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## **PURINE METABOLISM AND MICROALBUMINURIA IN PATIENTS WITH METABOLIC SYNDROME**

**Summary:** The aim of this work was to study the state of purine metabolism and microalbuminuria in patients with metabolic syndrome. We examined 50 patients aged 30-55 years, who were randomized into 3 groups: I (control) – healthy individuals – 15 people, II – patients with arterial hypertension – 18 people, group III – patients with arterial hypertension in combination with metabolic syndrome – 32 people. The results of the studies showed that the concentration of UA in the blood significantly correlated with the severity of obesity, hyperinsulinemia, triglyceridemia and glycemia - parameters that reflect the state of IR. Thus, the data obtained indicate that hyperuricemia is a metabolic disorder and one of the components inherent in the metabolic syndrome.

**Keywords:** metabolic syndrome, hyperuricemia, microalbuminuria, arterial hypertension, insulin resistance

**Management:** Recently, we have faced a new pandemic, i.e. a new term for metabolic syndrome (MS) has appeared in medicine and it summarizes the main factors leading to the development of atherosclerosis. In recent years, the literature has provided 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 [2,4,7,11]. MS is a complex of interrelated disorders of carbohydrate and purine metabolism, as well as mechanisms of regulation of blood pressure and endothelial reticula. The development of these disorders is based on a decrease in tissue sensitivity to insulin - insulin resistance (IR) [2,3,4,15].

According to studies performed at the Clinic of Internal Diseases of the RUDN, daily monitoring revealed the absence of a decrease in blood pressure in patients with high hyperuricemia and a reliable relationship between the left ventricular myocardial mass index and uric acid and serum levels 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 peculiarities of antihypertensive therapy in metabolic syndrome are associated with high uric acid levels [7,8,12,14]. Consequently, hyperuricemia (HUC) and microalbuminuria (MAU) are closely interrelated processes characterizing the clinical manifestation of MS. However, there is not enough work to study the state of purine metabolism and microalbuminuria in MS patients and this problem needs further comprehensive research.

**The purpose of the work.** To study the state of purine metabolism and microalbuminuria in patients with metabolic syndrome.

**Materials and methods.** 50 patients aged 30 to 55 years suffering from MS were examined, taking into account risk factors and lesions of target organs. In a hospital setting, 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 – 15 people; II – patients with arterial hypertension – 18 people at the age of 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. The body mass index (BMI) was determined using the formula: weight (kg)/height (m)<sup>2</sup>. According to the WHO classification, body weight is considered to be extremely accurate if the BMI exceeds 24.9.

2. Abdominal obesity was determined by measuring the waist circumference (FROM) between the edge of the lower rib and the wing of the ilium. The physiological indicator was taken as: for women less than 80 cm.

3. To determine metabolic disorders in patients, the level of total cholesterol (HC), triglycerides, very lowdensity 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). The state of purine metabolism was determined enzymatically by the colorimetric method by the level of uric acid in blood serum on an automatic analyzer Stat Fax Awakes technology INC (Italy), using reagents Hospitex diagnostics S.r.l. (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 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.** In the majority of MS patients, the disease was associated with a hereditary factor (31.5%), obesity (30.0%), an alimentary factor (28.4%), and low physical activity (inactivity – 10.1%). In the alimentary factor group, patients indicate excessive consumption of carbohydrates and fats. Overweight and obesity are considered to be the main components of MS. And at the same time, the interconnection between the components of the MS is of particular interest. In the examined patients, the Quetelet index (IC), body mass index and the degree of abdominal obesity (AO) were determined.

The measurement of waist circumference in group I showed  $78.8 \pm 1.14$  cm, in group II  $80.3 \pm 0.46$ , and in MS- $102.5 \pm 1.5$  cm (Tab -1). In patients with hypertension, AO was 1.9% higher than in the control group, i.e. the indicators were almost the same. When examining the IR in the control group, this indicator showed  $24.3 \pm 0.7$  m<sup>2</sup>, and in the II group the IR was equal to  $26.7 \pm 1.3$  m<sup>2</sup>. In the GB group, the IR was 4.9% higher, the indicators were almost the same. In MS, the IC averaged  $32.6 \pm 0.8$  m<sup>2</sup>, was 35% higher than in the control group, and 28.6% higher than in the II group.

The results obtained suggest that blood pressure and glycemc levels are related to body weight. Purine metabolism was evaluated based on the determination of uric acid concentration in plasma samples of venous blood taken on an empty stomach. Hyperuricemia with an MC level above 0.45 mmol/l was detected by us in 52.6% of patients suffering from MS and in 37.1% of patients who had an 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 the examined individuals into 3 clinical groups based on the results of the study. As the clinical picture of the syndrome increased, the prevalence of hyperuricemia also increased: in the HYPERTENSION group - in 22.2% of cases: in the MS group - in 50.7% of cases. The table shows the average values of purine

metabolism indicators, as well as other studied parameters reflecting the severity of disorders characteristic of MS.

A significant increase in the degree of uricemia occurred in the MS groups, i.e. at the stages when there was a statistically significant increase in TG concentration and obesity parameters. Although the deterioration of diastolic function correlated with an increase in the degree of hyperuricemia, the change in this parameter in patients with MS acquired a significant (compared with patients without the mentioned syndrome) character much earlier than the concentration of MC significantly increased in them. We did not find a reliable relationship between the magnitude of uricemia and the blood pressure level, but in individuals with a metabolic syndrome clinic without hypertension, the MC level was statistically significantly lower than in patients with an MS clinic, and there was also a tendency for a lower value of this parameter compared with all groups of patients who had MS with hypertension.

Analyzing the individual The distribution of MK concentrations among individuals of all clinical groups, we concluded that the level of uricemia characteristic of MS is the MK index of 0.45 mmol/l and higher. Patients with MS had this level of MC significantly more often than those with hypertension (chi-squared = 3.76,  $p < 0.05$ ). In our study, hyperuricemia was detected in 52.6% of patients with MS, which is slightly higher than the data of other authors. However, the frequency of purine metabolism disorders depended on the presence of concomitant components of MS: in its absence, it was only 22.2%, increased with the progression of the clinical picture of the syndrome and reached a maximum of 68.6% in patients with MS.

In addition, we noted that the concentration of MC in the blood was significantly correlated with the severity of obesity, hyperinsulinemia, triglyceridemia and glycemia - parameters reflecting the state of IR. Thus, the obtained data indicate that hyperuricemia is a metabolic disorder and one of the components inherent in the metabolic syndrome. We examined 26 MS patients for the presence of MAU. Patients were divided into groups. The criteria for the formation of groups were the stages of diabetic nephropathy (DN): group 1 – patients with normoalbuminuria: albumin excretion in urine below 30 mg/ day; group 2 – patients with MAU: albumin excretion in urine from 30-300 mg/day; group 3 - patients with proteus-nuria (PU), detected during the study of daily protein excretion with urine and with preserved nitrogen excretion 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, patients have nonselective proteinuria in 80.1% of cases. The degree of MAU and PU was directly correlated with the degree of DN: at the initial stage of DN – MAU at the level of microalbuminuria ( $< 30$  mg / day), at DN II stage of MAU from 30-300 mg / day, at DN III – IV degrees, PU is determined. The degree of PU severity is directly proportional to the degree of DN. At the bottom of stage III, PU was  $1.47 \pm 0.7$  g/ day, at the bottom of stage IV –  $2.7 \pm 1.9$  g/ day. Thus, in MS patients, the presence of normoalbuminuria indicates an adaptive-compensatory vascular reaction aimed at overcoming developing kidney pathology. The presence of MAU means that the MAU stage can be reversible with timely initiation of treatment and inhibits the progression of DN and its transition to the stage of PU and CRF. Studies performed in recent years on large groups of patients with MS have shown that most of the generally accepted risk factors retain their negative effect even in the presence of dyslipidemia, i.e. against the background of elevated levels of TG and HC, which is the dominant biochemical factor of atherosclerosis, in particular, it was shown that existing risk factors (age, diabetes mellitus, arterial hypertension, increased LDL levels, decreased

HDL levels) are risk factors for MS [2,5,7,12,13].

There are also papers emphasizing 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, and LDL is noted 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 the indicator of the control group by 53.8%, the LDL content in group III increased by 99.7% compared with 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%. When comparing the first and second groups, the difference in blood glucose levels was 7.1%, and in groups I and III - 47.6%. According to some authors, it is difficult to separate MS from hyperuricemia, as well as to determine cause-and-effect relationships, because, according to modern ideas about the pathogenesis of MS, these conditions mutually induce the occurrence 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 coronary 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 the metabolic syndrome. The degree of severity of GU is directly proportional to the increase in the clinical picture of MS. In MS patients, the presence of normoalbuminuria indicates an adaptive compensatory vascular response aimed at overcoming the developing kidney pathology. The presence of MAU means that the MAU stage can be reversible with timely initiation of treatment and will slow down the progression of DN and its transition to the stage of PU and CRF. The presence of MAU indicates glomerular hypertension and a decrease in glomerular filtration.

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