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CHRONIC OBSTRUCTIVE PULMONARY DISEASE AND THE METABOLIC SYNDROME: THE STATE OF THE PROBLEM

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ABSTRACT

The article provides an overview of published data on the state of the problem of combined chronic obstructive pulmonary disease and metabolic syndrome and the results of epidemiological studies on the combination of these nosological forms. The possible pathophysiological mechanisms of mutual worsening of these diseases are discussed. This review emphasizes the role of systemic inflammation, smoking, including passive smoking, as the leading risk factor. It also highlights the importance of determining the phenotype of chronic obstructive pulmonary disease to select the tactics for these patients. The value of adding obstructive sleep apnea syndrome was also considered. The indicated pathogenetic mechanisms that influence components of metabolic syndrome, including type 2 diabetes, on pulmonary function were considered. The article highlights the features of treatment, longtermtrends in therapy of these diseases.

KEYWORDS: *Chronic Obstructive Pulmonary Disease, Phenotypes Of Chronic Obstructive Pulmonary Disease, Metabolic Syndrome, Type 2 Diabetes Mellitus, Smoking.*

INTRODUCTION

As defined by the GOLD Working Group, chronic obstructive lung disease (COPD) is a group of chronic inflammatory diseases lungs, which is characterized by partially reversible airflow restriction flow. Obstructive ventilation problems are usually progressive and are associated with an unusual inflammatory response of the lungs to pathogenic gasesorparticles.

However, the views that COPD is primarily among lung disease, is currently contested. COPD will become the third leading cause of death worldwide and will have a significant impact on the overall health care system.

Type 2 diabetes mellitus and metabolic syndrome are also quite common causes that aggravate the course of a number of diseases and lead to mortality around the world.

An increase in the mass of visceral fat, in combination with a decrease in the sensitivity of peripheral tissues to insulin and hyperinsulinemia, is commonly called a metabolic syndrome, leading to a violation of carbohydrate, lipid, purine metabolism and arterial hypertension.

Isolation of the metabolic syndrome as a separate concept is of great clinical importance, since, on the one hand, this condition is reversible, and on the other, it precedes the onset of diseases such as type 2 diabetes mellitus and atherosclerosis, which are currently the main causes of mortality. Isolation of the metabolic syndrome as a separate concept is of great clinical importance, since, on the one hand, this condition is reversible, and on the other, it precedes the onset of diseases such as type 2 diabetes mellitus and atherosclerosis, which are currently the main causes of mortality.

In 2009, experts from the All-Russian Scientific Society of Cardiology proposed the following criteria for the diagnosis of metabolic syndrome. In 2009, experts from the All-Russian Scientific Society of Cardiology proposed the following criteria for the diagnosis of metabolic syndrome.

The main feature: central (abdominal) type of obesity - a waist volume of more than 80 cm in women and more than 94 cm in men.

Additional criteria:

—— arterial hypertension (blood pressure above 140/90 mm Hg);

—— an increase in triglyceride levels of more than 1.7 mmol / l;

—— lowering the level of high density lipoprotein cholesterol less

1.0 mmol / L in men, less than 1.2 mmol / L in women;

—— the increase in low-density lipoprotein cholesterol is greater

3.0 mmol / L;

—— fasting hyperglycemia (fasting plasma glucose above 6.1 mmol / l);

—— impaired glucose tolerance (plasma glucose after 2 hours

after glucose loading in the range of more than 7.8 mmol / l and less than 11.1 mmol / l).

The patient has central obesity and two of the additional criteria

riev is the basis for diagnosing his metabolic syndrome. There are different forms of metabolic syndrome depending on the number and combination of symptoms. The classic option is a combination of abdominal obesity, hyperinsulinemia, arterial hypertension, dyslipoproteinemia, impaired glucose tolerance (IGT), or type 2 diabetes mellitus.

The following combinations are available as alternatives:

—— hyperinsulinemia, arterial hypertension, dyslipoproteinemia, NTG

or type 2 diabetes mellitus ("European" variant - metabolic

non-obesity syndrome);

—— hyperinsulinemia, arterial hypertension, dyslipoproteinemia, abdominal

final obesity (option without NTG);

—— hyperinsulinemia, arterial hypertension, dyslipoproteinemia (in

non-obesity and IGT). Today, according to the World Health Organization, the prevalence of metabolic syndrome has become a pandemic.

In recent years, a large number of studies have been devoted to the combination of COPD and metabolic syndrome. According to various sources, metabolic syndrome suffers from 21 to 53%, and type 2 diabetes mellitus - 2–37% of patients with COPD. Among patients with type 2 diabetes mellitus, COPD occurs in about 10% of cases. A number of large epidemiological studies have found an increase in the incidence of obesity among patients with COPD compared to the general population.

Thus, in Northern California (USA), 54% of patients with COPD are obese: their body mass index (BMI) exceeds 30 kg / m2. For comparison: in general, obesity affects 20-24% of the population. A research group from the University of California at San Francisco studied 355 patients with the aim of studying the effect of body composition on the functional state of patients with various stages of COPD. Obesity (BMI ≥ 30 kg / m2) was diagnosed in 54% of study participants, which is significantly higher than in the general population of the United States. The same data are confirmed by a number of other authors from different countries.

K. Markis et al in their study showed the presence of one or more components of the metabolic syndrome in almost 50% of patients with COPD compared to 21% of the incidence in the control group without COPD, and the prevalence of obesity was about two times higher in the COPD group. Most often, elements of the metabolic syndrome are found in the early stages of COPD. Its combination with metabolic syndrome and type 2 diabetes mellitus leads to an increase in the number of exacerbations of COPD and a deterioration in the quality of life.

COPD metabolic syndrome and phenotypes. Back in 1968, G.F. Fille et al. Proposed to subdivide patients with chronic pulmonary pathology into two groups - "dyspnea" or "pink puffers" and "coughing" or "blue edema" (blue bloaters). These patient groups are also defined as emphysematous (A) and bronchitis (B) types of COPD. These views were developed and supplemented. So, with the development of computed tomography, a type with a predominance of emphysema and without it began to be distinguished. However, one thing remained indispensable: in contrast to the most common cachectic (emphysematous) type, there was a group of patients with increased body weight (metabolic syndrome).

S. Garra et al. In their case-control study studied the relationship between BMI and emphysematous and bronchitic phenotypes of COPD. In patients with bronchitic type of COPD in 25% of cases, BMI exceeded 28 kg / m2, compared with 16% in the control group. In addition, BMI ≥ 28 kg / m2. was associated with an increased risk of developing bronchitis, while the presence of emphysema was associated with low body weight. Most studies have noted

that the highest prevalence of obesity occurs in patients with mild to moderate COPD and low in patients with the most severe pulmonary dysfunction in an extremely severe stage.

However, in the study by R. Furtate et al., It was noted that patients with COPD have an excessive amount of visceral fat and its accumulation persists even in severe COPD with emphysema, despite the absence of obesity. It has been shown that in patients with COPD, there is a simultaneous decrease in skeletal muscle mass and excessive accumulation of visceral fat, especially in the more severe stage of COPD. There are several possible explanations for this phenomenon: skeletal muscle mass in severe stages of COPD decreases due to physical inactivity, decreased exercise tolerance, malnutrition and systemic inflammation;

a decrease in skeletal muscle mass leads to further physical inactivity, which leads to excess visceral fat accumulation, especially in more severe stages of COPD. Changes in the respiratory system with the association of metabolic syndrome and COPD are formed not only due to obstructive mechanisms due to COPD, but are also the result of limiting the respiratory excursion of the lungs with a decrease in the vital capacity of the lungs, tidal volume against the background of a high standing of the diaphragm as a result of pronounced abdominal obesity, which is the main a component of metabolic

At the same time, the normal movement of air through the bronchopulmonary system becomes difficult, the depth of breathing decreases and mucociliary clearance worsens. Thus, in the presence of concomitant pathology in the form of COPD and metabolic syndrome, there is an addition to obstructive disorders in the framework of COPD of the restrictive mechanism due to abdominal-visceral obesity. It is known that the life expectancy of patients with COPD correlates with their body mass index. Low BMI is a reliable predictor of mortality in COPD.

Thus, A. M. Schols et al. In their study showed that life expectancy at BMI ≤ 20 kg / m2 is two times lower when compared with the group of patients with BMI ≥ 29 kg / m2. However, according to the GOLD recommendations, it is not recommended to strive for a significant decrease in body weight in patients with severe COPD and elements of metabolic syndrome: the body mass index should be at least 21 kg / m2.

The prognostic significance of BMI assessment is also emphasized by the fact that this indicator was included in the integral scale for assessing the severity of systemic manifestations of COPD, presented as the abbreviation BODE, where B means body mass index (BMI), O - obstructive disorders of the ventilation function of the lungs, D - the degree of severity shortness of breath, E - exercise tolerance, which is established in the test with a six-minute walk. And, despite the fact that in the initial version of this scale only the group of people with a low BMI was singled out, proposals are made for correcting this criterion, taking into account excess weight.

It is important to note that the presence of recurrent subclinical thromboembolism of small branches of the pulmonary artery may contribute to the progression of pulmonary fibrosis. The role of systemic inflammation. The combination of COPD and metabolic syndrome is largely due to the common pathogenetic mechanisms leading to the development of these diseases. It is well known that the offspring of sick parents are more likely to develop both COPD and type 2 diabetes. A well-known risk factor for both diseases is low birth weight, which occurs, inter alia, as a result of maternal smoking during pregnancy.

Smoking, as a common risk factor for the development of COPD and metabolic syndrome, can be a common cause of the association of these diseases. IS Eze and co-authors in the course of the Swiss study SAPALDIA found that exposure to tobacco smoke increases the risk of diabetes mellitus and impaired glucose tolerance, even in never smokers, by 50%. At the same time, a dose-dependent effect was revealed.

In addition, smoking can contribute to the development of systemic inflammation and oxidative stress - a pronounced imbalance of oxidative-antioxidant systems, as a result of which a pathogenic concentration of active oxygen metabolites is produced. At the same time, their excess activates the transcription factors NF-kB and AP-1, MAP-kinases, which, in turn, induce the synthesis of pro-inflammatory cytokines (tumor necrosis factor-α, IL-8 and other chemokines), thereby increasing the influx of neutrophils and macrophages into the inflammation center with a further escalation of the production of active oxygen metabolite

Bronchoconstriction and vasoconstriction also develop through oxidative mechanisms. In addition, oxidants mediate many other pathological processes, such as DNA degradation, a decrease in surfactant activity, and an increase in the permeability of the epithelium and endothelium. In recent years, much attention has also been paid to the study of the role of oxidative stress in the development of endothelial dysfunction and insulin resistance, which is not only one of the main links in the pathogenesis of type 2 diabetes mellitus, but also the main component of the metabolic syndrome.

Lipid oxidation products stimulate the activity of protein kinase C, calcium release, disrupt endothelial cell replication and angiogenesis, and induce apoptosis. Adipose tissue is central to the development of insulin resistance under the influence of inflammation. The idea of it as an inert tissue serving only for the accumulation of energetic substances and triglycerides is a thing of the past.

It turned out that adipose tissue is metabolically very active, and can also be considered as an endocrine organ that produces substances such as leptin, lipoprotein lipase, apolipoprotein E, which are involved in the regulation of various physiological processes of the body, primarily eating behavior, energy balance and metabolism, mainly fats and carbohydrates. Moreover, the metabolic and hormonal activity of visceral fat is significantly higher than that of subcutaneous fat. It is important to emphasize that adipose tissue cells secrete pro-inflammatory cytokines (TNF-α, IL-6 and IL-1, resistin), as well as chemokines.

Increased secretion of these substances correlates with obesity, and to a greater extent with an increase in visceral fat mass. It is noted that with a combination of COPD and metabolic syndrome, the level of TNF-α is 38.3%, IL-6 - 28%, and IL-8 - 38% higher than in patients with isolated pathology. A correlation was also found between the content of TNF-α and the stage of COPD. Of decisive importance is the detection in obesity, insulin resistance and type 2 diabetes mellitus of an increase in the level of C-reactive protein in the blood - a generally recognized marker of the acute phase of inflammation, despite the absence of many other classic signs of inflammation in these conditions.

Thus, with the development of both COPD and metabolic syndrome, a similar shift in biochemical processes occurs, in particular, the activation of free radical oxidation due to imbalance in the oxidant – antioxidant system.

Metabolic syndrome and lung function. A number of authors note that the lungs, along with others, should be considered the target organ of diabetes mellitus. It is known that type 2 diabetes mellitus is often associated not only with arterial hypertension, abdominal obesity, and various cardiovascular diseases, but also with a reduction in pulmonary function and a decrease in forced expiratory volume in the first second (FEV1), worsening the clinical picture and evolution of COPD.

The study showed that baseline values of FEV1 and forced vital capacity (FVC) were inversely associated with the incidence of type 2 diabetes, and a recent crossover study found that decreases in FEV1 and FVC were directly related to the development of diabetes mellitus 2- th type. In the work, patients with diabetes mellitus and a smoker index of more than 10 pack / years showed a more pronounced decrease in lung function than in persons without diabetes, even if chronic lung diseases were not identified.

There are four main reasons for the decrease in lung function in diabetes mellitus. First of all, this is non-enzymatic glycosylation of collagen and elastin of the lungs by the end products of glycosylation, produced when glycemic control is impaired, which ultimately leads to a violation of the elasticity of the lungs. Thickening of the basal lamina of the alveolar epithelium and microvascular changes in the pulmonary capillaries, leading to a decrease in capillary blood volume and a decrease in the diffusion capacity of the lungs, are of potentially equal importance.

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Features of therapy. Currently, the question of the treatment of COPD against the background of metabolic syndrome remains largely open. An important role is played by the fact that exacerbations of COPD often require the use of glucocorticosteroids. Although the GOLD guidelines do not limit the treatment of patients with a combination of COPD and metabolic syndrome or diabetes mellitus, a number of studies indicate that the use of higher doses of corticosteroids may increase the risk of hospitalization for exacerbations of type 2 diabetes.

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Against the background of treatment with roflumilast, there is a decrease in body weight in obese patients, an improvement in the glycemic profile in patients with type 2 diabetes mellitus. It is also noted that the anti-inflammatory properties of statins have a beneficial effect on the course of COPD and metabolic syndrome. There was a decrease in the level of C-reactive protein in the blood, normalization of the lipid profile and glycemic parameters in patients with COPD and atherosclerosis against the background of metabolic syndrome when atorvastatin and metformin

were prescribed in addition to basic therapy. Treatment of diabetes mellitus in patients with COPD is recommended according to standard protocols.

Conclusion

Comorbidity in COPD is a serious problem due to the fact that mortality from COPD is largely due to the presence of comorbidities. Comorbidities affect the course of the disease, which in turn determines the choice of treatment and prevention programs. Diabetes mellitus and metabolic syndrome are today considered one of the leading risk factors for severe COPD.

Association with metabolic syndrome leads to an increase in the number of exacerbations of COPD, increases the risk of adverse outcomes In turn, some authors note that COPD can be considered as an independent marker of some components of metabolic syndrome, such as decreased carbohydrate tolerance or type 2 diabetes mellitus, arterial hypertension or a reduction in bone mineral density.

Meanwhile, the data of our review indicate insufficient study of the problem of the mutual influence of COPD and metabolic syndrome. The combination of these diseases can be fraught with a number of interesting discoveries. In particular, as is known, COPD through the cytokine proinflammatory cascade contributes to the development of lung cancer.However, in the course of studies, it was found that with a combination of COPD with diabetes mellitus, the relative risk of developing lung cancer is lower than with isolated COPD.

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