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NONSPECIFIC BODY REACTIVITY IN PATIENTS WITH DIABETES MELLITUS DEPENDING ON ITS DURATION

Introduction. Diabetes mellitus (DM) – is the most widespread form of the disturbance of all types of metabolism. As it is well known, body metabolic processes are significantly changed in case of DM, influencing on adaptive body potential and the degree of its immune reactivity [4]. Investigation of the adaptive body reserves, starting mechanisms of dysadaptation processes is of a high importance in relation to DM, known to be accompanied by the significant disturbances of natural and acquired immunity [2], serious disorders of neuroendocrine and immune interaction [7], that stipulates the severity and prognosis of the disease. That's why the comparative analysis of immune reactivity parameters in DM of various duration is of a special attention in concern of their timely correction and prognosis of the probable individual patient's response on administered treatment.

Considering that, the **objective** of this research was to study the changes of reactivity and adaptive body potential in patients with diabetes mellitus depending on its duration.

Materials and methodology. 33 patients with DM (17 men and 16 women – 52 and 48% respectively), aged between 19 and 78 years (mean age – $50,70 \pm 2,27$ years) and 10 healthy individuals, who served as control group, participated in the study. The verification of the diagnosis was based on thorough clinical-anamnestic and laboratory-instrumental investigations according to the WHO recommendations.

According to the results of complex patients' examination DM type 1 was established in 10 patients – 30% (mean age – $36,50 \pm 3,83$ years), whereas in 23 patients (70%) DM type 2 was diagnosed (mean age – $56,87 \pm 1,55$ years). The severity of the disease was assessed by the degree of clinical symptoms manifestation. Thus, moderate severity of DM was identified in 17 enrolled patients with overwhelming majority of DM type 2 patients (82%); severe form of the disease was observed in 16 examined patients, represented by 44% of type 1 diabetics and 56% of type 2 diabetics; individuals with mild diabetes were absent among those involved into the study. All participating patients were at the subcompensation stage of the disease.

In 12 of enrolled patients (group 1) the duration of diabetes was less than 5 years ($3,38 \pm 0,56$ years), in 11 participating individuals (group 2) diabetes lasted for 6-10 years ($7,82 \pm 0,56$ years), 10 of participants (group 3) had diabetes longer than 10 years ($15,10 \pm 1,11$ years). It should be noted, that the cohort of patients with DM type 1 in severe form was equally represented by cases of its duration less than 5 and more than 10 years, whereas in patients with DM type 2 severe form of the disease was mostly observed at the duration more than 10 years.

Integral haematological coefficients were used for the assessment of adaptive potential and general reactivity in diabetic patients [1, 9]: leukocytic index (LI), modified leukocytic intoxication index by B.A.Reys (LII), leukocyte shift index (LSI), neutrophils to lymphocytes ratio index (NLRI), leukocytes to sedimentation ratio index (LSRI), lymphocytic-granulocytic index (LGI), nuclear intoxication index (NII), neutrophils to monocytes ratio index (NMRI). Statistical processing of the obtained data was performed by means of «Biostat» software, using paired Student's t-criterion.

Results and discussion. Integral haematological indices calculation revealed substantial changes of nonspecific resistance indices in patients with diabetes depending on its duration. Thus, the decline of LI was found to be inversely proportional to the duration of diabetes and reliably significant at its duration over than 6 years (by 26,9% concerning controls, $P<0,001$), practically further unchanging (remaining by 23,1% lower at the duration of DM longer than 10 years as compared with that in controls, $P<0,001$, $P_2>0,1$). The decrease of NMRI had the same tendency with its unreliable elevation at diabetes duration over than 10 years ($P>0,5$). Meantime, other nonspecific resistance index – NLRI – enhanced proportionally to diabetes duration, ranking maximal level in patients with 6-10 years DM duration, remaining high at longer duration of the disease (NLRI increased by 31,1 and 28,4% in patients of group 2 and group 3 respectively, $P<0,001$, $P_2>0,5$).

Table.

Integral haematological indices in patients with diabetes mellitus depending on its duration ($X\pm Sx$)

Indices	Group, number of examined patients			
	Healthy individuals, n=10	Patients with DM, duration less than 5 years, group 1, n=12	Patients with DM, duration 6-10 years, group 2, n=11	Patients with DM, duration over than 10 years, group 3, n=10
Leukocytic index (LI)	0,52±0,02	0,44±0,04 $P>0,1$	0,38±0,01 $P<0,001$ $P_1>0,1$	0,40±0,01 $P<0,001$ $P_1>0,3$ $P_2>0,1$
Leukocytic intoxication index (LII)	1,70±0,05	2,02±0,13 $P<0,05$	2,14±0,07 $P<0,001$ $P_1>0,5$	2,11±0,06 $P<0,001$ $P_1>0,5$ $P_2>0,7$
Leukocyte shift index (LSI)	1,84±0,05	2,12±0,14 $P>0,09$	2,24±0,06 $P<0,001$ $P_1>0,4$	2,24±0,05 $P<0,001$ $P_1>0,4$ $P_2=1,0$
Leukocytes to sedimentation ratio index (LSRI)	1,85±0,20	0,97±0,11 $P<0,001$	1,54±0,28 $P>0,3$ $P_1>0,06$	1,95±0,39 $P>0,8$ $P_1<0,02$ $P_2>0,3$

Lymphocytic-granulocytic index (LGI)	4,38±0,15	3,86±0,31 P>0,1	3,35±0,10 P<0,001 P ₁ >0,1	3,43±0,10 P<0,001 P ₁ >0,2 P ₂ >0,5
Nuclear intoxication index (NII)	0,17±0,02	0,12±0,01 P<0,05	0,13±0,01 P>0,08 P ₁ >0,4	0,14±0,01 P>0,1 P ₁ >0,1 P ₂ >0,4
Neutrophils to lymphocytes ratio index (NLRI)	2,08±0,07	2,51±0,17 P<0,05	2,73±0,08 P<0,001 P ₁ >0,2	2,67±0,07 P<0,001 P ₁ >0,4 P ₂ >0,5
Neutrophils to monocytes ratio index (NMRI)	13,54±0,96	12,96±0,87 P>0,6	11,83±0,72 P>0,1 P ₁ >0,3	17,06±5,25 P>0,5 P ₁ >0,4 P ₂ >0,3

Note: values are expressed as means ± standard errors; number of patients in a group; P – significant difference in comparison with healthy individuals; P₁ – significant difference in comparison with patients of group 1; P₂ – significant difference in comparison with patients of group 2.

These findings evidence the impairment of nonspecific immune resistance (contributed mostly by microphages at DM duration for 6-10 years and macrophages – at its duration over than 10 years), as well as specific immune responsiveness, reliably significant already after 6th year of the disease.

Disturbance of the resistance, in its turn, determines the intensity and gravity of endogenous intoxication. Thereby, the signs of intoxication according to LII were found even in patients with non-protracted DM (LII exceeded control index by 18,8%, P<0,05, in patients of group 1), enhancing with its duration (LII was found to be elevated by 29,9 and 24,1% in patients of group 2 and group 3 respectively, P<0,001). LSI was also higher than of control by 14,6% (P>0,09) in case of diabetes duration less than 5 years and by 21,7% – in case of protracted diabetes (P<0,001, P₂=1,0).

The reduction of inflammation index LGI was found to be reliable in patients with DM duration for 6-10 years as compared with that in controls, continuing to remain lowered (LGI was by 23,5 and 21,7% lower than in controls in patients of group 2 and group 3 respectively, P<0,001, P₂>0,5). At the same time, inflammation index LSRI, maximally low in patients with DM duration for less than 5 years (by 1,9 times less than control level, P<0,001), tended to the increase proportionally to the duration of the disease, being twice higher in patients of group 3 (P₁<0,02).

Such changes of the studied parameters allow to suggest, that intoxication accompanying diabetes is endogenous, develops at the beginning of the disease and is caused, probably, by activation of the destructive mechanisms of tissue decomposition due to diabetes-

associated dysmetabolic processes [3, 11]. On the background of absent neutralizing opposition by detoxicating systems of the body, whose decompensation is evidenced by decreased NII in case of DM of various duration, and insufficient fermentative systems, dramatically disturbed in case of diabetes, autointoxication leads to the development of «metabolic immune defect», resulting in dysregulation of immunopoiesis, proliferation and metabolism of immunocompetent cells, autoregulation of immune response [8].

The accumulation of unphysiologic concentrations of intermediate and end products of metabolism, oxygen deficiency and oxidative tissues destruction, cellular stress mediators, other endotoxins, causative for toxemia [3], are found to be proportional to the duration of the disease. This explains more considerable autointoxication in patients with DM longer than 10 years, and, predictably, overexertion and exhaustion of macrophagic immune reactivity, directed mostly towards various products of tissue destruction [5]. Monocytic dysfunction, as well as inhibition of microphagic immune reactivity in patients with DM duration for 6-10 years, in its turn, provokes the disturbance of antigen presentation to immunocompetent cells, resulting in distortion of specific immunity [12].

Conclusions:

1) Dynamics of changes of integral haematological coefficients in case of diabetes mellitus is indicative for the development of endogenous intoxication, whose intensity enhances proportionally to the duration of the disease and is considered not only as the consequence of metabolism disturbances, typical for diabetes, but as the cause of pathological reactions as well, modulating the influence on body immunological reactivity and immune system disorganization in particular.

2) In case of diabetes mellitus the impairment of specific immunity as well as nonspecific one is formed, leading to dysregulation of cell-mediated and humoral reactions and depending on diabetes duration: at DM duration for 6-10 years the reduction of immune resistance is mostly contributed by macrophages, accompanied in the future by monocytic dysfunction on the background of significant deficiency of specific immune defense.

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ДИНАМИКА ЗАБОЛЕВАЕМОСТИ ВРОЖДЕННЫМИ ПОРОКАМИ РАЗВИТИЯ СРЕДИ ДЕТЕЙ ПЕРВОГО ГОДА ЖИЗНИ В АСТРАХАНСКОЙ ОБЛАСТИ

В статье рассматривается динамика заболеваемости врожденными пороками развития среди детей первого года жизни на территории Астраханской области за период 2004-2013 годы, порайонные соотношения уровней данной заболеваемости. Анализ показал рост данной патологии по всей области и преобладание в юго-западных сельских районах.