**GRADE OF ARTERIAL HYPERTENSION SEVERITY IN PATIENTS WITH 2 TYPE DIABETES MELLITUS AND ITS INTERACTION WITH ADIPOPOCYTOKINE MEDIATORS, CARBOHYDRATE AND LIPID METABOLISM**

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***Abstract.*** *The study describes the dynamics of parameters of carbohydrate and lipid metabolism, together with the activity of adipocytokine mediators, namely apelin-12 and obestatin, in patients with type 2 diabetes depending on the severity of arterial hypertension. In patients with arterial hypertension in combination with type 2 diabetes, there are synergistic attempts of apelin-12 and obestatin for normalizing blood pressure level, however, the concentration of these markers is inadequate for existing needs. The discrepancy between the levels of apelin-12 and obestatin in the activity of the renin-angiotensin-aldosterone system is accompanied by an increase in blood pressure of more than 180/100 mm Hg. in patients with type 2 diabetes mellitus.*

***Keywords:*** *arterial hypertension, 2 type diabetes mellitus, apelin-12, obestanin, carbohydrate metabolism, lipid metabolism*

**Introduction.** The prevalence of diabetes ranges from 6.5 to 34 % per 1000 population, and cases of impaired glucose tolerance rise up to 15 % among the adult population according to the Ministry of Health of Ukraine data for 2002-2012. In the latter group, there is a high risk of developing not only diabetes mellitus (from 24 to 48 %), but also severe forms of arterial hypertension, acute cerebrovascular dysoders [1].

In the general population comorbidity of arterial hypertension and type 2 diabetes is common [5]. This combination is due to pathogenetically justified presence of insulin resistance and hyperinsulinemia [14]. Comorbidity of arterial hypertension and type 2 diabetes is often associated with the presence of other components of the cluster of metabolic disorders - dyslipidemia and central obesity, which causes an increase in cases of complicated course of this pathology, a decrease of life length [8, 10, 13]. Due to the widespread occurrence of arterial hypertension in patients with type 2 diabetes, the researchers are interested in the study of new markers responsible for the growth of blood pressure on background of insulin resistance. Apelin-12 is a peripheral vasodilator, has a powerful positive inotropic effect on myocardial contractility, affects the water homeostasis and is involved in the pathogenesis of heart failure, in the development and progression of arterial hypertension [6, 7]. Obestatin refers to peptide [11]. It has been established that obestatin regulates the function of adipocytes and protects against the pathological effects caused by insulin resistance [9]. However, the problem of apelin-12 and obestatin changes in patients with arterial hypertension in combination with type 2 diabetes, depending on the level of blood pressure remains the subject of scientific discussion.

The aim of the study is to analyze the dynamics of parameters of anthropometry, carbohydrate and lipid metabolism, together with the activity of adipocytokine mediators, namely apelin-12 and obestatin, in patients with type 2 diabetes depending on the severity of arterial hypertension.

**Material and methods.** The study examined 100 patients with a combination of arterial hypertension and type 2 diabetes (mean age 60.03 ± 1.17). The patients were divided according to the severity of arterial hypertension. Verification of type 2 diabetes was carried out in accordance with standard protocols recommended by the Ministry of Health of Ukraine (Order No. 1118 of the Ministry of Health of Ukraine dated December 21, 2012) and Recommendations for Diabetes, Pre-diabetes and Cardiovascular Diseases of the EASD/ESC, 2014

Exclusion criteria were acute and chronic inflammatory processes, diffuse connective tissue diseases, oncological diseases, concomitant diseases of the thyroid gland, the presence of symptomatic ***Science Review***

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hypertension, and also chronic heart failure more than III functional class. All patients performed clinical and biochemical blood tests, instrumental studies.

Apelin-12 and obestatin were determined by the immuno-enzymatic method using the commercial test system of Human Apelin 12 (AP12) ELISA Kit and the Human Obestatin (OB) ELISA Kit, China. Statistical processing of the received data was carried out using the package of statistical programs "Microsoft Excel". The data is presented in the form of averages and average errors. The statistical significance of different averages was determined by the F-Fisher criterion. The analysis of interconnections was carried out using the Spirman correlation (r).

**Research results.** The level of haemoglobin A1c (HbA1c) in patients with type 2 diabetes with arterial hypertension varying grades of severity did not significantly differ (p> 0.05). Similar results are obtained from the level of glycaemia (p> 0.05). As for lipid profiles, the comparison of patients with varying grades of arterial hypertension in type 2 diabetes showed changes. Thus, the concentration of total cholesterol was significantly higher when comparing arterial hypertension of 3 degree with 1 degree arterial hypertension with concomitant diabetes mellitus type 2 by 7.8 % (p<0.05). By the parameters of low density lipoprotein and an coefficient of atherogenicity in patients with 3 degree arterial hypertension compared with 1 degree arterial hypertension in type 2 diabetes, a tendency to increasing, which did not reach the level of probability (p = 0.05), was found. Comparison of the content of total cholesterol, low-density lipoprotein, the coefficient of atherogenicity in patients with arterial hypertension of 3 degree versus 2 degree arterial hypertension, as well as arterial hypertension of 1 degree and arterial hypertension of 2 degree in type 2 diabetes showed that they corresponded to those in the comparable subgroup (p> 0.05). High density lipoprotein, triglycerides, and very low density lipoprotein were not significantly different in patients with type 2 diabetes with varying degrees of arterial hypertension (p> 0.05).

Comparison of concentrations of apelinemia in patients with type 2 diabetes and arterial hypertension of various degrees showed that in patients with 2 and 3 degree of arterial hypertension severity, the level of this mediator was higher than in patients with arterial hypertension of 1 degree. However, when comparing the concentrations of apelin-12 in patients with 2 and 3 degree of arterial hypertension severity, no significant differences were found (p> 0.05). The level of obestatin probably did not differ in patients with arterial hypertension of 1 and 2 degrees, but comparing the concentration of this mediator in patients with arterial hypertension of 1 and 3 degree found a significant decrease with increasing severity of arterial hypertension. The increase of apelin-12 in patients with arterial hypertension of 1 and 2 degree compared to each other can be considered as an adaptative reaction aimed at attempting to normalize blood pressure by inducing NO-dependent vasorelaxation, which causes the presence of hypotensive properties of apelin-12 [2, 3, 4]. The absence of proportional to the severity of arterial hypertension growth of the adipocyte mediator apelin-12 suggests the depletion of adaptive effects, which is accompanied by the development of 3 degree of arterial hypertension.

While comparison the concentration of obestatin in patients with arterial hypertension of 1 and 2 degree, as well as 2 and 3 degree significant differences were not found. This fact can be considered as an effect of obestatin, aimed at suppressing hyperinsulinemia, which results in the development of insulin resistance with the further potentiation of vasoconstrictor activity of angiotensin II [12]. However, further increases in blood pressure can be considered as evidence of the inadequate effect of existing levels of obestatin present at this stage, which can have inhibitory effects on the insulin-induced activity of the renin-angiotensin-aldosterone system. The presence of a cohort of patients with severe arterial hypertension suggests that the concentrations of the above-mentioned markers are not relevant to the needs at this stage.

**Conclusions.**

1. In patients with arterial hypertension in combination with type 2 diabetes, there are synergistic attempts of apelin-12 and obestatin for normalizing blood pressure level, however, the concentration of these markers is inadequate for existing needs.

2. The discrepancy between the levels of apelin-12 and obestatin in the activity of the renin-angiotensin-aldosterone system is accompanied by an increase in blood pressure of more than 180/100 mm Hg. in patients with type 2 diabetes mellitus. ***Science Review***

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