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SYMPTO-ADRENARAL SYSTEM AND IMMUNE INFLAMMATION IN METABOLIC SYNDROME

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Summary
Metabolic syndrome is characterized by dysregulation of many organs and systems of the body. There is no doubt about the important role of the sympathetic-adrenal system (SAS) in the processes of neurohumoral regulation. The addition of disimmunoregulation components exacerbates this condition. It has been shown that the high activity of S AS causes immuno-imbalance of humoral immunity.

Keywords: metabolic syndrome, sympathetic-adrenal system, monoamine oxidase, cytokines.

Relevance

Metabolic syndrome (MS) is considered a global medical and social problem due to its high prevalence and high mortality rate [1]. According to WHO experts, by 2050 the number of MS patients will exceed 550 million people [1]. In MS, the development and progression of insulin resistance (IR) and associated metabolic disorders play an important role in immune inflammation and neurohumoral disorders with an increase in SAS activity [2,4]. MS not only changes the reactivity of the immune and neuroendocrine systems, but also the mutual integration and interactions between them [3].

The aim of the study was study of the relationship and mutual influence of the sympathetic-adrenal system and immunoinflammatory changes in metabolic syndrome.

Material and Methods

The study included 100 patients (age from 35 to 57 years, on average 46.7 ± 2.1 years), of which 80 had MS. All patients were assessed the state of carbohydrate metabolism (glucose on an empty stomach, insulin on an empty stomach); the state of lipid metabolism (total cholesterol – total cholesterol, TG, HDL, LDL). IR was calculated using the HOMA index.
Biologically active amines were determined by the daily urinary excretion of free and

conjugated forms of catecholamines (CA) by the fluorimetric method modified by E.Sh. Matlina . The determination of the activity of monoamine oxidase (MAO) in the blood was carried out according to the method of A.V. Balaklevsky . Cytokine status (IL-6, TNF-α, IL-10) was studied by enzyme – linked immunosorbent assay.

Results and Discussion

All patients were randomized into three groups. Group I – control consisted of 20 healthy individuals aged 35 – 55 years. Group II consisted of 30 patients diagnosed with arterial hypertension (AH) II – III stage, Group III consisted of 50 patients diagnosed with MS.

When studying the daily excretion of CA and DOPA in patients with hypertension, a statistically significant increase in the excretion of adrenaline (A) by 52.7% was noted, which is 2.1 times higher than the values of the control group (P <0.001). The highest levels of A excretion were noted in the group of patients with MS, which is 61.1% and, accordingly, 2.6 times higher than the control values (P <0.001). The daily excretion of norepinephrine (NA) was also significantly increased in groups II and III . Thus, the content of NA in patients with AH is 63.2%, which is 2.6 times higher than in the control (P <0.001). The indicators of total NA in the group of patients with MS turned out to be maximally increased in relation to other biogenic amines and 73.0% (3.7 times; P <0.001) higher than the control values (Table 1). Data on the significance of insulinemia in the activation of the SAS in MS patients have been confirmed [8, 10]. A direct correlation was found between daily NA excretion and hyperinsulinemia (HI) (r =0.67, P <0.01), as well as NA with body mass index (r =0.65, P<0.01). A direct correlation was found between the daily excretion of NA and the level of blood pressure (r = 0.62, P < 0.01).

The release of dopamine (DA) in this category of patients did not change significantly both in relation to the control group and relative to other groups. Thus, the content of DA in patients with AH is reduced by 8.1% (p >0.05) compared with the control values. The results of DA in patients with MS also showed a tendency to a slight decrease in performance (Table 1). The level of DOPA was moderately increased in group II patients by 46.9%, which is 1.8 times higher than in the control group (p <0.01). The parameters of the group of patients with MS were 86.8±2.71 μg/ day, which is 51.8% higher than control (P <0.001) (Table 1).

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Table 1

Indicators of daily excretion of catecholamines (CA) in healthy people, patients with AH and MS (μg/ day)

Indicators \ Groups		Healthy (n =20)	AH (n =30)	MS (n =50)
A	free	4.29±0.33	8.9±0.38	11.3±0.45
	conjugated	3.9±0.35	8.4±0.32	9.72±0.36
	total	8.13±0.67	17.3±0.70*	21.02±0.81*
NA	free	8.1±0.31	21.3±0.63	27.6±0.68
	conjugated	7.15±0.36	20.1±0.71	28.9±0.81
	total	15.25±0.67	41.4±1.78*	56.5±1.48*
DA	free	176.0±9.07	149.5 ± 8.30	149.9±8.75
	conjugated	187.0±7.30	186.4 ± 7.20	199.1±9.2
	total	363.0±16.40	335.9 ± 15.60**	349.0 ±17.95**
DOPA		41.83±2.47	78.8±3.60*	86.8±2.71*
MAO (u/exc)		0.072	0.036	0.029

Note: * – reliability of differences between the indicators P <0.001

** – reliability of differences between the indicators P <0.05

Studies of the activity of MAO – the enzyme deamination of CA revealed that in parallel with the increase in the concentration of CA in daily urine, there was a significant decrease in MAO in all groups of patients: from moderate (group II by – 42.9%; 1.75 times, to pronounced (III group – by 71.5%; by 3.5 times) (Table 2). An inverse correlation of MAO with daily excretion of NA in patients with MS (r = -0.68, P <0.01) was revealed.

The immune system reacted with an imbalance of pro- and anti-inflammatory cytokines. In all groups of patients, an increase in proinflammatory cytokines was noted. Thus, IL-6 increased from moderate (group II by 64.0%) to a sharp increase by more than 3.7 times in patients with MS. The maximum increase was noted in TNF-α – in the group of MS patients up to 96.8±9.6 pg /ml (4.3 times). Antinflammatory IL-10 had only a slight tendency to increase both in patients with hypertension (by 24.5%) and in patients with MS (by 1.7 times compared with the control). Apparently, this is associated with a different immunological response to a chronic inflammatory process occurring in the vascular wall (Table 2).

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Table 2 Content of immunocytokines in healthy people, patients with AH and MS (pcg /ml)

No.	Groups	IL-6	TNF-α	IL-10
I	Healthy (n =20)	20.9±2.1	22.6±2.1	13.7±0.8
II	Patients with hypertension (n =25)	34.3±2.7**	34.7±2.7**	16.8±0.9**
III	Patients with MS (n =30)	78.3±6.7*	96.8±9.6*	21.1±1.9*

Note: * – reliability of differences between the indicators P <0.001

** – reliability of differences between the indicators P <0.01

A positive correlation was found between IL-6 and elevated blood pressure (r =0.67, P <0.01), IL-6 level and body mass index (r =0.59, P<0.01). A positive correlation was also found between the levels of IL-6 (r =0.53, P <0.01) and TNF-a (r =0.60, P<0.01) with an increase in daily excretion of NA.

The problem of the functional state of the SAS in patients with MS, its relationship with other clusters of the disease, in particular with the immune system, has become a subject of discussion in recent years [3]. The SAS and the immune system are closely related . GI leads to a significant increase in the activity of the SNS and, first of all, the SAS [2]. Under conditions of IR, hyperactivation of the SNS leads to the appearance of AH and the development of MS due to sympathetic stimulation of the heart, blood vessels, and kidneys [1,2]. On the other hand, endogenous CA can stimulate the production of cytokines and humoral immunity [3].

The conducted studies revealed the functional activity of CAS, especially NA in MS patients. At the same time, these same patients showed a violation of the immune response with an increase in pro- inflammatory cytokines – IL-6, TNF-a. The established correlation relationships between the content of CA and IL confirm the distinct effect of SAS activation on the state of the body's immune system.

Conclusions

1. Activation of the sympathetic-adrenal system in MS is associated with increased CA biosynthesis, especially norepinephrine and adrenaline.
2. The decrease in the activity of the key enzyme of CA deamination, monoamine oxidase, is inversely proportional to the increased activity of the sympathetic-adrenal system in MS, which causes a qualitatively reversible change in the catalytic properties of its activity.
3. It has been established that in MS there is an imbalance of the immune system, in particular, the cytokine link with an increase in the activity of proinflammatory cytokines (IL-6, TNF-α), which are markers of cardiovascular risk in MS.

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