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# HUMORAL REGULATION IN REMODELING OF ARTERIAL VESSELS IN PATIENTS WITH TYPE 2 DIABETES IN COMBINATION WITH OBESITY: FOCUS ON OMENTIN

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**Introduction.** The influence of various adipokines, as products of adipose tissue metabolism, on the development of angiopathy in patients with diabetes mellitus (DM) type 2 determines the relevance of the problem of vascular diabetic complications. [1]. The altered secretion of these substances is capable of simulating the mechanisms of formation of angiopathies in the mentioned persons [2]. An increase in the thickness of the intimo-medial segment (TIMS) is associated with cardiovascular risk factors, as well as vascular catastrophes [3]. An association between increased TIMS and the development of metabolic syndrome was established [4]. The association between the structural changes of arteries and the secretion of certain adipokines in obese type 2 DM patients remains unclear.

**Aim:** to determine the level of omentin-1 in obese patients with type 2 diabetes and to assess the presence and nature of the relationship between its level and TIMS of the carotid arteries in these individuals.

**Material and methods.** An examination of 90 patients with diabetes, who were treated in hospital conditions at the CI "OK Endocrinedispensary" of the ZRC, was carried out. Group 1 included 58 people (30 women and 28 men) with a body mass index  $> 25 \text{ kg/m}^2$ , the average age was  $56.6 \pm 10.33$  years, the average duration of diabetes was  $7.51 \pm 5.13$  years. Group 2 included 32 patients (17 women and 15 men) with a body mass index  $\leq 25 \text{ kg/m}^2$ , average age  $55.22 \pm 6.14$  years, average



duration of diabetes  $6.48 \pm 5.71$  years. The control group included 27 practically healthy individuals, which was comparable to groups 1 and 2 in terms of gender and age. All patients gave written consent to participate in the study for ethical reasons in accordance with the Declaration of Helsinki.

Omentin-1 level was determined by enzyme immunoassay using test systems from Bender MedSystems GmbH (Austria). Ultrasound of the carotid arteries was performed using a MyLab50X device with a 7 MHz linear sensor, TIMS was measured in B-mode at a distance of 1.0–1.5 cm proximal to the bifurcation of the common carotid artery according to generally accepted recommendations.

Correlation analysis using the Spearman correlation coefficient was used to determine the direction and nature of the relationship. The presence of intergroup differences was assessed by the Mann-Whitney method. Statistical analysis was performed using the program "Statistica 6.1" (StatSoft Inc., USA, serial number RGXR412D674002FWC7). Statistically significant differences were considered at  $p < 0.05$ .

**Results and discussion.** Patients with type 2 diabetes and obesity had a significantly lower level of omentin-1 compared to patients of group 2, the difference was 123.25% ( $p < 0.05$ ). When examining the level of omentin-1 in the subjects, depending on the degree of compensation of diabetes, it was found that in 1 group of patients with HbA1c values  $\geq 8\%$ , the level of omentin-1 was lower than in compensated diabetes - by 27.22% ( $p < 0.05$ ). In the subjects of the control group, the level of omentin-1 was 47.29% ( $p < 0.05$ ) higher than in patients of group 1 with compensated diabetes, and 63.11% ( $p < 0.05$ ) higher than in patients with HbA1c  $\geq 8\%$ . In patients with type 2 diabetes and normal body weight, the state of compensation of carbohydrate metabolism did not significantly affect the level of omentin-1.

In patients with type 2 diabetes in combination with obesity with a duration of diabetes of more than 5 years, level of omentin-1 was lower by 38.64% ( $p < 0.05$ ) than with a shorter history of the disease, in group 2 the difference was slightly lower and was 25.44% ( $p < 0.05$ ). The level of omentin-1 among individuals of the 1st group

with a duration of diabetes up to 5 years was lower than in the control group by 62.14% ( $p < 0.05$ ). With a longer duration of diabetes in patients of the 1st group, the level of omentin-1 was lower than in the control group by 77.05% ( $p < 0.05$ ). In the 2nd group with diabetes lasting more than 5 years, the level of omentin-1 was lower than in the control group by 32.15% ( $p < 0.05$ ). Thus, the duration of the course of type 2 diabetes contributed to a gradual decrease in omentin-1 values, especially with increased body weight.

The analysis of TIMS registration of carotid arteries in patients with type 2 DM showed that in group 1 the indicator was the maximum on both sides compared to the corresponding indicators of individuals in group 2 by 15.76% ( $p < 0.05$ ) and 20.72% ( $p < 0.05$ ) respectively. Between group 1 and practically healthy individuals, the TIMS difference was 38.69% ( $p < 0.05$ ) and 27.29% ( $p < 0.05$ ) on the right and left sides, respectively. In group 2, the corresponding indicators did not differ from the control group.

Compensation state of carbohydrate metabolism had a significant impact on pathological changes in arterial vessels in the combination of type 2 diabetes and obesity. In group 1, the TIMS indicator in persons with diabetes decompensation on the left was 15.68% ( $p < 0.05$ ) more than the corresponding indicator in persons with a HbA1c level  $< 8\%$ , when evaluating the corresponding indicator on the right, the difference was 16.27% ( $p < 0.05$ ). In group 2, the state of compensation of carbohydrate metabolism did not affect the value of TIMS on both sides.

The duration of diabetes for more than 5 years showed that in people of group 1, the TIMS values on the right were higher by 16.37% ( $p < 0.05$ ) compared to the data of people with a shorter history of diabetes, on the left the difference was 17.09% ( $p < 0.05$ ). In the control group, the TIMS indicator was lower on the left by 20.05% ( $p < 0.05$ ) and 33.14% ( $p < 0.05$ ) compared to the data of patients of group 1 under 5 years and older than 5 years, on the right the difference was 30.21% ( $p < 0.05$ ) and 47.74% ( $p < 0.05$ ), respectively. In group 2, the difference in TIMS values between individuals with different durations of DM was not significantly different.

Chronic diabetic complications in patients of group 1 affected the condition of

the carotid arteries. In the presence of complications, the TIMS indicator compared to the corresponding data of patients without complications was higher by 10.85% ( $p < 0.05$ ) on the left, and by 12.06% ( $p < 0.05$ ) on the right. The corresponding difference between the data of the control group and 1 group was 25.77% ( $p < 0.05$ ) on the right and 37.62% ( $p < 0.05$ ) on the left. In patients of 2nd groups, the TIMS indicator did not reliably differ in the presence or absence of chronic complications of diabetes.

Correlation analysis was conducted to assess the presence and directionality of the relationship between the studied indicators. A positive correlation was found between TIMS (especially on the right) and the level of omentin-1 in the blood ( $R_s = -0.52$ ,  $p < 0.05$ ).

Omentin-1 is considered an important prognostic adipokine of visceral adipose tissue [5]. The level of omentin-1 in type 2 diabetes depends on the level of physical exertion, an increase in the level of omentin-1 was observed against the background of aerobic exercise [6]. Pharmacological treatment can have the opposite effect [6, 7], because omentin-1 increases insulin sensitivity [8].

The role of omentin-1 in glucose metabolism and insulin-dependent tissues is not defined; the results of our study open new perspectives for pharmacological interventions in the pathogenetic mechanisms of diabetes and obesity.

Overweight plays an important role in the progression of the atherosclerotic process of blood vessels. This is clearly reflected in the visual examination of the carotid arteries. A decrease in the TIMS indicator is observed when using drugs that affect the level of lipids and blood pressure [9]. The TIMS index of the carotid arteries plays an important role in predicting vascular events in patients without any objective manifestations of vascular pathology, as well as in patients with certain clinical manifestations, in which case an increase in the TIMS index is associated with an increased risk of cerebral stroke and/or myocardial infarction [10].

The data of our study showed the importance of a decrease in the blood level of omentin-1 on the development of pathological changes on the part of arterial vessels, which was determined by an increase in the TIMS index of the carotid arteries, in

patients with type 2 diabetes in combination with obesity.

### **Conclusions:**

1. Comorbidity of obesity and type 2 diabetes leads to a decrease in omentin-1 levels compared to patients with type 2 diabetes with normal body weight. These processes were influenced by the decompensation of diabetes and the duration of the disease.

2. The rate of TIMS of carotid arteries in patients with type 2 diabetes in combination with obesity was higher, especially with decompensation of diabetes, long-term diabetes and the presence of chronic diabetic complications.

3. A negative correlation was established between the level of omentin-1 and the TIMS indicator of carotid arteries in patients with type 2 diabetes in combination with obesity.

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