HORMONAL-METABOLIC PHENOTYPES OF OLDER MEN WITH DIABETES MELLITUS TYPE 2

Background and aims. Bone tissue, in addition to the classic insulin target tissues, is subject to both diabetic complications and a potential pathophysiological factor in the disease itself. Osteocalcin (OK) is a marker of osteosynthesis that increases insulin sensitivity, stimulates insulin secretion, and is reduced in patients with type 2 diabetes mellitus (DM2). It is established that the risk of visceral obesity increases significantly with decreasing OK levels. However, the relationship between the OK level as a modulator of metabolic processes and the constitutional-metabolic phenotype of patients with DM2, including patients with normal body weight, remains insufficiently studied. The aim is to determine OK level in patients with DM2 and insulin resistance without obesity.

Materials and methods. The study involved 44 male patients with DM2, older than 50 years. Patients were divided into 2 groups by BMI. Group 1 - men with a BMI ≤ 29.9 kg/m² (n=23), group 2 - a BMI ≥ 30 kg/m² (n=21). Also, 49 postmenopausal patients with type 2 diabetes mellitus were involved in the study. They were divided into 2 groups according to BMI. Group 1 – women with BMI ≤ 29.9 kg/m² (n=24), group 2 – BMI ≥ 30 kg/m² (n= 25). Blood levels of OK, proinsulin, C-peptide, glycated hemoglobin (HbA1c) were determined, HOMA-IR index, total testosterone, testosterone-estradiol binding globulin (TEZG), free testosterone index were calculated. All patients signed the informed consent performed in accordance with the ethical standards laid down in the Helsinki Declaration and reviewed by the Local Ethics Committee. Statistical processing was performed by the Wilcoxon method. The probability of the obtained results at p<0.05 was regarded as significant.

Results. The data obtained are evidence of differences in carbohydrate metabolism in patients with DM2 with and without obesity. The end result of these disorders, which unites both groups, is decompensation of diabetes mellitus (>8%) and fasting glucose. But the path to this outcome in the two groups are different. Thus, in patients of group 1 there was a lower level of C-peptide (1,38 ng/ml [0,65-2,7] vs 2,71 ng/ml [2,05-3,41], p<0,05), insulinemia (9.1 mU/l [6,7-11] vs 14,5 mU/l [10,3-16,3], p<0,05) along with no changes in proinsulin level, compared with patients of group 2. The OK blood level in patients of group 1 without obesity is higher compared to group 2 with obesity (3.65 ng/ml [2,9-4,7] vs 2,8 ng/ml [2,3-3,1], p<0,05). The emphasis is on the fact that in group 1, despite the absence of obesity, there was an increased index of HOMA-IR 4,11 [2,7-5,4], which is evidence of insulin resistance, similar to group 2. The results obtained in women were very similar to the group of
men with type 2 diabetes. It was established that the level of osteocalcin is significantly higher in women with a normal body weight compared to obese patients [6.2 ng/ml [5.2-7.1] vs 2.98 ng/ml [2.2-3.3], p<0.01]. At the same time, in the group of patients with normal weight, a higher level of insulinemia (6.04 mU/l [2.2-9.9] vs 13.7 mU/l [11.4-15.9], p<0.05), C-peptide (1.43 ng/ml [0.9-2.0] vs 2.85 ng/ml [2.4-3.29], p<0.05), and the HOMA (2.8 ng/ml [2.16-3.44] vs 8.27 ng/ml [5.45-11.09], p<0.05) index was observed, compared to obese patients on the background of diabetes decompensation in both groups.

Given the involutive changes in men with diabetes, it was important to determine the possible impact of reduced androgen supply on these features of carbohydrate metabolism. However, we did not find a difference in total testosterone levels (TES) or free testosterone index depending on the presence or absence of obesity. Also, we did not find a significant difference in the levels of total testosterone, regardless of the presence or absence of obesity in postmenopausal patients.

The obtained results confirm the heterogeneity of DM2, which, in addition to the difference in the phenotype of patients, is characterized by different metabolic disorders. The increase in the concentration of osteocalcin in groups of men and women with normal weight, in our opinion, has a mostly compensatory effect, which, however, is not sufficient for a significant reduction in glycemia. With regard to obese patients, a decrease in the content of osteocalcin in the blood is a natural consequence of metabolic changes due to the implementation of the path of adipocyte increase and, accordingly, a decrease in the pool of osteoblasts during the differentiation of mesenchymal cells.

Conclusion. In patients with DM2 without obesity, there is an increase in osteocalcin level, compared with patients with obesity, which is compensatory in nature, but does not have a significant effect on glycemic control. Absence of obesity among men with DM2 does not increase androgenic performance against the background of involutive changes.