

Features of Anti-Hypertension Therapy in Overweight Patients

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Abstract: Arterial hypertension and lipid metabolism disorders are one of the most pressing problems of modern medicine, associated with age, and hence the increase in body weight in most cases, the development of Coronary heart disease (CHD), not regular and age-related physical activity, alcohol consumption and smoking, aggravated heredity. According to scientific studies, the prevalence of obesity in the general population of Uzbekistan was 20,4%. In the female population 22,1%, in the male population 11,5%, i.e., is half as low [B.A.Sultanov, author's abstract Diss. 2008]. The same study was conducted on the impact of obesity on the growth of Diabetes mellitus type 2 (DM2) and prediabetes in Uzbekistan: the obesity rate in the group with DM2 was 41.6% in the male population and 38.5% in the female population, respectively. Obesity rate in the group with prediabetes was 37.06% in the female population and 32.3% in the male population respectively. Increasing the weight by 1 kg increases the risk of cardiovascular disease by 3.1% and diabetes by - 4.5% -9%.

Introduction: In case of excess body weight there is adipocyte-cell infiltration of adipose tissue by macrophages with the subsequent development of inflammatory reactions, which changes the metabolic activity of adipose tissue. The expression of this inflammation clearly correlates with the degree of obesity. Since the inflammatory reaction occurs in the tissue, the proportion of which may be up to 50% or more of the total body weight, the assumption of systemic manifestations becomes natural. That is, local inflammatory processes in adipose tissue are accompanied by chronic mild inflammation.

Adipokins, hormones of adipose tissue, are a type of cytokines secreted by adipocytes. Adipokins are referred to as adipokins: IL-6 - interleukin-6; TNF α - tumor necrosis factor, leptin. The level of leptin increases in proportion to the weight of adipose tissue. The main target of leptin is the central nervous system, mainly hypothalamic structures. Leptin is the main regulator of the amount of fat in the body, helps reduce food intake and increase energy consumption. Leptin levels are closely correlated with body mass index (BMI) and blood pressure level (BP). In patients with AG and obesity, the dependence of BP level on the concentration of leptin, which was absent in patients with normal weight, was revealed. Plasma concentrations of leptin are higher in people with BP than in normal weight patients. It was found

that leptin stimulates the activation of the sympathetic-adrenal system, and catecholamines, in turn, suppress the production of leptin. However, in the development of metabolic syndrome, these interactions are disturbed and the increased level of leptin in combination with hyperactivation of neurohumoral systems promotes the emergence of AG, as well as inflammation and, ultimately, stenosis of coronary arteries.

In addition to leptin, C-reactive protein (CRP) levels change in patients with CHD and obesity.

Many studies have confirmed that CRP is a useful indicator of cardiovascular risk. Measuring basic CRP levels makes it possible to assess the risk of acute myocardial infarction, brain stroke and sudden cardiac death in people who do not suffer from cardiovascular disease. At concentration of CRP less than 1.0mg/l the risk of cardiovascular complications is minimal, at 1.1 -1.9 - low, at 2.0 - 2.9 - moderate, at large, more than 3 mg/l - high. These data are confirmed by the results of the Framingham study, where the level of CRP above 3 mg/l was associated with a high risk of cardiovascular complications. Meta-analysis of a number of prospective studies has shown that the risk of adverse cardiovascular events in individuals with the highest levels of CRP is two to three times higher than in individuals with the lowest levels of DRR. In adult patients with CRP above 3.0 mg/l the risk of cardiovascular disasters is 4 times higher than in healthy individuals. In Metabolic Syndrome (MS), increased CRP is associated with high risks of cardiovascular disease and diabetes. Thus, in patients with MS CRP is increased in 38.4%, and among people without MS it is increased only in 10.3%.

Interest in C-reactive protein as a marker of cardiovascular disease was not manifested until the publication of works that showed the connection between increased levels of CRP and "activity" coronary heart disease. For a very long time, the diagnostic value of CRP was correlated with its levels exceeding 5 mg/l. In case of CRP less than 5 mg/l the absence of systemic inflammatory response was stated and the precise determination of CRP in the range from 1 to 5 mg/l was not considered clinically significant. Then, the sets allowing to determine CRP levels, which are now called basic, were introduced into practice. The basic CRP level is a concentration that is consistently determined in virtually healthy individuals, as well as in patients with no risk factors. In the presence of overweight, hyperlipidemia, diabetes mellitus, arterial hypertension, metabolic syndrome, chronic inflammatory diseases, as well as in smokers, the level of basic CRP is higher. CRP levels were also higher in people who subsequently had a myocardial infarction (MI) or stroke. Reduced levels are observed in moderate alcohol consumption, increased physical activity, weight loss, and the use of drugs such as statins - drugs with hypolipidemic activity.

Currently, all patients with CHD, especially those with hypertension and obesity, are shown statin intake. They should be assigned regardless of the initial values of the lipid profile, and then the dose is titled until the target values of low-density lipoproteins are reached. At present, the main modern and effective representatives of this class in terms of their hypolipidemic ability are Rosuvastatin and Atorvastatin. In a randomized MERCURY I (70) study, the hypolipidemic effects of statins were evaluated in 3,140 patients with CHD, atherosclerosis or DM2 and hypercholesterolemia. In the course of treatment with Rozuvastatin, Atorvastatin, Simvastatin and Pravastatin it was supposed to trace their hypolipidemic effect of each and to change Atorvastatin for Rozuvastatin, Simvastatin for Atorvastatin within 8 weeks. As a result of the conducted research, when switching from different statins to Rosuvastatin, the percentage of patients with target values of low-density lipoproteins statistically significantly increased in comparison with patients who stayed on the previous therapy. So, after 8 weeks, patients who took Rosuvastatin in the dose of 10mg reached the target lipid level in 86% of cases, and the transition to 20mg dose of Rosuvastatin was achieved in 90% of patients ($p<0.01$).

At present, quite promising randomized studies have been conducted on the treatment of statistic patients with CHD, DM2, hypertension and related obesity, and MS patients. The point is that the achievement of low-density lipoproteins at the normal level is the goal of comprehensive treatment of patients with CHD. And in this complex treatment, a special place is given to statins.

Statins, in addition to hypolipidemic action, have a number of pleiotropic properties. They inhibit the formation of metalloproteinases, slow down myocardial fibrosis and can serve as a means of preventing chronic heart failure ischemic etiology.

At present, given the epidemic situation in the world, the coronavirus SARS-Cov-2 pandemic Russian, Chinese and Italian physicians noted that a positive clinical effect in coronavirus infection is associated with pleiotropic action of statins: reducing the severity of inflammation, the risk of thrombosis, restoration of endothelial function, immunomodulatory effect. The recommendations of all COVID-19 treatment societies note the importance and mandatory use of statins in hyperlipidemic patients infected with SARS-Cov-2. In nursing homes, patients who were treated with statins were almost 3 times less sick and had less severe course.

In addition, the literature presents data from a retrospective analysis of a database of 3,043 influenza patients who had received statins before and during inpatient treatment, and the outcome of the disease to reduce complications and death from influenza was related to the intake of statins. As a result, scientists strongly recommend continuing to take statistic medication from patients with COVID-19, and who are shown the medications, to begin taking them.

Conclusions: So what is the way to treat arterial hypertension complicated by such comorbidity as metabolic syndrome? The main hypotensive drugs currently include APF inhibitors, sartans or BRA (blockers of the rennin-angiotensin system), as well as dihydroperidin antagonists of calcium and diuretics. Adrenoblockers, α -adrenoblockers and imidazoline receptor blockers are used only for special indications. What are the special indications for which central action drugs, such as Moxonidine, are used? As it turned out, only 2 groups of drugs reduce the level of insulin resistance - Metaprolol and Moxonidine. The level of leptin in the blood is influenced by Carvedilol, Enalapril, Losartan, Amlodipine and Moxonidine. The level of adiponectin is influenced by Carvedilol, Telmisartan, Moxonidine, which also affects the level of resistance. As we can see, in MS accompanied by high arterial hypertension, Moxonidine is the drug of choice. Moxonidin reduces the activity of the sympathetic nervous system and leads to a decrease in AP. The high hypotensive efficiency of moksonidin in a dose of 0.2-0.4 mg/day allows achieving the target AP values in 52% of patients with obesity and SD2. If treatment in combination with iAPF in patients with AG and MS can be achieved up to 98% of the target AP level (CAMUS studies). In the same studies it was found that Moxonidine reduces blood insulin, leptin and glucose levels, reduces triglycerides and free fatty acids, and increases the level of high-density lipoproteins. Of all the hypotensive drugs currently used in the treatment of arterial hypertension in combination with metabolic syndrome and type 2 diabetes mellitus, only iAPF and ARA blockers to a lesser extent and Molsidomin 4 times more reduces the level of insulin resistance.

Thus, the selective inhibitor of I1-imidazoline receptor Moxonidine can be considered as a universal antihypertensive drug, effective both for long-term treatment of AG, and for the management of uncomplicated hypertensive crises. It affects carbohydrate and lipid metabolism and can be recommended for patients with arterial hypertension and metabolic syndrome as monotherapy, as well as in combination with iAPF, ARA blockers, calcium antagonists.

When carrying out rational pharmacotherapy and choosing a specific drug in patients with obesity and arterial hypertension it is necessary to follow the principles of personalized medicine, focused on the maximum convergence of the drug and the needs of the patient. In order to ensure the most appropriate therapy for a particular patient, it is necessary to take into account the latest achievements in molecular biology, which allowed studying the pathophysiological features of the emergence and progression of AG in a specific clinical situation. A number of hemodynamic changes occur in obesity, such as an increase in the volume of circulating blood, stroke volume and cardiac output with relatively normal vascular resistance. It is believed that high blood pressure in obese patients is mainly due to increased cardiac output with "inadequate" peripheral resistance.

Of course, each case requires serious consideration and analysis of the peculiarities of the clinical situation, which should be taken into account in selecting a particular class of drugs.

The mechanism of arterial hypertension, insulin resistance in individuals with metabolic syndrome is of great importance in the tactics of choice of drugs, dosage and duration of use, as well as combinations of hypotensive drugs, statins, biguanides, insulin drugs, hepato- and cardioprotectors. All these issues should now be carefully developed, studied and implemented in practical health care.

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