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PATHOGENETIC SIGNIFICANCE OF INSULIN-LIKE GROWTH FACTOR IN THE FORMATION OF CARDIOVASCULAR DISEASES

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✓ ***Resume***

In the review article, the author presents studies by foreign scientists devoted to the study of the importance of insulin-like growth factor in the pathogenesis of cardiovascular diseases. All data are systematized and generalized into a single pathogenetic mechanism, direct and indirect neuro-immuno-endocrine effects of the factor on the cardiovascular system are described. Insulin-like growth factors affect growth, metabolism and apoptosis. Most studies have shown a decrease in insulin-like growth factor levels in people with metabolic syndrome or its components and in patients with coronary heart disease. Insulin-like growth factor has anti-inflammatory, antioxidant, hepatoprotective, metabolic (anabolic) effects. Insulin-like growth factor tachycardia, headache and vomiting as a result of transient increase in blood pressure, lipohypertrophy at the injection site, hypertrophy of the tonsils and adenoids, swelling of the face, arthralgia, myalgia, asthenia, orthostatic hypotension and side effects such as hypoglycemia (due to activation of insulin receptors). Insulin-like factor reduces the manifestation of insulin resistance in diabetes, and may contribute to both platelet stabilization and growth in coronary heart disease. In hypertension, it causes vasodilatation, which lowers blood pressure, and stimulates the growth of smooth muscle cells and cardiomyocytes, increases blood pressure.

Keywords: Cardiovascular system; insulin-like growth factor; arterial hypertension; diabetes; insulin resistance.

ПАТОГЕНЕТИЧЕСКОЕ ЗНАЧЕНИЕ ИНСУЛИНОПОДОБНОГО ФАКТОРА РОСТА В ФОРМИРОВАНИИ СЕРДЕЧНО-СОСУДИСТЫХ ЗАБОЛЕВАНИЙ

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✓ ***Резюме***

В обзорной статье автором приведены исследования зарубежных ученых, посвященные изучению значения инсулиноподобного фактора роста в патогенезе сердечно-сосудистых заболеваний. Все данные систематизированы и обобщены в единый патогенетический механизм, описаны прямые и опосредованные нейро-иммуно-эндокринные воздействия фактора на сердечно-сосудистую систему. Инсулиноподобный фактор роста влияет на рост, метаболизм и апоптоз. В большинстве исследований показано снижение уровня инсулиноподобного фактора роста у лиц с метаболическим синдромом или его компонентами и у больных ишемической болезнью сердца. Инсулиноподобный фактор роста обладает противовоспалительным, антиоксидантным, гепатопротекторным, метаболическим (анаболическим) действием. Инсулиноподобный фактор роста имеет побочные как тахикардия, головная боль и рвота в результате транзиторного повышения АД, липогипертрофия в месте инъекции, гипертрофия миндалин и аденоидов, отек лица, артралгия, миалгия, астения, ортостатическая гипотензия и побочные эффекты, такие как как гипогликемия (вследствие активации рецепторов инсулина). Инсулиноподобный фактор уменьшает проявления инсулинорезистентности при диабете и может способствовать как стабилизации, так и росту тромбоцитов при ишемической болезни сердца. При артериальной гипертензии вызывает расширение сосудов, что снижает

артериальное давление, а также стимулирует рост гладкомышечных клеток и кардиомиоцитов, повышает артериальное давление.

Ключевые слова: Сердечно-сосудистая система; инсулиноподобный фактор роста, артериальная гипертония; сахарный диабет; инсулинорезистентность.

YURAK-QON TOMIR KASALLIKLARI SHAKLLANISHIDA INSULINGA O'XSHASH O'SISH OMILINING PATOGENETIK AHAMIYATI

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Buxoro davlat tibbiyot instituti

✓ ***Rezume***

Taxliliy maqolada muallif xorijiy olimlarning yurak-qon tomir kasalliklari patogenezida insulinga o'xshash o'sish omilining ahamiyatini o'rganishga bag'ishlangan tadqiqotlarini taqdim etadi. Barcha ma'lumotlar tizimlashtirilib yagona patogenetik mexanizmga umumlashtirildi, bu omilning yurak-qon tomir tizimiga bevosita va bilvosita neyro-immun-endokrin ta'siri tavsiflanadi. Insulinga o`xshash o`shish omili o'sishga, metabolizmga va apoptozga ta'sir qiladi. O'tkazilgan tadqiqotlarning aksariyati metabolik sindrom yoki uning tarkibiy qismlari bo'lgan odamlarda va yurak ishemik kasalligi bo'lgan bemorlarda insulinga o`xshash o`shish omili darajasining pasayishini ko'rsatadi. Insulinga o`xshash o`shish omili yallig'lanishga qarshi, antioksidant, gepatoprotektiv, metabolik (anabolik) ta'sirlarga ega. Insulinga o`xshash o`shish omili taxikardiya, qon bosimining vaqtincha ko'tarilishi natijasida bosh og'rig'i va qusish, in'ektsiya joylarida lipogipertrofiya, bodomsimon bezlar va adenoidlarning gipertrofiyasi, yuzning shishishi, artralgiya, miyalgiya, asteniya, ortostatik gipotenziya va gipoglikemiya (insulin retseptorlari faollashishi tufayli) kabi nojo`ya ta`sir qilishi mumkin. Insulinga o`xshash omil qon tomir devorining kardiomiotsitlari va silliq mushak hujayralarining o'sishini rag'batlantiradi, vazodilatatsiyani keltirib chiqaradi. U qandli diabetda insulin rezistentlikning namoyon bo'lishini kamaytiradi, yurak ishemik kasalligida ham blyashka barqarorlashishiga, ham o'sishiga hissa qo'shishi mumkin. Gipertenziyada qon bosimini pasaytiradigan vazodilatatsiyani keltirib chiqaradi va silliq mushak hujayralarni va kardiyomiyositlarning o'sishini rag'batlantiradi, qon bosimini oshiradi.

Kalit so`zlar. Yurak-qon tomir tizimi; insulinga o'xshash o'sish omili, arterial gipertenziya; qandli diabet; insulin rezistentlik.

Relevance

Insulin-like growth factor-1 (IGF-1) polypeptide is a representative of growth factors and is close to insulin by its physiological effects. This factor plays an important role in the mechanisms of regulation of the structure and function of the myocardium and blood vessels. IGF-1 is detected in the processes of hypertrophy of the heart and blood vessels. A number of authors link IGF-1 to prognostic biological signs of the development of heart failure.

To date, the pathogenetic role of IGF-1 in the development of injuries of the cardiovascular system, including arterial hypertension, type 2 diabetes and their combination, remains unclear. In this regard, it is of great scientific interest to determine the relationship between the level of IGF-1 in the blood and the structural and functional parameters of the heart and carotid artery in patients with type 2 diabetes, hypertension. Treatment with metformin in patients with hypertension with type 2 diabetes resulted in a significant decrease in IGF-1 levels in the blood. This was particularly evident in patients with concentric left ventricular hypertrophy prior to treatment and with elevated IGF-1 levels. However, the addition of long-acting glyclazide to metformin, no decrease in IGF-1 levels in the blood of patients after treatment was not observed [1].

Both hypertension and obesity lead to structural and functional remodeling of the myocardium and the formation of left ventricular hypertrophy associated with the development of interstitial fibrosis. Cardiovascular fibrosis is a humoral process in which angiotensin II (ATII), endothelin-I, and aldosterone play a central role.

Angiotensin II stimulates type I collagen production and stimulates the involvement of profibrogenic peptide growth factors such as insulin-like growth factor-1 (IGF-1) and transformational growth factor b1, which alter ATII response. Activation of these humoral factors leads to the proliferation of fibroblasts and the development of imbalances in the process of collagen synthesis and degradation, its excessive accumulation in the interstitial space. An important representative of profibrogenic growth factors is IGF-1, which is produced in the liver, cardiomyocytes, smooth muscle cells, and fibroblasts under the influence of growth hormone. IGF-1 is believed to be partially structurally close to insulin, has an insulin-like metabolic effect, lowers glucose levels, and reduces insulin resistance. This factor plays an important role in the mechanisms that regulate the structure and function of the myocardium and blood vessels. Experiments have shown that IGF-1 plays a leading role in the protection of cardiomyocytes from apoptosis, both in vivo and in vitro. In experimental myocardial infarction in mice, a decrease in apoptosis was observed against the background of increased production of IGF -1, and in the absence of IGF-1 decreased DNA synthesis and increased apoptosis in cardiomyocytes. In recent years, the association of IGF-1 as an independent risk factor in cardiovascular disease has been discussed, but the results of these studies are highly controversial. A number of studies have shown that increased IGF -1 levels lead to a higher risk of developing ischemic heart disease, while other studies have shown that lower IGF-1 levels increase the risk of developing ischemic heart disease and death. There are studies showing the role of IGF-1 as a biological marker of prognostic significance for the development of heart failure. The results of clinical studies evaluating the level of IGF-1 in the blood of patients with hypertension are also not the same.

Thus, the study found that IGF-1 concentrations were higher in patients with hypertension than in normotonics, and in other studies, in contrast, in patients with hypertension, compared with controls, decreased, or with type 2 diabetes and arterial hypertension. in patients with pathological types of myocardial remodeling, its low level was noted. However, studies aimed at evaluating the effects of profibrotic growth factors on hemodynamic parameters and left ventricular remodeling in patients with arterial hypertension and metabolic syndrome are rare. Among the humoral factors that stimulate the growth of cardiomyocytes and myocardial fibroblasts, the sympathetic and renin-angiotensin systems play an important role, and the contribution of insulin and insulin-like growth factors in the regulation of connective tissue production has been studied. , especially in metabolic syndrome. IGF-1 is the main representative of the family of insulin-like growth factors, carries out endocrine, autocrine and paracrine regulation of growth processes and is actively involved in anabolic reactions in connective tissue, muscle and heart. IGF-1 levels are regulated by growth hormone, and its concentration depends on the effects of both growth hormone and sex steroids, thyroid hormones, glucocorticoids, and insulin on the liver. At the same time, insulin and estrogens increase the synthesis of IGF-1 in the liver, while glucocorticoids reduce it, which provides a synergistic effect of insulin, somatotropin, sex and thyroid hormones on the growth and differentiation of cells and body tissues. IGF-1 is known as insulin-like growth factor because of its ability to stimulate glucose absorption by muscle and adipose tissue in a very similar and insulin-like manner to proinsulin [2,8]. The role of IGF-1 factor in the development of many pathological processes in vascular disease has been demonstrated in experimental and clinical studies [8, 9, 10]. However, the effect of IGF-1 on hemodynamics and the prognosis of cardiovascular disease are highly contradictory. Thus, low levels of IGF-1 are associated with a risk of coronary heart disease (CHD), including cardiovascular death. However, there are conflicting data, suggesting that individuals with high levels of IGF-1 are more likely to develop UIC disease [8]. On the other hand, in a study evaluating the relationship between life expectancy and IGF-1 levels in older men, IGF-1 levels were higher in both the longest-lived general population and those with a poor cardiovascular history. which was. The literature data showing changes in IGF-1 levels in patients with hypertension are also contradictory. In addition to studies showing an increase in IGF-1 activity in hypertensive patients compared to normotonic patients, there are also studies showing a decrease in IGF-1 concentration in the blood of hypertensive patients compared to control groups. Changes in IGF-1 levels in the blood of patients with AG and MS were found to be related to the severity of obesity and to reflect myocardial left ventricular remodeling characteristics. Level ventricular concentric hypertrophy in grade 1 obesity is characterized by hyperproduction of IGF-1 and eccentric left ventricular hypertrophy at levels 2-3 of obesity is apparently associated with decreased IGF-1

synthesis, the lack of which contributes to increased cardiomyocyte apoptosis and the development of myocardial fibrosis. The results are consistent with data from other studies in which a decrease in IGF-1 activity was noted in AH patients with severe left ventricular hypertrophy, as well as in combination with diabetes mellitus. A correlation analysis in patients with grade III obesity and AG revealed a close relationship between IGF-1 levels and left ventricular mass index. The results of the study showed that IGF-1 deficiency in women with hypertension and MS plays an important role in the development of myocardial remodeling and fibrosis, and prone to the development of heart failure. On the other hand, in obese women with hyperinsulinemia, IGF-1 production in the liver and myocardium is reduced. Against the background of its deficiency develops left ventricular hypertrophy. It is known that insulin is an important modulator of the effect of IGF-1, the effect of insulin on myocardial remodeling processes, apparently, both through its direct effect on IGF-1 receptors in cardiomyocytes, and indirectly by stimulating IFR-1 synthesis can be done. However, unlike insulin, which is not synthesized in the myocardium, local secretion of IGF-1 and its receptors occurs in cardiomyocytes due to its synthesis by autocrine or paracrine mechanisms. Therefore, myocardial remodeling, apoptosis, and the development of interstitial fibrosis in AG and obesity may occur with IGF - 1 mediation [2]. In addition, a physiological decline in growth hormone and IGF-1 levels begins after puberty, which develops in proportion to a decrease in the hormonal function of the gonads (7). Decreased levels of growth hormone secretion associated with aging may decrease IGF-1 synthesis and its levels in the blood and tissues. There is evidence that IGF-mediated involvement in the regulation of the normal menstrual cycle in young women, while IGF-1 expression in endometrial stromal cells is stimulated by estrogens. An increase in estradiol levels in the proliferative phase of the cycle leads to the stimulation of IGF-1 expression in the blood and endometrium, which then leads to its increase. It is known that estradiol levels decrease in postmenopausal women, so the proliferative effect of IGF-1 on the endometrium is reduced. IGF-1 levels in the blood and endometrium are significantly reduced. Therefore, against the background of hypoestrogenemia in postmenopausal women, IGF-1 deficiency leads to the development of obvious changes in the cardiovascular system, such as apoptosis and a decrease in the number of cardiomyocytes, remodeling of the myocardium and fibrosis. On the other hand, IGF-1 deficiency in patients with MS with MS, which develops against the background of severe obesity and hypoestrogenemia, significantly enhances the processes of myocardial remodeling and fibrosis, leading to the early development of heart failure. In addition, there is evidence that low levels of IGF-1 are a biochemical sign of deterioration of anabolic processes [1] and are a predictor of chronic heart failure decompensation, indicating an unfavorable prognosis and a high risk of death (11). Thus, IGF-1 deficiency in postmenopausal patients with AG and MS is associated with a variety of structural, metabolic, and hormonal disorders, the most important of which is the development of hypertrophic forms of myocardial remodeling and subsequent heart failure.

AG and MS are related to the severity of obesity and reflect myocardial remodeling properties. In patients with hypertension and grade 1 obesity, concentric remodeling of the left ventricle predominated, and an increase in IGF-1 activity was noted.

The formation of hypertrophic types of myocardial remodeling at levels 2-3 of obesity is characterized by a decrease in IGF-1 levels, the minimum values of which were found in patients with AG with grade 3 obesity, with eccentric left ventricular hypertrophy predominating [2,11].

Of IGF-1 on cell growth and differentiation processes, the participation of cytokine in the regulation of carbohydrate metabolism and the functioning of the cardiovascular system in obese patients is highly controversial. Data are described. Thus, in a study by Zakirova NE et al (2017), high levels of IGF-1 were observed in patients with stage 1 AG and primary obesity, and a gradual decrease in blood pressure and TMI was observed. In another study, by contrast, the highest levels of IGF1 were observed in patients with combined AG and type 2 diabetes. However, IGF-1 levels showed a stable correlation with cytokine profile indicators, impaired carbohydrate metabolism, and diastolic dysfunction [3, 12].

Insulin-like growth factor 1 (IGF-1) plays an important role in the energy balance of the newborn’s body, it is associated with protein reserves, and its level is seen as an indicator of nutritional status. can exit. Based on the literature, it can be said that, in general, IGF-1 levels in premature infants are relatively low in premature infants. Analysis of the content of IGF-1 in the blood of premature infants showed that the values of this indicator in the neonatal period are very different: in the first study their

range of values was 1.0-48.13 μg / l, in the second 3, 14–60, 3 mkg / l. Two variants of IGF-1 and blood nutrient dynamics of the studied nutrients were identified during early postpartum adaptation in preterm infants [4].

IGF-1 **is** a polypeptide hormone produced primarily by the liver in response to growth hormone stimulation. It is formed in smaller amounts in other organs and tissues and has an auto- or paracrine effect there. The nature of insulin, cortisol, and nutrition significantly affects hormone expression. Growth factor and IGF-1 functions are not fully separated.

IGF-1 acts on growth hormones, as well as has its own activity - anabolic, antioxidant, anti-inflammatory and cytoprotective effect. It affects the development, growth and differentiation of cells, tissue regeneration. Unlike the growth factor, IGF-1 levels are constant throughout the day and do not depend on food intake. Plasma IGF-1 concentrations are associated with moderate levels of growth hormone throughout the day in both healthy individuals and patients with acromegaly . The amount of IGF-1 secreted depends on the basal level of growth hormone and is not related to the amplitude of its secretion peaks [13]. In infancy, IGF-1 promotes growth, neuro- and sympathogenesis, and overall development; in childhood it mainly affects bone metabolism, anabolic processes and proliferation; affects glucose and lipid metabolism in young and middle age, has antioxidant and anti-inflammatory properties, is a hepato- and cardioprotector; in old age it provides neuroprotection, mitochondrial protection, and reduces apoptosis. IGF-1 deficiency is observed in children with Laron syndrome (congenital short stature - due to a defect in the gene for somatotropic hormone receptors), cirrhosis of the liver in adults, cardiovascular and nervous system diseases in the elderly, and underdevelopment of fetal growth. The maximum concentration of IGF-1 is observed in the prepubertal period and early adolescence, over the years it gradually decreases. In healthy people over 65, IGF-1 secretion is 50-70% lower than in young people. The amount of IGF-1 depends not only on age but also on gender. In women aged 25-34 years, the concentration of IGF-1 is higher than in men, and vice versa at the age of 55-64 years. Blood IGF-1 concentrations are inversely related to age, body mass index, SAB, and total cholesterol levels in men and women. There is a positive correlation between IGF-1 composition and growth [7].

The components of the IGF-1 system, including itself, its receptors and binding proteins, are regulated by many factors, including other hormones, cytokines, lipoproteins, and hemodynamic load. In the uterus and ovaries, IGF-1 secretion is regulated by estrogens and follicle-stimulating hormone. Thrombin, tumor necrosis factor, and estrogens reduce IGF-1, mRNA production, and protein levels in smooth muscle cells.

Active forms of oxygen and angiotensin II have the opposite effect. The effect of LDL and platelet growth factor on IGF-1 secretion is unclear. IGF-1 promotes tissue growth, which is not possible without increasing their nutrition, which means increased blood flow. The effect of the hormone on blood vessels is associated with its vasodilating effect, as well as with the good absorption of glucose (including by microvascular endothelial cells), ie insulin-like effect. In vessels, IGF-1 is involved in the development of atherosclerosis, restenosis, diabetic injury, and angiogenesis [8]. IGF-1 is involved in the activation of vascular endothelial growth factor and stimulates endothelial cell growth. In experiments, the introduction of IGF-1 is accompanied by an increase in the density of cerebral vessels, and antibodies against it block this effect. IGF-1 is 50% similar to proinsulin and provides sensitivity to up to 10%. Both insulin and IGF-1 can activate each other’s receptors, but have a much lower affinity for foreign receptors than their own receptors. Decreased plasma IGF-1 concentrations are associated with the development of insulin resistance and metabolic syndrome, which are less common when IGF-1 and hydroxyvitamin D (calcifediol) concentrations are high. In metabolic syndrome, high levels of insulin lead to a decrease in IGF-1 production in the liver and tissues. A decrease in IGF-1 concentration, along with an increase in blood pressure, has a significant effect on the occurrence of vascular complications in diabetes. This is because IGF-1 may stimulate more smooth muscle cell migration and proliferation during hyperglycemia than euglycemia. IGF-1 contributes to the stabilization of atherosclerotic plaques by reducing oxidative stress, apoptosis, inflammatory signals, and endothelial dysfunction. Risk factors for the development of cardiovascular complications are increased PZXL, impaired insulin resistance, central obesity, smoking and AG, endothelial dysfunction with a decrease in IGF-1 levels [3] are associated with an increased risk of

ischemic heart disease, stroke, and heart failure [7]. Growth factor and IGF-1 deficiency worsen NO-dependent vasodilation associated with blood flow, increasing cardiovascular disease and mortality.

In vitro and in vivo experiments have shown that IGF-1 partially reduces vascular resistance by increasing NO synthesis by endothelial and smooth muscle cells, partially by inhibiting intracellular calcium flow, and by stimulating Na / K-ATPase. Much of its effect on vascular tone is due to endothelial NO synthase activity of IGF-1 and growth hormone is made by the activation of potassium channels and a decrease in the sensitivity of smooth muscle cells to calcium ions. In addition, IGF-1 reduces vasoconstriction induced by endothelin-1 by acting on endothelin receptors in smooth muscle cells. IGF-1 and its receptors are expressed in the myocardium, aortic wall and vascular endothelium. IGF-1 stimulates the growth of cardiomyocytes and vascular endothelium, proliferation and migration of smooth muscle cells in the vascular walls , leading to an increase in blood pressure.

Left ventricular hypertrophy in arterial hypertension can be explained only by partial pressure overload, IGF-1 is involved in its development, which stimulates cardiomyocyte hypertrophy. Insulin can also cause myocardial hypertrophy by stimulating IGF receptors as a result of the structural similarity of these molecules. In patients with untreated hypertension, left ventricular myocardial mass was associated with body mass index, postprandial insulin level, insulin resistance index, IGF-1 levels after starvation and glucose, and mean SBP and DBP during 24-hour monitoring. Blockade of IGF-1 receptor synthesis is observed with a decrease in the density of angiotensin II receptors in the arteries, which leads to a significant decrease in the pressor response to angiotensin II and adrenaline. However, it does not alter blood pressure and intima-media thickness at rest in spontaneous hypertensive mice.

Have shown that there is an inverse relationship between IGF-1 levels and the prevalence of hypertension. When the amount of IGF-1 is in the lower limit of the norm , hypertension is observed more often than when the normal concentration is higher. This situation is different for women, where the presence of high levels of IGF-1 is accompanied by a decrease in the risk of developing arterial hypertension.

The Framingham study confirms that the mean blood pressure of IGF-1 concentration is inversely related to the pulse wave velocity. A decrease in IGF-1 concentration to the lower limit of normal is associated with AG and diabetes mellitus in patients without pituitary disease and cardiovascular disease.

There is a negative correlation between the free concentration of IGF-1 and blood pressure in patients with type 1 diabetes, which is also observed when taking into account age, sex and anamnestic data, IGF-binding protein and the relationship between AB is less pronounced.

Separate studies in the last century have found no association between IGF-1 and AG, or correlated IGF-1 levels in patients with AG depending on the degree of left ventricular hypertrophy (6,7). When observed in young men for 10 years, no correlation was found between IGF-1 and blood pressure levels, although a weak correlation was found between IGF-binding protein-3 and blood lipid content.

Myocardial stem cells, increases telomerase activity and slows replicative aging; in the myocardium - neovascularization of the affected areas is observed. Therefore, it can have a healing effect on the aging process of the heart and blood vessels. In healthy longevity, the ratio of IGF-1 to IGF - binding protein is related to blood pressure levels.

IGF-1 maintains endothelial function and affects the balance of calcium and magnesium ions, which helps to lower blood pressure in the long-lived compared to the elderly. IGF-1 receptors are present in all tissues and are tetramers, consisting of two extracellular α -chains and two intracellular b -chains in which the tyrosine kinase domain is located. Its activation stimulates cell growth, differentiation, migration, and survival. The effects of IGF-1 are modulated by binding proteins, the activity of which varies as a result of phosphorylation, proteolysis, polymerization, and binding to cells or matrices. Because IGF has a clear affinity for IGFBO, they are used to transport and accumulate the hormone.

75-90% of IGF-1 in the blood is associated with IGFBO-3, which increases the half-life of the hormone to several hours, regulates its adequacy and its effect at the cellular level. This protein itself can affect growth, metabolism, and apoptosis. IGFBO -1, 2, 4 enters the vascular wall and transports the hormone to the organs.

The content of IGFBO -1 in middle-aged men is lower than in women. Regardless of gender, a decrease in IGFBO-1 concentration is associated with an increase in blood pressure and an increased risk of developing vascular disease. As a marker of insulin sensitivity, IGFBO-1 can be used to assess the risk of developing metabolic syndrome, the IGF-1 / IGFBO-3 ratio provides less information in this regard.

Most studies in the last decade have shown a decrease in IGF-1 levels in people with MS or its components and in patients with ischemic heart disease. Similarly, a further decrease in IGF-1 levels is observed in patients with growth factor deficiency, and substitution therapy has a clear positive effect. The results of experimental and clinical studies on the use of IGF-1 in the treatment of ischemic heart disease and MS are insufficient [13,14].

IGF-1 is a mitogen for smooth muscle cells, stimulating their migration and reducing apoptosis. Therefore, its inhibition may be beneficial in AG and in the early stages of atherosclerotic plaque growth, but it is considered harmful in the presence of unstable plaque. Recombinant IGF-1 has been available since the late 1980s. It is widely used as a substitute therapy for congenital or acquired growth factor deficiency.

In children with severe IGF-1 deficiency, such treatment increases the annual height by 3 to 8 cm. Growth factor hypersecretion is observed in patients with type 1 diabetes mellitus, accompanied by absolute insulin deficiency. A decrease in IGF-1 and IGFBO-3 and an increase in IGFBO-1 are detected in the blood. Recombinant IGF-1 is therefore promising in treatment alone or in combination with IGFBO-3.

However, in many cases, the use of recombinant IGF-1 is limited to substitution therapy if it is a systemic deficiency. It is rarely used to optimize the level of IGF-1 in the blood, because in order to achieve a good effect, it is advisable to use an optimal combination of growth factor, IGF -1 and its binding proteins. the combination has not yet been found (14,15).

Prescribing IGF-1 in the absence of deficiency includes its use of anti-inflammatory, antioxidant, hepatoprotective, metabolic (anabolic) effects, but due to side effects, only with short courses limited. It is preferable to use low doses of the hormone as they are sufficient to develop a therapeutic effect and do not cause the complications typical of high doses.

The side effects of IGF-1 disappear quickly after discontinuation of the drug. These include tachycardia, headache and vomiting as a result of a temporary increase in blood pressure, lipohypertrophy at the injection site, hypertrophy of the tonsils and adenoids, swelling of the face, arthralgia, myalgia, asthenia, orthostatic hypotension and hypoglycemia (due to activation of insulin receptors). enters. Although IGF-1 concentrations are often high in cancer, its use in low doses does not stimulate oncogenesis [16].

Patients with type 2 diabetes receive an increase in IGF expression when taking pioglite, which is an activator of PPAR- g receptors, which improves insulin sensitivity and reduces lipolysis in liver and adipose tissue, resulting in increased growth factor synthesis and, consequently, The formation of IGF-1 is also stimulated. IGF-1 has a significant effect on the condition of the cardiovascular system in adults.

And smooth muscle cells of the vascular wall , causes vasodilation, and has insulin-like properties. IGF-1 influences the development of diseases that play an important role in cardiovascular pathology - ischemic heart disease, hypertension and diabetes. Reduces the manifestation of insulin resistance in diabetes; may contribute to both plaque stabilization and growth in ischemic heart disease; causes vasodilatation, which lowers blood pressure in hypertension, and stimulates the growth of smooth muscle cells and cardiomyocytes, increases blood pressure [17,18].

Due to the wide range of multidirectional effects, the only recognized indicator of IGF-1 use in these diseases is clearly enhanced insulin resistance. In other cases, the combination of positive and negative effects requires a more in-depth study of the IGF-1 system to create drugs with minimal side effects [5,19].

PAPP-A is an acute phase protein that reflects atherosclerotic plaque damage. Increased concentrations of PAPP-A occur in acute coronary syndrome and massive vascular inflammation of atherogenic etiology. IGF-I is a growth protein that reflects the process of vascular repair. Increased IGF-I concentrations are associated with the development of ischemic heart disease and arterial hypertension [6,12,20].

Conclusion

The absence of gender characteristics of PAPP-A and IGF-I has been confirmed, and the patterns of gender-specific acute coronary syndrome outcomes have not been established. However, a negative statistical correlation was found between IGF-I levels and the age of patients with acute coronary syndrome . Thus, older patients have lower concentrations of IGF-I and a relatively low reparative ability to repair damaged vessel wall and myocardium.

Pregnancy-related plasma protein A and insulin-like growth factor 1 are new hypersensitive biochemical markers of vascular inflammation and injury. Their level can be used to predict atherosclerotic plaque instability in acute coronary pathology and disease prognosis.

Abbreviations:

IGF1 - insulin-like growth factor
IGFBO - is a protein that binds to an insulin-like growth factor
SBP - systolic blood pressure
DBP - diastolic blood pressure

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