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ADIPONECTIN IN PATIENTS WITH TYPE 2 DIABETES MELLITUS WITH NORMAL BODY WEIGHT

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Resume. It was found that in patients with type 2 diabetes mellitus against the background of normal body weight, the average level of adiponectin (AN) in blood plasma, unlike patients with overweight and obesity, is within the reference norms. At the same time, about half of them (54.5%) have a reduced AH level. The subgroup with a reduced level of AH is characterized by a large age of patients and the duration of diabetes, as well as an increase in the levels of triglycerides and very low-density lipoproteins, a more frequent increase in waist circumference. At the same time, in patients with type 2 diabetes mellitus with normal body weight, there were no significant associative links between the level of AN and indicators of carbohydrate metabolism - blood glucose and fasting insulin levels, the NOMA-IR index. The obtained data substantiate the need to timely identify and correct lipid metabolism disorders in patients with type 2 diabetes mellitus with normal body weight.

Keywords: type 2 diabetes mellitus, normal body weight, adiponectin.

Introduction. Currently, adipose tissue is considered as an active metabolic and endocrine organ that plays a key role in the formation of obesity, metabolic syndrome and type 2 diabetes mellitus (DM) [1]. It has been established that even a small increase in the volume of visceral fat plays a significant role in metabolic disorders and an increased risk of cardiovascular diseases [2].

Adipose tissue is capable of secreting a large number of factors with various effects — adipokines [1]. The increased scientific interest in establishing the mechanisms of influence of each of them on the development of OH, insulin resistance (IR) and cardiovascular pathology is due to the need to obtain new data that can form the basis of diagnostic and therapeutic technologies.

Recently, significant attention has been attracted by adiponectin (AN) — adipokine, discovered in 1995 [3]. This protein is secreted in white adipose tissue and participates in the regulation of energy homeostasis of the body. It was revealed that the plasma concentration of AN is inversely correlated with the body mass index (BMI) in case of Lv [4]. The level of this hormone increases significantly during fasting and weight loss on the background of a hypocaloric diet in patients with acute respiratory failure [5]. AN indicators have a positive correlation with insulin sensitivity, and its low level in the blood precedes the development of IR [6]. The experiment showed that adiponectin reduces IR by activating the action of insulin in skeletal muscle and liver tissue [7]. IR — TNF-alpha mediators and glucocorticoids inhibit the secretion of AN [8]. It is not excluded that there is a feedback relationship between AH levels and cardiac risk factors, such as dyslipidemia and arterial hypertension (AH) [9, 10-15]. A hypothesis has been put forward according to which

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the trigger mechanism for the development of hypertension in children with LV is a combination of IR and hypoadiponectinemia [16-21].

It should be stated that the main body of publications on the effect of adipokines, including AN, on the progression of LV and the formation of cardiovascular pathology is based on the study of overweight persons (IbsMT) or with Lv. At the same time, the contingent of people with metabolic coolant against the background of normal body weight (NormMT) is practically not represented in the scientific literature, and this cohort, as it turned out, has a negative prognosis regarding mortality, including from cardiopathology, which determined the purpose of this study — to establish the levels of adiponectin in the blood plasma of patients with a clinical phenotype of type 2 diabetes against a background of normal body weight.

Materials and methods of research. The study group included 33 patients with type 2 diabetes with NormMT, whose BMI was below 25.0 kg/m2 at the time of diabetes diagnosis and the titers of antibodies to pancreatic islets (ICA) and glutamic acid decarboxylase (GAD) were not increased, which is characteristic of latent autoimmune diabetes in adults (LADA). The comparison groups consisted of 15 patients with type 2 diabetes with IBS and 11 with LV, who did not significantly differ in age (56,01 ± 1,69; 54,23 ± 2,01; 55,64 ± 1,87 years) and the duration of SD (8.69 ± 1.08; 7.87 ± 1.22 and 7.18 ± 1.58 years). In patients with the enzyme immunoassay, the level of adiponectin in blood plasma was studied using the EA2500-1 kit, Human Adiponectin ELISA (laboratory norm 4-16 ng/ml), immunoreactive insulin (IRI) was studied using the Inculin DRG ELISA kit, REF EIL-2935 (laboratory norms for the kit were 2-25 μed/ml) using enzyme immunoassay analyzer Stat Fax 4700. The glucose level in blood plasma was also determined by glucose oxidase method on the BIOSENC-LINE ECF Diagnostic device (laboratory norm 3.8–6.2 mmol/L). The HOMA-IR index was calculated using the formula: fasting blood glucose level (mmol/L) multiplied by fasting insulin level (mcEd/ml) and divided by 22.5. Normally, the indicator should not exceed 2.77.

The patients were measured waist circumference (FROM) with a centimeter tape made of flexible-rigid material. The OT indicator was evaluated taking into account the IDF criterion: the norm for men < 94 cm, the norm for women < 80 cm.

Blood cholesterol was determined by colorimetric method on a set with pL, Kharkiv. The Solar PM 2111 device (norm < 4.5 mmol/l). The level of triglycerides was determined using a set of CpL, Kharkiv (norm < 1.7 mmol/l). The level of very low density lipoproteins (VLDL) is calculated by the formula: VLDL = triglycerides • 0.45 (norm < 0.76 mmol/L).

Quantitative signs were checked for the normality of the distribution by the Shapiro—Wilk method. Statistical analysis of normally distributed quantitative data was carried out by the Student's method. The arithmetic mean values of X, the standard deviation of S, and the statistical error of the arithmetic mean of SX are

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calculated. The reliability of the difference in average values was determined by the Student's t-criterion. To establish the relationship between the indicators of adiponectin and other studied values, a correlation analysis using the Pearson method was carried out.

Results and their discussion. The conducted studies have shown that the average levels of AN concentration in the blood of patients with DM against the background of IBS and LV were reduced (2.97 ± 0.49 and 2.83 ± 0.46 ng/ml, respectively). At the same time, in the group of patients with NormMT, they were within the normal range — 4.36 ± 0.52 ng/ml and were significantly ($p < 0.05$) higher than with IbsMT and with Lv. This confirms the literature data that the concentration of circulating AN decreases as the body weight of patients with type 2 diabetes increases [6]. At the same time, in 18 of 33 patients with NormMT (54.5%), the level of AN in the blood was reduced. Considering that this factor is considered unfavorable in terms of the prognosis of cardiac pathology, it was analyzed by what parameters the subgroups with normal and reduced levels of AN differ (Table 1).

Table 1

Dependence of characteristics of patients with type 2 diabetes mellitus on the background of normal body weight on the level of plasma adiponectin

Indicator, unit of measurement	X ± SX		p
	Adiponectin > 4.0 ng/ml r (norm)	Adiponectin < 4.0 ng/ml (reduced)	
Age of patients, years	52,40 ± 2,54	59,00 ± 2,09	< 0,05
Duration of SD, years	6,34 ± 0,80	10,70 ± 1,77	< 0,05
FROM, the frequency of magnification, %	46,7	61,1	-
IRI, mmol/l	14,4 ± 2,6	11,90 ± 1,43	-
Blood glucose, mmol/l	8,79 ± 0,35	8,49 ± 0,42	-
HOMA-IR	5,32 ± 0,87	4,54 ± 0,61	-
Triglycerides, mmol/l	1,63 ± 0,18	2,29 ± 0,26	< 0,05
Cholesterol, mmol/l	5,26 ± 0,27	5,73 ± 0,24	-
HC VLDL, mmol/l	0,74 ± 0,08	1,08 ± 0,14	< 0,05

It turned out that in the group with a reduced level of circulating AN, the age of patients and the duration of diabetes were significantly greater ($p < 0.05$). This group also significantly differed in the level of TG and VLDL, and the values of these two

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indicators exceeded the reference norms, in contrast to the group with a normal concentration of plasma AN. In the group with hypoadiponectinemia, the frequency of increase in OT was unreliably ($p > 0.05$) higher by 30.8%, as well as the level of total cholesterol was 8.9% higher.

As for the characteristics of carbohydrate metabolism, they showed the opposite trend: against the background of hypoadiponectinemia, the level of IRI was within the normal range and 17.4% lower, and the level of NOMA-IR was 14.7% lower than in the group with AN > 4.0 ng/ml, but the differences were not significant ($p > 0.05$). It should be noted that at the same time, the NOMA-IR index exceeded the norm in both groups, and the level of IRI — only in the group with a normal level of AN.

We have traced associative links between AN and a number of characteristics of patients with type 2 diabetes with Norms (Table 2).

Table 2

Correlations between circulating adiponectin and a number of characteristics of patients with type 2 diabetes mellitus with normal body weight

Indicator	r	p
Age of patients	–0,251	-
Duration of diabetes	–0,397	< 0,05
Waist circumference	–0,07	-
IRI	–0,100	-
Fasting glycemia	–0,019	-
NOMA Index-IR	0,071	-
General Cholesterol	–0,254	-
VLDL	–0,354	< 0,05
tg	–0,357	< 0,05

It was found that in individuals with Norm, the concentration of circulating AN significantly negatively correlated with the duration of type 2 diabetes, the level of VLDL and TG. At the same time, there was no significant correlation with the indicators of carbohydrate metabolism.

One of the methodological approaches in the study of the mechanisms of formation of a particular pathology is the identification of the relationship between different "participants in the process" in groups that differ in some way. The principal feature of our study is the selection of a group of patients with type 2 diabetes at the age of IV-VI decades of life with normal BMT (BMI < 25.0 kg/m2), and in this group a significant negative correlation was established between circulating AN and the duration of type 2 diabetes, VLDL and TG levels. According to the literature, adolescents with LV have a negative correlation of AN with the age of the child, an increase in OT, IRI, the NOMA-IR index, BMI and HDL [12]. In men with abdominal LV [5], a negative correlation was found between AN and BMI, OT,

OT/OB, IRI. T. Lindstrom et al. [13] in women with type 1 diabetes, a negative correlation was found between AN and the duration of diabetes and a positive one with HDL, and with type 2 diabetes type —negative correlation of AN with BMI and NOMA-IR, TG and positive — with HDL. Scientists from the St. Petersburg Research Institute of Experimental Medicine [14] have studied in detail the associative relationships between the concentration of AN and metabolic parameters in patients with a BMI < 28 kg/m2 (with normal and moderately increased body weight) and with Lv (BMI 28 kg/m2) and found that in the first of these groups AN It correlated negatively with IRI and NOMA-IR, and with the frequency of development of type 2 diabetes in case of LV. At the same time, the correlation with TG did not reach a statistically significant level. It should be noted that in this study, the group of patients with a BMI < 28 kg/m2 included individuals with both NormMT and partially with IbsMT, therefore, it does not seem quite correct to compare the results of this group with those of patients with NormMT. Nevertheless, attention is drawn to the fact that in people of different age groups, as a rule, against the background of LV, the correlation of AN is revealed not only with metabolic characteristics — BMI, OT, OT / OB, manifestations of dyslipidemia, but also with indicators of carbohydrate metabolism. In our study concerning patients with type 2 diabetes with NormMT, the correlation between AN, TG and VLDL comes to the fore.

Conclusion. 1. Approximately half of patients with type 2 diabetes mellitus have hypoadiponectinemia against the background of normal body weight.

2. The duration of diabetes and the age of patients are factors contributing to a decrease in the level of adiponectin in patients with normal body weight.

3. The level of circulating adiponectin in patients with type 2 diabetes mellitus on the background of normal body weight negatively correlates with the level of triglycerides and very low density lipoproteins.

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