity of the SAS is aimed at mobilizing the internal reserves of the body. However, at one of the stages of this process, the catabolic orientation of the effects of SAS begins to manifest itself, and a further increase in the activity of which becomes one of the main elements of the formation of this pathology and its complications [2, 12].
3. According to our research results, there is a decrease in the catalytic activity of MAO, which is associated with the activation of POL and a qualitative change in the properties of MAO.
4. The results obtained by us indicate an increased intensification of POL processes in MS.
5. Based on our clinical data, it could be assumed that disorders of KA metabolism in MS could have pathogenetic significance. At the same time, perhaps the main role should have been given to strengthening the GENDER in this pathology. It could be expected that if the intensification of POL plays an important role in disorders of the metabolism of biogenic amines, then in the body of MS patients there could be analogies with a number of other pathological processes in which the accumulation of POL products occurs.

CONCLUSION. The study of patients with metabolic syndrome showed a change in the functional activity of the sympathetic-adrenal system and the metabolism of biogenic amines, which is expressed by an increase in the content of adrenaline and norepinephrine in the blood and increased urinary excretion of free and conjugated forms of catecholamines, and therefore early correction is necessary to prevent the

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development of complications. Also, with the metabolic syndrome, there is a marked decrease in the activity of the key enzyme deamination of catecholamines (MAO), as a result of their prolonged toxic effect on the myocardium.

In metabolic syndrome, there is a significant activation of lipid peroxidation products, which is of great interest in identifying the mechanism of development of the metabolic syndrome.

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