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Навчук І.В.,
кандидат медичних наук, доцент кафедри
соціальної медицини та організації охорони здоров'я
ВДНЗ України «Буковинський державний медичний університет»
Навчук Г.В.,
кандидат філологічних наук, доцент кафедри
суспільних наук та українознавства ВДНЗ України
«Буковинський державний медичний університет»
Собко Д.І.
лікар-терапевт

FEATURES OF COURSE OF ARTERIAL HYPERTENSION COMBINED WITH TYPE II DIABETES MELLITUS AND OSTEOARTHROSIS IN THE FIELD OF OBESITY

Navchuk I.V.,
PhD, Associate Professor of the Department of Social Medicine and the Organization of Health Care of Higher State Educational Establishment of Ukraine «Bukovinian State Medical University»
Navchuk H.I.,
PhD, Associate Professor of Social Sciences of Higher State Educational Establishment of Ukraine «Bukovina State Medical University»
Sobko D.I.
Physician

Анотація

Артеріальна гіпертензія у поєднанні з такими чинниками ризику як куріння, гіподинамія, дисліпідемія, ожиріння, цукровий діабет стає причиною 70-75% інсультів та 80-90% інфарктів міокарда і є основним чинником розвитку низки серцево-судинних ускладнень, які призводять до передчасної інвалідизації та смертності пацієнтів. Тому аналіз даних наукових праць щодо особливостей перебігу артеріальної гіпертензії у поєднанні з атеросклерозом, ожирінням і цукровим діабетом ІІ типу, а також щодо їх ранніх біомаркерів є актуальним для розробки алгоритму первинної, вторинної та третинної їх профілактики.

Abstract

Hypertension in combination with risk factors such as smoking, hypodynamia, dyslipidemia, obesity, diabetes mellitus causes 70-75% of stroke and 80-90% of myocardial infarctions and is a major contributor to the development of a number of cardiovascular complications that lead to premature infertility and mortality of patients. Therefore, the analysis of scientific data on the characteristics of the course of arterial hypertension in combination with atherosclerosis, obesity and type II diabetes, as well as their early biomarkers is relevant for the development of an algorithm for primary, secondary and tertiary prevention.

Ключові слова: артеріальна гіпертензія, цукровий діабет ІІ типу, остеоартроз, ожиріння, серцево-судинні ускладнення.

Keywords: arterial hypertension, type II diabetes mellitus, osteoarthritis, obesity, cardiovascular complications.

Arterial hypertension (AH) is an important medical and social problem of health care in many countries of the world, as it affects about a quarter of the world's population. In combination with such common risk factors as smoking, hypodynamia, dyslipidemia, obesity, diabetes mellitus (DM), hypertension is the cause of at least 70-75% of stroke cases, 80-90% of myocardial infarctions, and it is a major factor the risk of developing a series of cardiovascular complications that lead to premature disability and mortality of patients. AH significantly increases the risk of kidney damage, stroke cases (in Ukraine, the frequency of stroke is twice the rate of myocardial infarction), heart failure (HF), peripheral vascular disease and cardiovascular death.

The report of the World Health Organization (WHO) estimates that obesity in the modern world is comparable to the epidemic. The results of sample surveys conducted in Ukraine suggest that today, at least 30% of the working population of our country has an overweight and 25% obesity. The steady increase in the prevalence of obesity is observed in almost all countries of the world. In the last 10 years in the world, it has grown by an average of 75%. Obesity leads to the development of insulin resistance (IR) of peripheral tissues, which plays a key role in the development of diabetes.

Today, over the world, over 400 million people suffer from diabetes, more than one million in Ukraine. The main reason for the disability and mortality of patients with diabetes is cardiovascular disease, the development of which has a leading AH, which, according to official statistics, is noted in 80% of patients with diabetes type II.

A similar situation is characteristic for osteoarthrosis (OA). Osteoarthrosis of the knee joints attracts special attention due to significant prevalence, progressive course and early disability, persistent pain syndrome, motor activity and quality of life. There is no doubt about the role of obesity in the development and progression of OA.

Osteoarthrosis is often pathogenetically linked to the components of the metabolic syndrome (MS) (insulin resistance, type II diabetes, obesity, hyperlipidemia, arterial hypertension and coronary heart disease (CHD). OA against the background of MS is an important medical and social problem even in Moreover, the presence of MS accelerates the pace of progression of pathology of the joints, in connection with which the study of clinical and pathogenetic features of the combination of OA with MS is quite relevant.

The purpose of the study is to analyze the data of scientific works on the characteristics of the course of arterial hypertension in combination with osteoarthritis, obesity and type II diabetes, as well as their "early" biomarkers.

The object of the study were literary sources for the last 15 years, which studied the peculiarities of the course of diseases such as hypertension, osteoarthrosis, type II diabetes, metabolic syndrome, obesity, and the like. The subject of research is «early» biomarkers of hypertension in combination of OA and type II diabetes on the background of obesity. In the process of research, the following methods were used: description, analysis, synthesis, comparison, contrast, etc.

A number of population studies have shown the relationship between obesity, especially abdominal, and the frequency of hypertension. According to them, indicators of blood pressure increased in proportion to the excess body weight. Certain roles in the genesis and development of hypertension also played a dysfunction of the endothelium of the vessels. However, the effect of hypertension and its combination with obesity on the clinical manifestations and the course of OA is not sufficiently studied.

Underlying development of hypertension during obesity is insulin resistance (IR). Many studies have found a positive correlation between the level of blood pressure and the concentration of insulin in the blood. Against the background of hyperinsulinaemia, reverse transport of sodium and water in the kidneys increases, which leads to hypervolemia. It is also believed that IR/hyperinsulinemia promotes hypertension due to anomalies of the signaling pathway of insulin and is associated with cardiovascular and metabolic disorders. This includes increased activity of the sympathetic and renin-angiotensin systems, reduces the synthesis of atrial natriuretic peptide, causes sodium retention with subsequent volume increase, promotes kidney damage, hyperactivity, left ventricular hypertrophy, dyslipidemia, chronic hyperglycemia and an increase in oxidative stress.

The development of insulin resistance, hyperlipidemia and hypertension contributes to abdominal obesity, which is a frequent companion of patients with hypertension with type II diabetes. In adipose tissue, the synthesis of numerous biologically active substances, to which, in particular, belongs, is leptin, tumor necrosis factor-α (FNP-α), IL-6, IL-8. Recently, angiotensin-II (A-II), an inhibitor of plasminogen-1 activator (IPA-1), a transforming growth factor-β1 (TGR-β1), adiponectin, and others, are attributed to substances that are synthesized by adipocytes. It is believed that periarterial and periateriolary fatty tissue may have the same properties as visceral fat, and therefore play a role in the development of vascular complications and IR. Most of the population surveys show a direct correlation between IOP and obesity, but IOP may not be accompanied by excess body weight. Thus, there was no relationship between obesity and IR during lipodystrophy, when there is no abdominal and visceral adipose tissue.

According to various studies, it can be assumed that the interaction between central obesity and hypertension can lead to a decrease in adiponectin, which more than likely increases the TNF-a concentration. These altered adipocin patterns (low circulating adiponectin and high TNF-a) indicate that complications from obesity can progress more rapidly when there is hypertension and vice versa. However, the results of this study are specific to adult women, a similar study for men has not yet been conducted. Additional studies that would clarify the mechanisms of the origin of adipose tissue, including adipokines and cytokines, will help to understand the peculiarities of the emergence, development and combination of these diseases and to prevent serious consequences.

In addition, literary sources indicate that the concentration of leptin is also increased in the case of metabolic syndrome, probably due to resistance to leptin. At the same time, the concentrations of anti-inflammatory cytokines (IL-10), grilin, adiponectin and antioxidant factors (PON-1) were, conversely, lowered, which correlated with specific disorders within the cluster.

Consequently, the aforementioned biomarkers are significantly correlated with metabolic syndrome and can (provide a minimally invasive means) to be clinical and laboratory indicators for early detection of hypertension in combination with type II diabetes and OA against obesity. Further studies are encouraging to determine the effectiveness of the use of these biomarkers for early diagnosis and specific treatment of these diseases.

On the other hand, studies point to the involvement of oxidative stress as an imbalance between prooxidant and antioxidant systems to pathogenesis and OA progression. Intensification of peroxide lipid oxidation (LPO) leads to the release of proinflammatory cytokines, microcirculatory disturbances, collagen structure and contributes to the progression of the degenerative process in the articular tissues. Peroxidation products cause damage to the vessel's endothelium, vasospasm, and increased general peripheral resistance, which may lead to an increase in blood pressure in patients with OA, in the context of reducing the effect of antihypertensive drugs. At the same time, the presence of hyperglycemia in patients with OA leads to activation of the polyol route of glucose metabolism and non-enzymatic glucosylation of proteins, which causes

damage to the muscles and periactricular tissues. Hyperglycemia affects the course of OA both at the local and at the systemic levels: in particular, local effects of oxidative stress and glycosylation of end products increase cartilage tissue damage, and the accumulation of toxic glycolysis products can lead to OA progression. Dahaghin S. et al. found the association of diabetes mellitus (DM) with OA of the joints of the brushes in people aged 55 to 62 years, with the highest frequency of OA of the joints of the brushes was noted in the subgroup of patients with a combination of excess body weight, DM and AH. Type II diabetes complicates destructive processes in the tissues of the knee joints, in connection with which, in its presence, the stage III of OA is detected 2 times more often.

Data from literature show that adiponectin, leptin and vsfatin can affect both the large joints and the joints of the bristles. These adipokines are involved in the regulation of glucose metabolism and adipocytes, as well as immune and inflammatory responses. Increasing their serum level is a predictor X-ray progression of OA of the joints of the hands.

The adipose tissue contains macrophages, forming a coronoid structure around hypertrophied adipocytes. In contrast to fatty tissue, thin, containing mainly anti-inflammatory M2-macrophages, in the case of obesity, fatty tissue primarily contains inflammatory macrophages M1. In addition, fatty fat is rich in dendritic cells, T- and B-cells, neutrophils and adipocytes. During obesity, the production and release of proinflammatory cytokines and adipokines - leptin, resistin, liponquine-2, RBP4, interleukins (IL) -6, 18, an alpha-tumor necrosis factor (FNP-a), which is accompanied by the emergence of low-intensity systemic inflammation, is increasing. The source of adipocyne is also its own fatty tissue of the joints, in particular, the infralateral fatty tissue (ILFT) of the knee joint. Due to its location, ILFT can play an important role in local inflammation of the knee joints. Today, at least 3 cytokines are produced, which are produced at the same time by adipose tissue and IPLT: IL-6, FNP-a and VEGF (vascular endothelial growth factor).

It has been established that the high level of some adipokines (IL-1, IL-4 and 6, leptin) is associated with the progression of articular cartilage defeat in OA.

Consequently, metabolic syndrome (MS) is a risk factor not only for development, but also for the progression of OA, because there is an interconnection of OA with metabolic changes occurring during obesity: both in one and in another state, there is an increased circulation of systemic inflammatory markers (C-reactive protein, IL-1 and FNP-a) [27]. In addition, leptin, produced by macrophages of adipose tissue, is a key mediator of metabolic disorders in OA. Leptin is capable of causing the synthesis of metalloproteinases (MPP) (collagenase, stromelysin, gelatinase, membrane proteinase, and metalloelastasia) that cause damage to the cartilage during OA, and the degree of increase in the activity of these enzymes is mostly correlated with the degree of damage to cartilage tissue. Leptin enhances the synthesis of proinflammatory mediators (IL-6, IL-8 and prostaglandin E2) in Cartilage in the case of OA.

Thus, during the metabolic syndrome, higher levels of insulin and leptin are also observed. The pro-inflammatory state of the immune system illustrates the increase in the content of S-RB and IL-1. In the presence of a metabolic syndrome, a more pronounced progression of joint damage is observed, indicating a negative role of insulin resistance and adipokines (leptin, C-reactive protein and interleukin-1) in articular cartilage metabolism during OA.

An important role in the progression of OA belongs to AG, and the use of non-steroidal anti-inflammatory drugs (NSAIDs) for anti-inflammatory and analgesic effects in patients with heart disease in a history of 10 times increases the likelihood of hospitalization for heart failure and leads to destabilization and progression of hypertension.

In addition, NSAIDs can reduce the effectiveness of antihypertensive drugs, especially those whose effects are mediated through the renin-angiotensin system (angiotensin-converting enzyme (ACE) inhibitors, diuretics, angiotensin II receptor antagonists), which have been shown to reduce left ventricular hypertrophy and rigidity of arteries in patients with hypertension and diabetes. However, an advantage should be given to ARIs, since they most often reduce the mass of myocardial infarction, decrease the activity of angiotensin II, have less adverse reactions, have a mild effect on renal hemodynamics.

According to researchers, one should not forget that the development of dystrophic changes in the vascular wall and articular cartilage, the progression of hypertension and OA may contribute to lipid metabolism disorders, which become the general pathogenetic mechanism of these diseases. Under dyslipidemia, oxidized low-density lipoproteins (LDL) reduce the activity of endothelial NO synthase (NOS) and the bioavailability of NO. Therefore, the analysis of factors of endothelial dysfunction in patients with a combination of OA and hypertension on the background of obesity is well grounded.

Today, researchers have proven that the regression of the intima-media complex correlates with a decrease in LDL cholesterol levels . At the same time, the risk of developing a stroke increases with an increase in the thickness of the intima-media complex of the vessels, and the growth of the of the total carotid artery at 0.2 mm is associated with an increased risk of stroke from 33 to 43%. In general, thickening of intima-media complex is an independent predictor of an unfavorable cerebrovascular prognosis. Proceeding from this, binding of statins is obligatory.

So, after analyzing the literature on the peculiarities of hypertension in combination with OA and type II diabetes against obesity, as well as their «early» biomarkers, the following conclusions can be drawn:

First, the combination of arterial hypertension and obesity significantly affects anthropometric parameters, blood pressure, parameters of intracardiac hemodynamics and increases the disturbance of carbohydrate metabolism.

Secondly, in the case of the combination of arterial hypertension and obesity as a result of vascular, meta-

bolic and hormonal changes, the latter has a more pronounced effect on the severity of clinical manifestations and functional deficiency of joints in patients with osteoarthritis than arterial hypertension.

Third, AH in combination with type II diabetes is characterized by high prevalence, more frequent and severe damage to target organs, decreased insulin sensitivity, accompanied by hyperinsulinemia, atherogenic dyslipidemia, a violation of the daily profile of AT, which significantly increases cardiovascular risk, and activation of proinflammatory drugs cytokines and growth factors not only enhance dysmetabolic manifestations, but also leads to the development of hypertrophy and myocardial fibrosis, causing its pathological remodeling.

Prospects for further research are to increase the efficiency of complex treatment of osteoarthritis combined with type II diabetes, based on the study of clinical and pathogenetic features of combined pathology.

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