



State Of Purine Exchange And Microalbuminuria In Patients With Metabolic Syndrome

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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 monoaminooxidase) desamidization 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 catecholamins on myocardium.

KEYWORDS

Metabolic syndrome, sympathetic-adrenal system, catecholamins, arterial hypertension, insulinresistens.

INTRODUCTION

Recently, we have faced a new pandemic, i.e. in medicine, a new term for metabolic

syndrome (MS) has appeared and it summarizes the main factors leading to the

development of atherosclerosis. In the literature in recent years, there is a lot of information about the main role of MS in the development of various diseases. This is evidenced by the data on MS caused by multiple disorders [2,3,4,7,17,18,20]. MS represents a complex of interrelated disorders of carbohydrate and purine metabolism, as well as mechanisms of regulation of arterial pressure and endothelial reticula. The development of these disorders is based on a decrease in tissue sensitivity to insulin - insulin resistance (IR). This symptom complex is also known under the names "metabolic syndrome", "well-being syndrome", "polymetabolic syndrome" "syndrome X", "deadly quartet", "insulin resistance syndrome". More often than others, the names "meta-bolic syndrome" and "insulin resistance syndrome" [2,3,4,15,18,20].

Glucose and insulin are important factors in uric acid homeostasis, involved in the secretion and reabsorption of uric acid. An imbalance in these indicators leads to either hypouricemia or hyperuricemia. So, hyperuricemia contributes to uricosuria, so the level of uric acid in the blood in patients with de-compensated diabetes mellitus of any type can decrease. The effects of insulin on uric acid secretion are opposite to those of glucose. At the same time, normal levels of insulin have practically no effect on renal hemodynamics, glomerular filtration, and permeability of the renal filter in relation to albumin. The hyperinsulinemia seen in IR and type 2 diabetes mellitus contributes to a decrease in the excretion of lactic acid. This was found in patients with metabolic syndrome and healthy volunteers in whom acute euglycemic hyperinsulinemia leads to transient hyperuricemia as a result of increased

reabsorption of sodium and uric acid [12,13,20]. According to studies carried out in the clinic of internal diseases of the RUDN University, with daily monitoring, there was no decrease in blood pressure in patients with high hyperuricemia and a reliable relationship between the left ventricular myocardial mass index and the level of uric acid and blood serum in patients with metabolic syndrome. In patients with hypertension and left ventricular hypertrophy, the concentration of uric acid in the blood is one of the most significant determinants of left ventricular hypertrophy and indicates its resistance to standard antihypertensive therapy. The high level of uric acid is associated with the features of antihypertensive therapy in metabolic syndrome [7,8,12,14].

Consequently, hyperuricemia (HUA) and microalbuminuria (MAU) are closely interrelated processes that characterize the clinical manifestation of MS. However, studies on the state of purine metabolism and microalbuminuria in MS patients are insufficient and this problem needs further comprehensive research.

PURPOSE OF THE WORK

Study of the state of purine metabolism and microalbuminuria in patients with metabolic syndrome.

MATERIAL AND METHODS.

50 patients aged from 30 to 55 years old, suffering from MS, were examined, taking into account the risk factors and damage to organs - targets. In a hospital, 18 male (34.7%) and 32 female (65.3%) patients aged 30 to 55 years were examined, who were randomized into the following 3 groups: I (control) - healthy individuals aged 25-40 years old - 15 people; II -

patients with arterial hypertension - 18 people aged 30-59 years; Group III - patients with MS – 32 at the age of 30-59 years.

The following methods were used to diagnose MS:

1. Determination of body mass index (BMI) was carried out according to the formula: weight (kg) / height (m) 2. According to the WHO classification, body weight is considered overweight if the BMI exceeds 24.9.
2. Abdominal obesity was determined by measuring the waist circumference (WT) between the edge of the lower rib and the wing of the ilium. The physiological indicator was taken: for women less than 80 cm.
3. To determine metabolic disorders in patients, the level of total cholesterol (CS), triglycerides, very low density lipoproteins (VLDL), LDL, high density lipoproteins (HDL), atherogenic coefficient (lipid spectrum was determined by biochemically express analyzer "Reflotron-Roche"), blood glucose (glucose oxidase method) .The state of purine metabolism was determined enzymatically by the colorimetric method according to the level of uric acid in the blood serum on an automatic analyzer StatFax Awareness technology INC (Italy), using reagents Hospitex diagnostics.rl (Italy). The results of clinical trials were processed using the applied statistical processing programs of the Excel program, as well as by the method of variation

statistics using the tables of Student's t-tests. Differences between the arithmetic mean values were considered statistically significant at $p < 0.05$.

RESULTS AND DISCUSSION

In the majority of patients with MS, the disease was associated with a hereditary factor (31.5%), obesity (30.0%), an alimentary factor (28.4%), and low physical activity (hypodynamia -10, 1%), (Fig. 1). In the alimentary factor group, patients indicate excessive consumption of carbohydrates and fats. Excess body weight and obesity are considered the main components of MS. And at the same time, the relationship between the components of the MS is of particular interest. In the examined patients, the Quetelet index (IR), body weight and the degree of abdominal obesity (AO) were determined. Measurement of the waist circumference in group I showed 78.8 ± 1.14 cm, in group II 80.3 ± 0.46 , and in MC-102.5 ± 1.5 cm (Tab -1). In patients with AH, AO was 1.9% higher than in the control group, i.e. the figures were almost the same. When examining the IC in the control group, this indicator showed 24.3 ± 0.7 m2, and in the II group, IC was equal to 26.7 ± 1.3 m2. In the GB group, IK was higher by 4.9%, the indicators were almost the same. In MS, IC averaged 32.6 ± 0.8 m2, was higher than the indicators of the control group by 35%, indicators of the second group by 28.6%. The results obtained suggest that blood pressure and glycemic levels are related to body weight. Purine metabolism was assessed by determining the concentration of uric acid in fasting venous blood plasma samples.

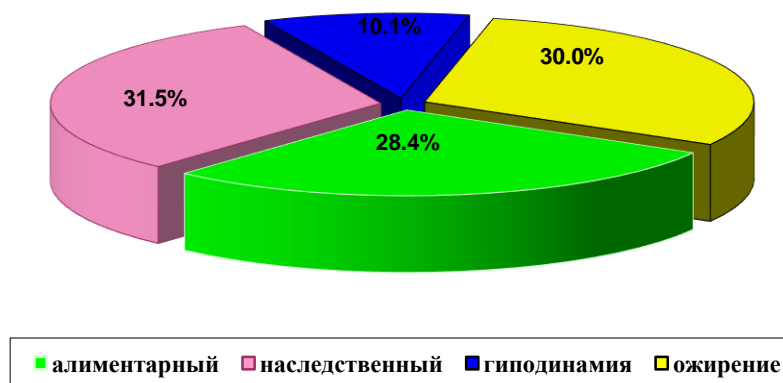


Figure: 1. Etiological factors of MS

Hyperuricemia, a MC level of more than 0.45 mmol / L, was detected by us in 52.6% of patients with MS, and in 37.1% of patients with a hypertension clinic.

For the purpose of a more in-depth analysis of the relationship between the level of uricemia and other parameters of MS, we divided all examined persons according to the results of the study into 3 clinical groups. As the clinical picture of the syndrome grew, the prevalence of hyperuricemia also increased: in the AH group - in 22.2% of cases: in the MSv group in 50.7% of cases. The table shows the average values of the indicators of purine metabolism, as well as other their studied parameters, reflecting the degree of severity of violations, characteristic of MS. A significant increase in the degree of uricemia took place in the MSt groups. at the stages when there was a statistically significant increase in the concentration of triglycerides and obesity parameters. The deterioration of diastolic function, although it correlated with an increase in the degree of hyperuricemia, but the

change in this parameter in patients with SMS acquired a significant (compared with patients with the absence of the mentioned syndrome) character much earlier than in them the concentration of MC increased significantly ... We did not find a reliable relationship between the magnitude of uricemia and the level of blood pressure, but in persons with a clinical picture of metabolic syndrome without hypertension, the level of MC was statistically significantly lower than in patients with a clinical picture of MS, and there was also a tendency for a lower value of this parameter in comparison with all groups of patients in which MS proceeded with AH. After analyzing the individual distribution of the values of MC concentration among the individuals of all clinical groups, we came to the conclusion that the level of uricemia characteristic of MC is the MC value of 0.45 mmol / L and higher ... Patients who had MS had this level of MC significantly more often than those with AH (chi-square = 3.76, p < 0.05)

Table 1

Indicators of purine metabolism, blood pressure, fat and carbohydrate metabolism, in patients with varying degrees of MS severity (M ± m)

Index	MS		
	I st group	II nd group	III rd group
Age, years	44,6±1,2	46,5±1,6	50,2±2,2*
MC, mmol / l	0,37±1,7	0,59±2,0*	0,71±2,0*
waist circumference	78,8±1,14	80,3±0,46,**	102,5±1,5***
Quetelet index, kg / sq.m	24,3±0,7	26,7±1,2**	32,6±0,8***
SBP, mm Hg	125,6±1,8*	150,0±2,9	152,4±5,0
DBP, mm Hg	85,2±2,2	101,2±2,1	100,7±1,7

Note: * p<0,05,**p<0,01,***p<0,001

In our study, hyperuricemia was detected in 52.6% of patients suffering from MS, which is slightly higher than the data of other authors. However, the frequency of violations of purine metabolism depended on the presence of concomitant components of MS: in its absence, it was only 22.2%, increased as the clinical picture of the syndrome progressed and reached a maximum of 68.6% - in patients with MS. In addition, we noted that the concentration of MC in the blood significantly correlated with the severity of obesity, hyperinsulinemia, triglyceridemia, and glycemia - parameters reflecting the state of IR.

Thus, the data obtained indicate that hyperuricemia is a metabolic disorder and one of the components inherent in metabolic syndrome.

We examined 26 MS patients for MAU. The patients were divided into groups. The criteria

for the formation of the groups were the stages of diabetic nephropathy (DN): 1 - group - patients with normoalbuminuria: urinary albumin excretion below 30 mg / day; Group 2 - patients with MAU: urinary albumin excretion from 30-300 mg / day; 3 - group - patients with proteinuria (PU) detected in the study of daily excretion of protein in the urine and with preserved nitrogen excretory function of the kidneys (serum creatinine level below 110 mmol / L). The results of the study showed that MAU was expressed in patients with hypertension in 22.4% of cases, in patients with MS - in 75.2% of cases.

In the presence of MS in patients, non-selective proteinuria is noted in 80.1% of cases.

Table 2

Clinical characteristics of MS patients according to MAU level

Index	Control	AG	MK
Creatinine	72,3±4,2	73,5±10,0	99,0±10,5**
Urea	4,7±0,96	4,7±1,0	5,36±1,0
MAU, mg / day		10,7±6,9	
PU g / day			1,47±0,7

Note: differences with control are significant *p<0,02, **p<0,01

The degree of MAU and PU directly correlated with the degree of DN: at the initial stage of DN - MAU at the level of microalbuminuria (<30 mg / day), with DN II stage MAU from 30-300 mg / day, with DN III - IV degree, PU is determined ... The degree of manifestation of PU is directly proportional to the degree of DN. At stage III DN, PU was 1.47 ± 0.7 g / day, with stage IV DN - 2.7 ± 1.9 g / day.

Thus, in patients with MS, the presence of normoalbuminuria indicates an adaptive-compensatory reaction of the vessels, aimed at overcoming the developing kidney pathology. The presence of MAU means that the MAU stage can be reversible if treatment is started on time and will slow down the progression of DN and its transition to the stage of PU and CRF.

Most cases of MS occur against the background of long-term coexistence of risk factors, which include an increase in triglycerides, low-density lipoproteins (LDL-C) and a decrease in plasma HDL levels. Studies carried out in recent years on large groups of patients with MS have shown that most of the

generally accepted risk factors retain their negative effect in the presence of dyslipidemia, i.e. against the background of an increased level of TG and cholesterol, which is the dominant biochemical factor of atherosclerosis, in particular, it was shown that the existing risk factors (age, diabetes mellitus, arterial hypertension, an increase in LDL, a decrease in HDL) are risk factors for MS [2,4,5, 7,8,12,13,16,18,20]. There are also works that emphasize that the listed parameters cannot fully explain the variability of the clinical course of MS.

As can be seen from table 3, 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 patients 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 that of the control group by 53.8%, the LDL level in group III increased by 99.7% compared to the healthy

group. HDL in groups II and III is reduced compared to 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%. When comparing the first and second groups, the difference in blood glucose levels was 7.1%, and in groups I and III - 47.6%.

Table 3.

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

Groups	Total cholesterol, mmol / l	Triglycerides, mmol / l	LDL, mmol / l	HDL, mmol / l	VLDL, mmol / l	Index atherogen., units	Glucose plasma, 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
P 1-2	P<0,001	P<0,05	P<0,001	P<0,05	P<0,05	P<0,01	P<0,05
P 1-3	P<0,001	P<0,001	P<0,001	P<0,05	P<0,05	P<0,001	P<0,001
P 2-3	P<0,05	P<0,001	P<0,01	P<0,05	P<0,05	P<0,001	P<0,01

According to a number of authors, it is difficult to separate MS from hyperuricemia, as well as to determine causal relationships, because, according to modern ideas about the pathogenesis of MS, these states mutually induce the emergence and consolidation of each other. Hyperuricemia is detected in 25% of MS patients. The importance of the relationship between hyperuricemia and the development of MS, atherosclerosis and ischemic heart disease is evidenced by the relationship of hyperuricemia as a factor.

CONCLUSION

Thus, the data obtained indicate that hyperuricemia is a metabolic disorder and one of the components inherent in metabolic syndrome. The severity of GU is directly

proportional to the increase in the clinical picture of MS. In patients with MS, the presence of normoalbuminuria indicates an adaptive-compensatory vascular reaction aimed at overcoming the developing pathology of the kidneys. The presence of MAU means that the MAU stage can be reversible if treatment is started on time and will slow down the progression of DN and its transition to the stage of PU and CRF. The presence of MAU - about glomerular hypertension and a decrease in glomerular filtration.

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