THE STATE OF PURINE METABOLISM AND MICROALBUMINURIA IN PATIENTS WITH METABOLIC SYNDROME

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SUMMARY

The aim of this work was to study the state of purine metabolism and microalbuminuria in patients with metabolic syndrome. 50 patients aged 30-55 years were examined, who were randomly assigned to 3 groups: I (control) - healthy people - 15, II – patients with hypertension - 18 people, III group - patients with arterial hypertension and metabolic syndrome - 32 people. Results of the research have shown that the concentration of MC in the blood significantly correlated with the severity of obesity degree, hyperinsulinemia, and triglyceridemia and glikemia – parameters which reflect the state of IR. So, the findings suggest that hyperuricemia is metabolism disturbtion and one of the components of metabolic syndrome.

Keywords: metabolic syndrome, hyperuricemia, microalbuminuria, 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, there has been a lot of information in the literature about the main role of MS in the development of various diseases. This is indicated by the data on MS caused by multiple disorders [1,2,10]. 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) [9,12]. Glucose and insulin are important factors in uric acid homeostasis involved in ensuring its secretion and reabsorption. An imbalance of these indicators leads either to hypouricemia or hyper-rickemia. Thus, hyperuricemia contributes to uricosuria, so the level of uric acid in the blood of patients with decompensated diabetes mellitus of any type may decrease. The effects of insulin on uric acid excretion are opposite to the effects of glucose. At the same time, normal insulin levels have virtually no effect on renal hemodynamics, glomerular filtration, and the permeability of the renal filter in relation to albumin [4,8,13].

Consequently, hyperuricemia (HUC) and microalbuminuria (MAU) are closely interrelated processes that characterize 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.

Objective: 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 hospital conditions, 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. To determine metabolic disorders in patients, the level of total cholesterol (HC), triglycerides, very low-density lipoproteins (VLDL), LDL, high-density lipoproteins (HDL), atherogenicity coefficient were studied (the lipid spectrum was determined biochemically by the Reflotron-Roche express analyzer). The state of purine metabolism was determined enzymatically by colorimetric method by the level of uric acid in the blood serum on an automatic analyzer Stat Fax Awarenes technology INC (Italy), using reagents Hospitex diagnostics s.r.l. (Italy). 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 $R<0.05$.

Results and discussion. In the majority of MS patients, the disease was associated with a hereditary factor (31.5%), obesity (30.0%), alimentary factor (28.4%), and low physical activity (inactivity – 10.1%), (fig.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 communication between the MS components is of particular interest. In the examined patients, the Quetelet index (IC), body mass index and the degree of abdominal obesity (AO) were determined. Measurement of waist circumference in group I showed 78.8 ± 1.14 cm, in group II 80.3± 0.46, and in MS-102.5 + ± 1.5 cm (Tab -1). In patients with hypertension, AO was higher than the control group by 1.9%, i.e. the indicators were almost the same. When examining the IR in the control group, this indicator showed 24.3 ± 0.7 m2, and in the II group the IR was equal to 26.7 ± 1.3 m2. In the GB group, the IR was

4.9% higher, the indicators were almost the same. In MS, the IC averaged 32.6± 0.8 m2, was 35% higher than the indicators of the control group, and the indicators of the II group by 28.6%. The results obtained suggest that blood pressure and glycemic level 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.

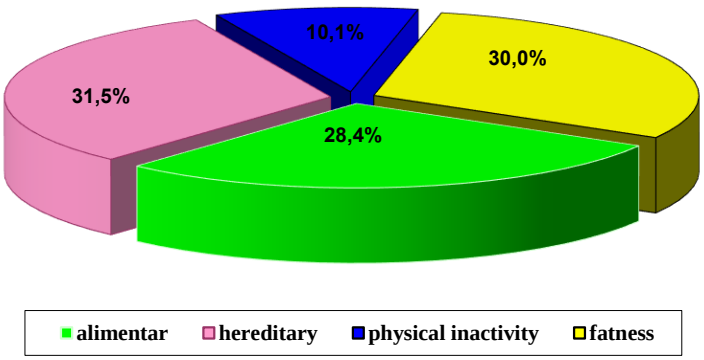

Рис. 1. *Etiological factors of MS*

Hyperuricemia MC level over 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 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 MS group in 50.7% of cases. The table shows the average values of purine metabolism indicators, as well as other parameters studied, 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 the concentration of TG and the parameters of obesity. 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 character (compared with patients with the absence of the mentioned syndrome) 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 to all groups of patients whose MS occurred with hypertension. Analyzing the individual distribution of values the concentration of MC among individuals of all

clinical groups, we came to the conclusion that the level of uricemia characteristic of MS is the MC index of 0.45 mmol/l and higher. Patients who had MS had this level of MC significantly more often than those with hypertension ($p<0.05$).

Table -1

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

Indicator	**MC**		
	I Group	II Group	III Group
Age, years	44,6±1,2	46,5±1,6	50,2±2,2*
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 ***
Ketle index, kg/sq.m	24,3±0,7	26,7± 1,3**	32,6± 0,8***
SAP, mmHg.	125,6±1,8*	150,0±2,9	152,4±5,0
DAP, mmHg.	85,2±2,2	101,2±2,1	100,7±1,7

Note: * R<0,05, ** R<0,01, *** R<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 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 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 the metabolic syndrome.

We examined 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: 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 proteinuria (PU), detectable in the study of the daily excretion of protein in the 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.

Table -2

Clinical characteristics of MS patients by MAU level

Indicator	Control	AP	MC
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: the differences with the control are significant *R-<0,02, **R<0,01

In the presence of MS, patients have nonselective proteinuria in 80.1% of cases. 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), at DN II stage of MAU from 30-300 mg / day, at DN III – IV degree, PU is determined. The degree of PU severity is directly proportional to the degree of DN. At stage III DN, the PU was 1.47 ±0.7 g/day, at stage IV DN – 2.7±1.9 g/day.

Thus, in MS patients, the presence of normoalbuminuria indicates an adaptive-compensatory vascular reaction aimed at overcoming the developing kidney pathology. The presence of MAU means that the stage of MAU 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. Most cases of MS occur against the background of a long-term coexistence of risk factors, which include an increase in TG, LDL cholesterol and a decrease in HDL levels in blood plasma [2,10,12]. There are also works 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, 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 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%. 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 HS, mmol/l	Triglycerides, mmol/l	LDL, mmol/l	HDL, mmol/l	VLDL, mmol/l	The atherogen index.,ед	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
R 1-2	R<0,001	R<0,05	R<0,001	R<0,05	R<0,05	R<0,01	R<0,05
R1-3	R<0,001	R<0,001	R<0,001	R<0,05	R<0,05	R<0,001	R<0,001
R2-3	R<0,05	R<0,001	R<0,01	R<0,05	R<0,05	R<0,001	R<0,01

According to a number of 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 artery 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 reaction aimed at overcoming the developing kidney pathology. The presence of MAU means that the stage of MAU 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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