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METABOLIC SYNDROME: METHODS OF PREVENTION AND TREATMENT

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ABSTRACT
Metabolic syndrome (MS) is a complex of interrelated and modifiable risk factors for the development of cardiovascular diseases (CVD) and type 2 diabetes mellitus (diabetes) (as defined by the World Health Organization (WHO, 1999) and NCEP ATP III (2001) - National Cholesterol Education Program Adult Treatment Panel III - US National Cholesterol Reduction Program, III revision of therapy for adults) [1]. The main components of MS are disorders of carbohydrate metabolism, abdominal obesity, dyslipidemia, and arterial hypertension.
KEYWORDS: metabolic syndrome, diabetes mellitus, cardiovascular diseases, obesity, prevention.

INTRODUCTION

According to D.L. Sprecher et al., In patients with MS and coronary heart disease (CHD) mortality from CVD increases 5 times for women and 2 times for men [2], and myocardial infarction and stroke occur 3.5 times more often [3] . From the point of view of public health and clinical practice, the obesity epidemic, the pathogenetic basis of which is insulin resistance (IR), is becoming the main socio-economic problem of mankind, for which early diagnosis and timely effective treatment of the main components of MS are extremely important [4].

Given the continuing disagreement in the definition of MS, in November 2009 a preliminary joint opinion was published by IDF, the National Heart, Lung, and Blood Institute (NHLBI), the American Heart Association (American Heart Association - AHA), World Heart Federation (WHF), International Atherosclerosis Society - IAS, and International Association for the Study of Obesity (International Association for the Study of Obesity - IASO) [9]. The main purpose of this document was to develop unified criteria for the diagnosis of MS. As a result, IDF, NHLBI, AHA, WHF, IAS and IASO (2009) identified the following MS criteria (if any 3 criteria are found, MS is diagnosed below):

• abdominal obesity: waist circumference (OT)> 80 cm in women, OT> 94 cm in men;
• triglycerides> 1.7 mmol / L (150 mg / dl) or drug therapy for hypertriglyceridemia;
• a decrease in the concentration of high density lipoproteins (HDL): <1.0 mmol / l (40 mg / dl) in men, <1.3 mmol / l (50 mg / dl) in women or drug therapy of dyslipidemia;

• high blood pressure:> 130/85 mmHg. Art. or taking antihypertensive therapy with a patient with a history of arterial hypertension;
• increased fasting glycemia:> 6.1 mmol / L (100 mg / dl) and> 7.8 mmol / L 2 hours after an oral glucose tolerance test or taking a hypoglycemic therapy [9].

The prevalence of MS and its individual components

Due to the high prevalence of MS, its early detection is of great importance for the timely start of the prevention of complications. So, in the Russian Federation (RF), according to the results of a study conducted by Yu.P. Nikitin et al., 40% of the population have 2 components of MS, 10.7% - 3 or more of its components [12].

According to the INTERHEART study, MS (according to NCEP ATP III criteria) on average have 26% of the adult population of the planet. Its prevalence among obese patients is high - 49%; among people with impaired glucose tolerance, the frequency of MS is 50%, and in diabetes - 80% [13]. In addition, there is a steady upward trend in the prevalence of MS. To date, the number of patients with MS is 2 times the number of patients with type 2 diabetes, and an increase in the frequency of MS by 50% is expected in the next 20 years [14]. It must be emphasized that most patients with MS are a population of people of active working age, the most productive and significant for society. In addition, over the past two decades, the frequency of the syndrome studied has shown steady growth among young people. WHO experts assessed the situation as follows: “We are facing a new pandemic of the 21st century, encompassing industrialized countries. This could be a demographic disaster for developing countries as well. ”

The close relationship of MS with CVD, type 2 diabetes, polycystic ovary syndrome, non-alcoholic fatty liver disease, chronic renal failure, certain types of cancer ultimately leads to increased mortality, morbidity and psychological problems, worsening the quality of life of patients.

The most frequent outcomes of MS - CHD and type 2 diabetes - play a leading role in the structure of mortality in the Russian Federation and represent a global problem for the healthcare system due to the high cost of treatment procedures, the duration of the course of diseases, and high disability of the population.

In industrialized countries, coronary heart disease is the most common cause of death and the main cause of disability due to illness. Every year in Russia, more than 1 million people die from CVD (431.5 people per 100 thousand people) [15]. According to the Ministry of Health of the Russian Federation, in 2007 the share of CVD in the structure of causes of death was 56.9%. In this regard, the identification of individuals at high risk of early development of coronary heart disease and the implementation of special individualized measures for the prevention of atherosclerosis have reduced mortality from complications of coronary heart disease in many economically developed countries [16]. Correction of MS is an important step in the prevention of CVD.

In addition, many modern researchers consider MS as a “prelude” of type 2 diabetes. The increase in the number of patients with type 2 diabetes in recent years is a serious public health problem. International and national recommendations for the prevention of type 2 diabetes are aimed at solving the problem of reducing the impact of all risk factors [17]. Type 2 diabetes is characterized by an asymptomatic course with the development of various complications leading to disability and an increase in the frequency of early death. In type 2 diabetes, at the time of diagnosis, 80% of patients have obesity, 80% have fasting hyperinsulinemia, 50% have essential hypertension, 50% have dyslipidemia, 15% have neuropathy, and 5% have diabetic neuropathy [18].

PRINCIPLES OF THERAPY FOR MS

To date, there is no single treatment strategy for MS. The presence in patients of a wide variety of non-modifiable risk factors (gender, heredity, age, ethnicity) in combination with modifiable factors (overweight or abdominal obesity, a sedentary lifestyle, arterial hypertension, dyslipidemia, impaired glucose tolerance and / or impaired fasting glucose) determines the existence of a huge number of phenotypic variants of MS, requiring a personalized approach to the selection of therapy of its individual components. In this regard, the use of the concept of MS, according to WHO experts, is limited as a diagnostic and therapeutic tool [11].

Scott Grundy, who led the third panel of NCEP experts in 2006, in his article “Medical Therapy for MS. Minimization of the polypharmacy crisis ”reflects the general treatment strategy for this violation:
• Strengthening activities to change lifestyle to minimize problems associated with polypharmacy;

• delaying the initiation of drug therapy as much as possible (without worsening long-term clinical outcomes; exceptions are possible - these are drugs for lowering low-density lipoprotein (LDL) cholesterol and blood pressure in individuals with an increase in relevant parameters);
• the use of the lowest possible doses of drugs, consideration of the possibility of an early start of the use of low-dose drugs with high levels of LDL cholesterol and high blood pressure;
• the use of the least amount of drugs to correct each risk factor: combining drugs in one dosage form, increasing the effectiveness of drugs without increasing toxicity, developing multifunctional drugs;
• increasing the degree of adherence to the regimen of drugs by simplifying treatment regimens;
• improving understanding of the variability of drug efficacy (eg, pharmacogenomics) [19].

The main therapeutic measures for MS include lifestyle changes, as the main way to correct metabolic risk factors, and drug treatment of the combined components of MS.

Lifestyle modification - the basis for the treatment of patients with MS

Despite the fact that the views on the beginning and tactics of drug therapy may differ, most researchers are unanimous that the basis for successful treatment and first-choice therapy is lifestyle change. First of all, we are talking about a decrease in body weight against the background of hypocaloric nutrition and an adequate regime of physical activity, since approximately 85% of all patients with MS are overweight. In addition, it is important to reduce alcohol consumption, stop smoking, reduce food intake high in saturated fatty acids and include foods rich in unsaturated fatty acids and fish oil in the diet. An increase in physical activity has a positive effect on all MS parameters. The effect is achieved by increasing energy expenditure and the associated reduction in body weight. Physical exercise also leads to an increase in tissue sensitivity to insulin, even without a decrease in body weight.

The high effectiveness of non-drug measures is beyond doubt and was proved by the results of a number of randomized clinical trials: TOMS, TORN, TAIM. The average life expectancy of overweight people is 8–10 years less than in the population as a whole, and more than 2.5 million people die every year from diseases associated with obesity. A decrease in body weight of 9–10 kg contributes to an increase in the life expectancy of patients: a decrease in overall mortality by 25%, mortality from cancer by 30–40%, and from type 2 diabetes by 30–40% [20].

The above data demonstrate that in the case of the successful implementation of the task to reduce body weight, there is a constant non-drug therapeutic effect on the whole complex of pathogenetic disorders in patients with MS.

Nevertheless, the results of the Cochrane review [21], which included 55 studies on primary prevention of CVD, showed that counseling and educating patients about lifestyle changes do not reduce overall mortality and mortality from CVD in the general population. Only patients with arterial hypertension and type 2 diabetes showed a good effect from the use of such therapeutic strategies, which may be associated with a higher adherence of such patients to treatment. In addition, lifestyle changes are often very problematic for patients, and the result of weight loss is not kept for a long period of time, so the effectiveness of this therapeutic strategy decreases over time. According to statistics, only 5% of patients manage to maintain a decrease in body weight achieved through diet and exercise over 1.5–2 years.

For many people, lifestyle modification measures cannot completely correct existing disorders, and the severity of risk factors increases with age, so the need for drug therapy increases.

Today, there are no drugs that can significantly reduce all metabolic risk factors for a long time. For this reason, drug treatment may include the correction of each risk factor separately, for example, a combination of lipid-lowering drugs, antihypertensive drugs and hypoglycemic therapy. Unfortunately, as the disease progresses, a single drug no longer provides effective control of the corresponding risk factor, therefore, several drugs are required. The problem is complicated when multiple medications are required to control several risk factors. For example, when a patient develops type 2 diabetes mellitus on the background of MS, therapy with 10 or more drugs is often required, most of which are aimed at correcting risk factors, but others may be needed to treat complications, exacerbating the problem of polypharmacy.

All of the above indicates the relevance of a comprehensive study of MS and the search for the most rational, patient-friendly and highly effective methods of pharmacotherapy.

PHARMACOTHERAPY OF OBESITY IN PATIENTS WITH MS

The appointment of drug therapy for abdominal obesity can be thought of if the change in lifestyle did not allow to reduce body weight by 5% for three to six months. In addition, drug therapy is indicated if the patient has obesity (body mass index (BMI)> 30 kg / m², or if there are other, in addition to increased body weight (BMI> 27 kg / m²), MS components.

Currently, two drugs are recommended for the treatment of obesity and overweight: orlistat and sibutramine. But both drugs are effective only in combination with lifestyle changes. This therapy, together with a change in lifestyle, leads to a decrease in body weight of approximately 10 kg. In addition to the positive effect on risk factors for CVD during pharmacotherapy, it is possible to improve the quality of life of patients.

Pharmacotherapy of dyslipidemia and non-alcoholic fatty liver disease

Atherogenic dyslipidemia is one of the main components of MS described by G. Re¬aven in 1988. In the process of studying the concept, it became clear that another common disease associated with MS is non-alcoholic fatty liver disease (NAFLD), which occurs in two forms, or successive stages: liver steatosis and non-alcoholic steatohepatitis (NASH). According to Russian authors, in patients with MS and abdominal type of obesity NAFLD occurs in 100% of cases, and NASH - in 41.7% [24]. It is proved that the leading mechanisms of the development of this disease are the pathological activation of lipolysis processes with the release of a large amount of free fatty acids in individuals with abdominal obesity, associated with IR and oxidative stress, which provokes an inflammatory reaction in hepatocytes and leads to the formation of steatohepatitis.

In those cases where a hypocaloric and hypocholesterol diet and a change in physical activity do not allow you to adjust the lipid spectrum and the activity of liver enzymes, it is necessary to consider the possibility of using drug therapy.

PHARMACOTHERAPY OF HYPERTENSION

The frequent development of arterial hypertension in MS is due to a whole complex of the previously described pathogenetic mechanisms of the development of the syndrome, against the background of the polygenic nature of the inheritance of concomitant diseases - obesity, type 2 diabetes and dyslipidemia, as well as hyperactivation of the renin-angiotensin-aldosterone system.

Antihypertensive therapy for MS should be carried out to achieve a target blood pressure level of less than 130 and 80 mm RT. Art., especially in the presence of type 2 diabetes. Numerous studies using a wide range of antihypertensive agents have proven that effective blood pressure control significantly reduces the risk of CVD and mortality. Moreover, strict control of blood pressure in patients with type 2 diabetes leads to a more significant decrease in the frequency of macrovascular complications of diabetes than the achievement of target glycemic levels.

The general principles of the medical treatment of arterial hypertension are: continuous, long-term therapy, starting treatment with the minimum doses of one drug, switching to drugs of another class with insufficient treatment effect (at the maximum dosage) or poor tolerance, the use of drugs mainly of long duration, the use of optimal combinations of drugs to achieve maximum hypotensive effect and minimize side effects.

Pharmacotherapy of insulin resistance and disorders of carbohydrate metabolism

One of the main dramatic outcomes of MS is the development of type 2 diabetes. This disease is characterized by a gradual onset - it begins with mild or moderate disorders of carbohydrate metabolism due to IR and functional hyperinsulinemia, which over time cause beta-cell dysfunction and impaired insulin production, which leads to the occurrence of prediabetes. Then, already for a much shorter period, the manifestation of type 2 diabetes occurs.

In conclusion, we note that, despite the exclusion of MS from the ICD-10 as a condition that does not meet the definition of the concept of “disease”, this concept still causes great scientific interest. The early identification of metabolic risk predictors is of great clinical importance in order to start the timely prevention of CVD and type 2 diabetes, the main causes of death among the world's population. In our country, it is necessary to actively develop effective prevention strategies based on available resources that will complement preventive strategies, focusing on controlling and reducing metabolic and behavioral factors by affecting key determinants [11].

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