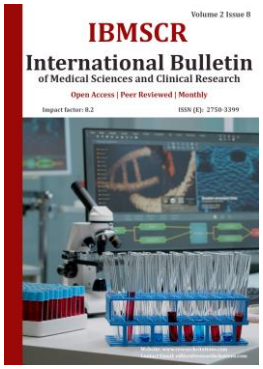

SPECIFICITY OF METFORMIN IN COMBINATION THERAPY OF HYPERTENSION WITH METABOLIC SYNDROME

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Metabolic syndrome (MS) in recent years has attracted more and more attention of doctors around the world, which is associated with its wide distribution, reaching 25-30% in the adult population, and increasing with age [1, 2, 7].

More than 70-80% of patients with type 2 diabetes have premature disability and early death from cardiovascular complications. Increase in diastolic blood pressure for every 6 mm Hg . increases the risk of developing coronary artery disease by 25%, and the risk of developing stroke - by 40%. The risk of developing coronary artery disease and stroke without type 2 diabetes increases 2-3 times, kidney failure - 15-20 times, blindness - 10-20 times, gangrene - 20 times. With a combination of DM and arterial hypertension (AH), the risk of these complications increases by another 2–3 times even if carbohydrate metabolism is satisfactorily compensated [3].

The key element of MS that triggers the pathological mechanisms of metabolic processes is insulin resistance [4, 8]. Insulin resistance even before the development of clinical manifestations of diabetes mellitus and hypertension leads to damage to the vascular wall. The stiffness of the vascular wall is a predictor of the development of arterial hypertension: with a decrease in the elasticity of the vascular wall by one standard deviation, the risk of developing arterial hypertension increases by 15%.

Normally, insulin through the vascular wall receptor IRS-1 activates phosphatidylinositol-3-kinase, protein kinase B, which ultimately initiates endothelial NO synthase and leads to NO synthesis and, accordingly, vasodilation . On the other hand, insulin stimulates the synthesis of endothelin-1 through its effect on the mitogen -activated protein kinase MAPK, i.e., causes vasoconstriction

Thus, the effect of insulin on the endothelium creates a balance between vasodilatory , antithrombotic , and anti-inflammatory effects and vasoconstrictive , inflammatory, and thrombotic effects.

With insulin resistance due to phosphorylation of IRS-1, NO synthesis decreases, i.e., the process of vasodilation is disrupted . At the same time, the vasoconstrictor effects of insulin are preserved. Thus, insulin resistance provokes an increase in stiffness and rigidity of the vascular wall, which leads to the development of arterial hypertension [5, 6] .

In this regard, the use of a superselective β-blocker in this group of patients, which is a nitric

oxide donator with a drug of the biguanide group, is of interest. metformin , which reduces the degree of insulin resistance and has a positive effect on carbohydrate and lipid metabolism.

Objective: to study the clinical and biochemical efficacy of metformin in combination with the superselective β-blocker nebivalol in the treatment of hypertensive patients with MS.

Methods and material: 145 men were examined, of which 105 were patients aged 25 to 60 years with AH duration of 2-4.5 years. The body mass index in the group of patients examined was more than 25.0 kg/m, the average body weight was 93.6 kg. The study did not include patients with secondary hypertension, a history of strokes and heart attacks, respiratory, cardiac, hepatic and renal insufficiency.

The control group of healthy individuals consisted of 40 men of the same age.

Patients were collected a family history, smoking status, alcohol consumption, a survey about the features of the course of hypertension and concomitant diseases.

Anthropometric data (height, weight, body mass index , waist circumference, hip circumference) were determined in all the studied individuals . BMI was calculated using the Quetelet formula as the ratio of body weight (kg) to height (m) squared.

According to the study, it can be seen that the majority of patients suffered from stage II hypertension, and among them, patients with a BMI of 25-30 amounted to 45 patients (42.85%), and with a BMI of more than 30-24 patients (22.8%). Grade 1 AH was observed in 14 (13.3%) patients with BMI 25-30, grade III AH in 7 (6.7%) patients in both cases, both with BMI 25-30 and with BMI over 30.

, patients with a disease duration of 2-5 years prevailed . Thus, in 11 (10.47%) patients, the duration of the disease was up to 2 years, in 59 (56.2%) patients - from 2 to 5 years, and in 35 (33.4%) patients - over 5 years.

Laboratory studies were performed with venous blood serum taken in the morning on an empty stomach after a 12-hour fast. The blood lipid spectrum was determined: total cholesterol, α-lipoproteins, β-lipoproteins, triglycerides. The state of carbohydrate metabolism was determined by gender indicators: glycated hemoglobin , the level of basal blood insulin . Test for glucose tolerance. After that, patients were randomly divided into 2 groups (15 people each), which, against the background of hypocaloric nutrition, were taken for 3 months: group 1 - superselective β-blocker - nebivalol at a dose of 5-10 mg per day . from the biguanide group) at a daily dose of 500 mg and nebivalol at a dose of 5-10 mg.

After a 3-month course of treatment, repeated instrumental and laboratory studies were performed. The effectiveness of treatment was assessed by the dynamics of the clinical manifestations of the disease, blood pressure indicators according to the Korotkov method, as well as biochemical blood parameters.

In group 1, it was possible to achieve a significant decrease in the level of SBP (daily, daytime and night - by 12.1; 13.0 and 8.0%, respectively) and DBP (by 13.2: 13.5 14.7%, respectively). A significant decrease in the level of heart rate was not obtained.

The absence in group 1 of nebivalol typical of therapy is significantly significant, the decrease in heart rate can be explained; several reasons. Firstly, antihypertensive therapy did not affect the severity of insulin resistance in this group of patients, and secondly, a decrease in blood pressure could in itself cause a compensatory increase in heart rate, which was additionally stimulated by chronic hyperinsulinemia (preservation of the latter at night - helps explain the lack of decrease in heart rate) . nocturnal HR , with a tendency to its

decrease during the day).

When analyzing the results of biochemical; There were no statistically significant differences in hormonal studies in group 1 against the background of ongoing therapy .

In the 2nd group, there was a significant decrease in blood insulin levels by 27.8%. glycated - hemoglobin by 13.8%. Decrease in the concentration of triglycerides by 18.1%, cholesterol by 12.1% and β-lipoproteins by 35% increase in the level of α-lipoproteins by 22%.

Conclusions **:** Thus , therapy with a drug of the biguanide group (metformin 500 mg/ day) in patients with metabolic syndrome is associated with a significant decrease in glycated hemoglobin and insulin in the blood, a significant, significant decrease in the level of cholesterol, triglycerides, β-lipoproteins and an increase in the concentration of antiatherogenic α-lipoproteins, in contrast to the standard monotherapy of arterial hypertension with corvitol .

The inclusion of medformin in the complex therapy of patients with metabolic syndrome leads to an additional more pronounced decrease in nighttime values of systolic and diastolic blood pressure and heart rate and contributed to the improvement of the oral glucose tolerance test.

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