ISSN 2181-3187

IMPACT OF ANTIHYPERTENSIVE MEDICATIONS ON INSULIN RESISTANCE AND LIPID PROFILE MODULATION

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Relevance: The mechanism of developing arterial hypertension and insulin resistance in individuals with excess body weight is of great importance when determining the treatment strategy, including the selection of medications, dosage, and duration of use, as well as the combination of antihypertensive agents, statins, biguanides, insulin medications, and hepatoprotective and cardioprotective agents. In this regard, antihypertensive drugs, such as losartan and nebivolol, used to treat patients with excess body weight and/or insulin resistance, must meet several criteria: effectively reduce blood pressure throughout the day, have no adverse effects on carbohydrate, lipid, and purine metabolism, possess organoprotective effects, and reduce the risk of developing metabolic syndrome (MS).

Key words: Arterial hypertension, metabolic syndrome, lipid spectrum, HOMA index , insulin resistance.

Excess body weight and insulin resistance are associated with impairments in endothelial function, which contribute to the development of arterial hypertension. In these cases, increased blood pressure is most often due to increased peripheral vascular resistance and disturbed renal regulation of blood volume. Reduced tissue sensitivity

ISSN 2181-3187

to insulin leads to elevated insulin levels in the blood, which in turn stimulates the sympathetic nervous system and raises blood pressure. Losartan, as an angiotensin II receptor antagonist, effectively reduces blood pressure and has a nephroprotective effect, improving kidney function, which is particularly important in patients with obesity and insulin resistance. Nebivolol, a beta-blocker with vasodilatory properties, also helps reduce blood pressure while having minimal impact on glucose metabolism, making it safer for patients at risk of developing diabetes. It is important for the therapeutic approach to be multifaceted, combining antihypertensive therapy with the correction of disturbances in carbohydrate metabolism, lipid profiles, and cardiovascular risk. The use of combined therapy including statins, biguanides, and cardioprotective agents allows not only effective blood pressure control but also reduces the risk of cardiovascular diseases and prevents the progression of metabolic syndrome and type 2 diabetes.

Arterial hypertension and lipid metabolism disorders are one of the most pressing problems of modern medicine, associated with age, and hence an increase in body weight in most cases, the development of coronary artery disease, irregular and age-appropriate physical activity, alcohol consumption and smoking, and family history.

In blood plasma, lipids such as TC and TG are present in various forms, in combination with proteins, with apoproteins . The extent to which lipoproteins cause the development of atherosclerosis depends on the type, particle size and concentration in the plasma. HDL-C is not the cause of atherosclerosis, but they have an antiatherogenic effect. In contrast to LDL and, in particular, LDL and VLDL have an atherogenic effect if they are modified i.e. oxidize. VLDL do not have an atherogenic effect, but their increased concentration in the blood serum may cause the development of pancreatitis. Most of the total cholesterol is found in LDL, which, according to most researchers, is the cause of the increased risk of CVD, especially in men. In women, the level of risk in connection with cholesterol is lower before menopause, and after the period, the level of cholesterol increases, and the risk of developing CVD in women equalizes and even increases. A 10% increase in TC blood concentration is associated

ISSN 2181-3187

with a 27% increase in the risk of CAD, which is an indicator of a problem associated with DLP. On the other hand, a 10% decrease in the concentration of total cholesterol in the blood is associated with a 25% decrease in the risk of coronary artery disease over 5 years. A decrease in the concentration of LDL cholesterol in the blood by 1 mmol/l. associated with a 19% reduction in risk from MI and 21% from IHD. In the CAMUS studies , Nebivolol was found to reduce insulin, leptin and blood glucose levels, reduce triglycerides and free fatty acids, and increase high-density lipoprotein levels. Of all the antihypertensive drugs that are currently used in the treatment of arterial hypertension in combination with metabolic syndrome and type 2 diabetes mellitus, only ACE inhibitors and ARB blockers reduce the level of insulin resistance to a lesser extent and Nebivolol 4 times more.

Purpose of the study: To evaluate the dynamics of insulin resistance and biochemical parameters of lipid metabolism in patients with metabolic syndrome during long-term therapy (6 months) with antihypertensive drugs **.**

Materials and methods of research: 70 patients were examined. Of these, 35 patients had arterial hypertension with varying degrees of obesity depending on their body mass index . The control group consisted of 35 patients with arterial hypertension with a normal body mass index. Laboratory data included general blood tests, blood sugar, biochemical parameters (triglycerides, total cholesterol, low-density lipoproteins - LDL, high-density lipoproteins - HDL), C-reactive protein, blood fibrinogen, prothrombin index, prothrombin time, glucose level fasting, glycosylated hemoglobin, blood insulin, insulin resistance index (HOMA index).

Results: Against the background of complex therapy of patients with hypertension and obesity, a significant decrease in central average daily, daytime and nighttime SBP was noted in all groups. In all groups there was a tendency towards a decrease in central DBP, which reached significant differences in group 2. When analyzing the average values of daily, daytime and nighttime blood pressure in the aorta, a significant decrease was revealed in all groups.

ISSN 2181-3187

Indicators of lipid parameters of blood plasma of patients with hypertension and obesity are presented in table. 1.

Indicators	1 group (35)	2nd group (35)
Total cholesterol (mmol/l),	5.6±0.9	5.3±1.1
HDL cholesterol (mmol/l)	1.4(1.1-1.9)	1.3 (1.1-1.8)
LDL cholesterol (mmol/l)	3.3 (2.1-3.8)	2.9 (1.9-3.7)
Triglycerides (mmol/l)	1.4 (1.1-2.1)	1.9(1.3-2.4)

Note: HDL cholesterol is high-density lipoprotein cholesterol, LDL cholesterol is low-density lipoprotein cholesterol.

When analyzing the lipid profile data, attention is drawn to a moderate increase in the level of total cholesterol and LDL in both groups, while an increase in triglycerides is observed only in patients with grade 2-3 obesity. Moreover, the average level of HDL cholesterol in both groups was above 1.2 mmol/l, which is a favorable factor. However, obesity of 2-3 degrees (group 2) is accompanied by a significant increase in the level of fasting insulin and the calculated index of insulin resistance (HOMA-III) compared to patients of the 1st group . The average HOMA-III value in group 2 exceeds the threshold (<2.7), which indicates impaired carbohydrate metabolism and a higher risk of developing diabetes mellitus in these patients. According to the literature, grade 2-3 obesity is often accompanied by more pronounced disorders of lipid and carbohydrate metabolism. However, in our study, despite more pronounced disorders of lipid metabolism in patients of group 2, the lack of significant differences between groups is apparently due to the selection criteria, according to which patients with clinical signs of atherosclerosis were excluded from the study.

ISSN 2181-3187

Indicators	1 group (35)	2nd group (35)
Glucose (mmol/l),	5.4 (5.1-6.5)	5.7 (5.1-6.7)
Fasting insulin (μU /ml)	8.9 (6.9-14.5)	13.8 (9.9-19.7)1
HOMA-IR	2.1 (1.6-4.2)	3.5 (2.2-5.7)*

Dynamics of laboratory parameters during therapy with Losartan and Nebivolol : In all groups, an increase in insulin levels and the calculated index of insulin resistance (HOMA - IR) was initially noted. By the end of complex therapy, the insulin level and the calculated index of insulin resistance (HOMA - IR) decreased to threshold values, but a significant decrease was detected in the 1st and 3rd groups of patients compared to the first visit. There were no significant differences between the groups.

Conclusions: For hypertension, treatment of concomitant obesity with Nebivolol at a dose of 5 mg/ day and losartan 50 mg and 100 mg is effective and safe enough in combination for use in the therapeutic practice of a general practitioner and a cardiologist. To ensure the safety of treatment and assess the effectiveness of antihypertensive therapy, ABPM is also recommended to obtain more complete information on the degree of blood pressure control.

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