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OBESITY AS A POWERFUL RISK FACTOR FOR ARTERIAL HYPERTENSION

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Abstract.

In recent years, researchers have been paying more and more attention to the study of molecular genetic factors of hypertension, the search for genes and the analysis of the association of their polymorphisms with various components of the metabolic syndrome. The ethnic features of predisposition to the development of hypertension have been revealed, which confirms the role of genetic factors. Significant changes in arterial hypertension within the framework of the metabolic syndrome are mutations of genes responsible for the balance of pressor and depressor pathogenetic links.

Key words: arterial hypertension, genes, polymorphism, metabolic syndrome, obesity.

SEMIZLIK ARTERIAL GIPERTENSIYA RIVOJLANISHINI KUCHLI OMILI SIFATIDA

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Annotatsiya

So'nggi yillarda tadqiqotchilar arterial gipertenziyaning molekulyar genetik omillarini o'rganishga, genlarni izlashga va ularning polimorfizmlarining metabolik sindromning turli tarkibiy qismlari bilan bog'liqligini tahlil qilishga tobora ko'proq e'tibor qaratmoqdalar. Gipertenziya rivojlanishiga moyillikning etnik xususiyatlari aniqlandi, bu genetik omillarning rolini tasdiqlaydi. Metabolik sindrom doirasida arterial gipertenziyadagi muhim o'zgarishlar pressor va depressor patogenetik bog'lanishlar muvozanati uchun javob beradigan genlarning mutatsiyasidir.

Kalit so'zlar: arterial gipertenziya, genlar, polimorfizm, metabolic sindrom, semizlik.

ОЖИРЕНИЕ КАК МОЩНЫЙ ФАКТОР РИСКА АРТЕРИАЛЬНОЙ ГИПЕРТЕНЗИИ

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Аннотация.

Последние годы исследователи всё более пристальное внимание уделяют изучению молекулярно-генетических факторов артериальной гипертензии, поиску генов и анализу ас-

социации их полиморфизмов с различными компонентами метаболического синдрома. Выявлены этнические особенности предрасположенности к развитию гипертонической болезни, что подтверждает роль генетических факторов. Значимыми изменениями при артериальной гипертензии в рамках метаболического синдрома являются мутации генов, ответственных за баланс прессорных и депрессорных патогенетических звеньев.

Ключевые слова: артериальная гипертензия, гены, полиморфизм, метаболический синдром, ожирение

Relevance. A sharp increase in the incidence of overweight and obesity in adolescents was first noted in the 80s of the 20th century, with a subsequent rise in the incidence of arterial hypertension (AH) and prehypertension. Trends in blood pressure (BP) lag behind body mass index (BMI) by about 10 years, which appears to explain some of the variability in the relationship between BP and BMI. Long-term trends in changes in these indicators in young people indicate a relationship between excess weight and hypertension [3].

Currently, the generally accepted criteria for diagnosing and classifying high blood pressure in adolescents are the criteria proposed by the National High Blood Pressure Education Program (NHBPEP). According to this classification, blood pressure levels between the 90th and 95th percentiles in patients according to their gender, age and height indicate the presence of a "pre-hypertensive" state; A blood pressure value between the 95th and 100th percentiles indicates the presence of arterial hypertension. The classification applies to adolescents up to 17 years of age inclusive. When assessing blood pressure in young people aged 18–19 years, the adult classification is used [1].

The main proportion of patients with increased blood pressure are those with signs of prehypertension. Although the relationship between obesity and hypertension has now been demonstrated in a number of studies, the mechanism by which obesity contributes to the development of hypertension is still debated.

A number of studies have shown that the relationship between blood pressure and BMI is not linear. Specifically, the researchers demonstrated that there was a downward trend in BP between 1963 and 1988, but BMI values remained constant during the same period. C. Koebnick et al. [2] showed that the prevalence of hypertension among adolescents 12–19 years old with overweight (2.1%) is twice as high as that among adolescents with normal weight (0.8%). The frequency of detection of high blood pressure increases stepwise with increasing weight in young people of both sexes and of any age. These data were confirmed by the results of a number of studies, which

showed that the likelihood of developing hypertension at a young age with excess body weight is significantly higher than in individuals with normal and low weight [7].

Currently, overweight and obesity are considered key risk factors for hypertension, although a number of other risk factors are known. Thus, hypertension in adolescents is associated with the use of diets high in fat and sodium, a sedentary lifestyle, insufficient physical activity, the presence of cardiovascular diseases (primarily hypertension) in the family history, and low birth weight [5]. The influence of ethnicity and gender on the development of hypertension has less evidence, but it is assumed that these factors influence the severity of the relationship between blood pressure and obesity.

Activation of the sympathetic nervous system, accumulation of visceral fat and fat deposition in the vascular wall, sodium retention, and activation of the renin-angiotensin system are considered important elements in the pathogenesis of hypertension in overweight [6]. Genetic predisposition may be a major factor, although diet and physical activity have been shown to play a more significant role [4]. A sedentary lifestyle, psychological factors (depression, low self-esteem) and lack of sleep at night also significantly contribute to weight gain. Obesity is likely the result of the influence of a combination of factors, including genetic ones, which affect the implementation of satiety mechanisms and the rate of metabolic processes [9].

Large amounts of dietary fat may have a greater effect on weight than the overall caloric intake of the diet. A significant portion of the energy consumed from fat is stored in adipocytes, increasing body weight and waist circumference as the number and volume of adipocytes increases, while carbohydrates contained in cereals, breads, fruits and vegetables, as well as proteins, are catabolized almost immediately after consumption. In addition, high fat content in food leads to hypercholesterolemia [9].

A change in the ratio of fractions of saturated and unsaturated fatty acids (in favor of the former), circulating in the blood as part of fats, affects the function of the liver and kidneys, and also leads to direct damage to the walls of blood vessels due to the formation of atherosclerotic plaques. One of the mechanisms for the development of metabolic syndrome is damage to the media of large arteries due to cholesterol deposition in the vessel wall [10].

Fat accumulates in the wall of the vessel, narrowing its lumen and preventing normal blood flow. An increase in the thickness of the intima-media

complex of the carotid artery in obese patients is observed even with normal blood pressure values, which indicates an early onset of atherosclerotic changes in obesity. Fat accumulating in the wall of the vessel gradually forms plaques, which continue to grow, leading to stenosis of the vessel, up to its complete obliteration, as a result of which the blood supply to organs and tissues suffers, creating conditions for the development of a number of acute and chronic diseases, including lethal ones [10] .

Another negative effect of a high-calorie diet is an increase in the synthesis and concentration of norepinephrine (an indicator of the activity of the sympathetic nervous system). It is assumed that a diet high in fat and carbohydrates leads to activation of peripheral adrenergic receptors, which causes an increase in blood pressure [8]. It has been shown that with simultaneous blockade of α- and β-adrenergic receptors, blood pressure in obese patients decreases.

The effect of obesity on the condition of many organs can lead to serious health problems, but the most obvious is the dependence of the condition of the kidneys on body weight. Accumulation of adipose tissue around the kidney, together with increased intra-abdominal pressure, is considered an additional cause of impaired sodium reabsorption. Initially, obesity leads to vasodilation and glomerular hyperfiltration, which maintains sodium balance despite increased tubular reabsorption. Together with an increase in blood pressure and some other factors (inflammation, oxidative stress and lipotoxicity), this can aggravate kidney damage and lead to the formation of renal failure [9]. Clinically, this process is manifested by proteinuria, which usually precedes a decrease in glomerular filtration rate by several years.

Leptin, by inducing cytokine signalin, promotes kidney damage. Adipose tissue, especially visceral fat, has systemic effects by secreting various hormones and cytokines. A diet high in fat and carbohydrates, leading to hypercholesterolemia and an increase in the concentration of free fatty acids in the blood, directly affects the ion channels of the cell membranes of smooth muscle cells and cells of other tissues [9].

Free fatty acids can also activate phosphorylation of the calcium-independent protein kinase C isoenzyme, an important element of cellular regulation. The binding of free fatty acids to Na+/K+-ATPase leads to the formation of multiple signaling modules, resulting in the activation and synthesis of the epidermal growth factor receptor and an increase in the

concentration of reactive oxygen species [10]. Changes in endothelial function result from decreased NO synthesis due to activation of oxidative stress or under the influence of proinflammatory cytokines. Increased production of cytokines, activation of oxidative stress and decreased NO concentrations lead to vasoconstriction and increased overall vascular resistance, which in turn contributes to the development of venous insufficiency, venous thrombosis and pulmonary embolism, cardiovascular diseases, especially hypertension [10].

Conclusion. The mechanisms of the pathogenesis of hypertension in overweight have not been sufficiently studied; this applies to all age groups. Most researchers point to the similarity of the mechanisms of development of hypertension in obesity in young and adulthood. Recording risk factors and subclinical markers is useful in identifying young people who are overweight and at high risk of developing hypertension. Hypertension in combination with overweight or obesity is more likely to contribute to the development of cardiovascular disease than either condition alone. That is why hypertension, associated with excess body weight at a young age, has been the subject of close attention of the medical community in recent years. There are no universal recommendations for determining the low risk of hypertension in overweight at a young age. However, European, North American and International guidelines emphasize the importance of assessing the complications and comorbidities associated with excess weight. Most guidelines recommend BP screening in all overweight and obese adolescents.

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