EUROPEAN JOURNAL OF LIFE SAFETY AND STABILITY (EJLSS)
ISSN 2660-9630
www.ejlss.indexedresearch.org Volume 15, 2022 ||

Relationship of Catecholamine Metabolism Disorders and Lipid Peroxidation Processes in Women with Metabolic Syndrome

I. M. Tashtemirova, G. I. Kodirova, H. N. Kodirov, M. D. Yusuvaliev
Andijan State Medical Institute

Abstract: *The aim of the given work was study interactions of impairments sympathetic – adrenal systems functional condition and processes of peroxidal oxidation of lipids in woman with metabolic syndrome. 107 women at the age of 25-49 were observation. They were randomized into 3 groups: I (control) – 15 healthy persons, II – 43 patients with arterial hypertension, III – 49 women with arterial hypertension in combination with metabolic syndrome.*

The results of carried investigations showed that activation of sympathetic adrenal system and processes of peroxidal oxidation of lipids took place in metabolic syndrome. Marked lowering of sympathetic – adrenal system key ferment catecholamins (MAO monoaminooxidaze) desalinization activity and considerable activation of peroxidal oxidation of lipid products which have great significance in revealing the mechanism of metabolic syndrome development were observed in metabolic syndrome. This results in the prolonged toxic influence of catecholamine on myocardium.

Keywords: *metabolic syndrome, sympathetic–adrenal system, catecholamins, arterial hypertension, insulinresistens.*

Date of Submission: 29-02-2022 ***Date of Acceptance: 31-3-2022***

Introduction. The frequency and severity of obesity-related disorders and diseases depend not only on the degree of obesity (according to BMI), but also on the characteristics of adipose tissue deposition in the body. In subsequent years, numerous observations and studies have confirmed that excessive accumulation of abdominal adipose tissue is usually accompanied by metabolic disorders and significantly increases the risk of developing hypertension, type 2 diabetes, and atherosclerotic diseases. In industrial countries, the prevalence of metabolic syndrome among the population over 30 years of age is, according to various authors, 10-20% (1,2,4,5,13,14,15).

Clustering of risk factors for cardiovascular diseases (CVD) in recent decades has shown that the mortality rate is largely influenced by the following 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 (2,3,5,11,12,14). Hypertension is often one of the first clinical manifestations of MS.

Recent data indicate a 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 (7, 8, 12, 15).

The processes of lipid peroxidation (LPO) lead to the accumulation of oxidized low-density lipoproteins (LDL), which leads to a violation of microcirculation. From this point of view, the study of LPO processes in MS has become particularly interesting, since one of the main biochemical parameters of blood in this case is an increase in the level of biogenic amines in the blood. Recent studies suggest that understanding atherosclerosis, hypertension, CHD, and diabetes mellitus (DM) requires studying biogenic amines (epinephrine, norepinephrine, serotonin, etc.) and their precursors, metabolic products, and enzymes involved in their metabolism [4,7,8,9]. 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 degradation products in MS patients were studied. A study of the functional state of the CAC by the level of excretion of all CA fractions with a parallel study of the composition of LPO in women with MS was not conducted.

Objective: To study the relationship between age-related disorders of the functional state of the sympathetic-adrenal system (SAS) and metabolic syndrome.

Materials and methods. In hospital 107 of the surveyed women aged 25-49 years were randomized into the following 3 groups: I (control) healthy individuals aged 25-40 years – 15 people; II – patients with arterial hypertension and 43 people aged 29-49 years; III group – patients with arterial hypertension in combination with MS -49 women aged 26-49 years.

The following methods were used to diagnose MS:

1. 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 (OT) between the edge of the lower rib and the iliac wing. For the physiological indicator, we took: for women less than 82cm.
3. To determine metabolic disorders in patients, the level of total cholesterol (CH), triglycerides, very low-density lipoproteins (VLDL), LDL, high-density lipoproteins (HDL), the coefficient of atherogenicity (the lipid spectrum was determined biochemically by the rapid analyzer "ReflotronRoche"), and 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, etc.).

Determination of epinephrine (A), norepinephrine (NA), dopamine (DA), and DOPA in daily urine was performed by the trioxyindole fluorimetric method modified by E. Sh.Matlina, Z. M. Kiseleva, and I. E. Sofieva (1965). Determination of the content of catecholamine (CA) conjugates in urine was performed according to the method described by T. I. Lukicheva, V. V. Menshikov, and T. D. Bolshakova (1971). The blood CA level was determined by ELISA on CatCombi a CatCombi ELISA device [10]. LPO products in 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 trials were processed using the applied statistical processing programs of the Excel program, as well as the method of variation statistics according to Fischer using Student's t-criteria tables. Differences between the arithmetic mean values were considered statistically significant at p

Results and discussion. As can be seen from the table, the maximum level of total cholesterol, triglycerides, LDL is observed in IIIgroup III, compared with the control and II groups. In comparison with the control group, the total cholesterol level in patients with hypertension increased by 31.5%, and in women with MS - by 48.5%. The triglyceride content in IIIgroup III exceeded the control value by 67%, in IIgroup II by 44.7%. The LDL level in IIgroup II exceeded the control group by 54.7%, the LDL content in IIIgroup III increased by 84.3% compared to the healthy group. HDL in groups II and III was reduced compared to the control group. When comparing the first and second groups, the difference in blood glucose level was 8.4%, and in groups I and III – 49.8%.

Table 1. Content of lipids and glucose in blood serum in practically healthy people and patients with arterial hypertension and metabolic syndrome

Groups	Total HC, mmol/l	Triglycerides, mmol/l	LDL, mmol/L	HDL, mmol / L	VLDL, mmol/L	Atherogen index, units	Glucose plasma mmol/l
of the I group	and 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 band	of 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	and 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
R 1-2	R<0,001	R<0,05	R<0,001	R<0,05	R<0,05	R<0,01	R<0,05
P1-3	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

The second table shows the average values of daily urinary excretion of CA in all groups examined. During the study, we noted a statistically significant increase in the excretion of A and HA in the daily urine of patients with hypertension and MS. Thus, the daily excretion of the totalAnd in patients with hypertension with healthy individuals, it is increased by 42% (P<0.001), the total by 37.1%. Daily urinary excretion of all DA and DOPA fractions in patients with hypertension is statistically significantly lower than the control level. The elimination of free, conjugated, and total A and HA in MS patients was statistically significantly higher than in healthy subjects. The difference in DOPA excretion in MS was 32.2,2% (P<0.01) (Table 2).

Table 2. Daily urinary excretion of catecholamines in healthy subjects and patients with metabolic syndrome

Groups	Catecholamines			
	A, mcg / day	TO µg/day	YES, mcg/day	of l-DOPA, mg/day
I	SV. 4,5±0,1 Con. 3,7±0,2 Sum. 8,2±0,2	SV. 8,9±0,2 Con.9,2±0,1 Sum.18,1±0,2	SV.Of 279.2±6,2 Con.182,6±5,8 Sum.461,8±6,4	47,3±0,8
II	SV.6,0±0,1*** Con.5,8±0,2 *** Сум11,8±0,2***	St. 11,8±0,1*** Con.12,3±0,1*** Sum.24,1±0,2***	St. 159,8±5,1* Con. 168,3±4,6^ Sum.328,1±8,6^	50,2±0,6*
III	SV. 9,2±0,3*** Con.8,2±0,2*** Sum.17,4±0,2***	St. 12,9±0,4*** Con.12,2±0,3*** Sum.25,2±0,2***	St. 165,2±4,4* Con. 159,4±2,8^ Sum. 324,6±9,4*	58,8±0,8**

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

The third table 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. (For example, the level of A in MS patients was 3 times higher than in healthy patients, and in AH patients it was 1.5 times higher. The content of NA in the blood of MS patients was increased 2.5 times in the control group, and 1.3 times in comparison with the examined AH patients.) When analyzing the MDA data, we noted a statistically significant increase in the content in IIIgroup III compared to group I by 97.5%, and the difference between groups I and II was 42.3%.

The MAO study showed a statistically significant decrease in its level in groups II and III (P

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

Groups	Epinephrine, nmol / l	Norepinephrine, nmol / l	MDA nmol / ml.	MAO, ed / ex.
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
p-1-2	p<0.001	p<0.001	p<0.01	p<0.001
P-1-3	p<0.001	p<0.001	p<0.01	p<0.001
P-2-3	p<0.05	p<0.001	p<0.01	p<0.001

Thus, we found a statistically significant increase in the daily excretion of free and conjugated forms of CA (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 LPO products, and MAO was also reduced.

Thus, the results of the conducted studies showed that in MS, CA activation occurs, expressed by an increase in the content of A and HA in the blood and urinary excretion of CA (A, HA, DA, their DOPA precursor). A further increase in the intensity of CAC activity 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, and the further increase in the activity of which becomes one of the main elements in the formation of this pathology and its complications [6, 12].

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.

Our results indicate an increased intensification of LPO processes in MS.

Based on our clinical data, it was possible to assume that disorders of CA metabolism in MS could have pathogenetic significance. At the same time, perhaps the main role should have been assigned to the strengthening of GENDER in this pathology. It could be expected that if LPO intensification plays an important role in biogenic amine metabolism disorders, then in the body of MS patients there could be analogies with a number of other pathological processes in which LPO products accumulate.

Conclusion. A 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 epinephrine and norepinephrine in the blood and increased urinary excretion of free and conjugated forms of catecholamines, and therefore an early correction is necessary to prevent the development of complications. Also, in the metabolic syndrome, there is a marked decrease in the activity of the key catecholamine deamination enzyme (MAO), as a result of which their long-term toxic effect on the myocardium occurs.

In the 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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