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# STUDY OF THE MORPHO FUNCTIONAL STATE OF THE VASCULAR ENDOTHELIUM OF THE LUNGS IN DIABETES MELLITUS BASED ON EXPERIMENTAL STUDIES

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**Abstract:**

The main category of patients is persons of working age (from 40 to 67 years). The severe course of COPD, the frequency of hospitalizations, disability and mortality of patients are associated with the presence of concomitant diseases, one of which is diabetes mellitus.

**Keywords:** Diabetes, inflammatory response, condition of patients

Diabetes mellitus is also an important medical and social problem, which is due to its high prevalence, chronic course, high disability of patients and mortality due to complications. The number of patients with diabetes in Russia, according to the International Diabetes Federation (2014), is currently at least 12.1 million people. According to forecasts, by 2040, the number of people with diabetes in the world will increase from 415 million currently to 642 million people. In developed countries, type 2 diabetes accounts for 87-91 % of all cases of diabetes. Among patients with diabetes mellitus, mortality from heart disease and stroke is observed 2-3 times, blindness-10 times, nephropathy-10-15 times, gangrene of the extremities-20 times more often than in the general population [1].

Co morbidity in COPD is an actual problem of modern medicine. In the management and treatment of patients with COPD in combination with diabetes mellitus, it is necessary to take into account the risk factors and mechanisms of development and progression of both diseases.

Currently, COPD is considered as a disease that can be prevented and treated. It is characterized by persistent restriction of the air flow velocity, which is usually progressive and is associated with a pronounced chronic inflammatory response of the lungs to the action of pathogenic particles or gases. In a number of patients, exacerbations and co morbidities may affect the overall severity of COPD.

A special role in the development of COPD belongs to chronic inflammation, which is the basis for the progression of the disease. The pathogenesis of chronic inflammation includes oxidative stress, proteolysis tissue destruction, immune insufficiency, and microbial colonization. At the beginning of COPD disease, the implementation of these components of pathogenesis is carried out under the influence of risk factors, and when the disease is formed, it takes the character of a self-supporting process. Inflammation engulfs all layers of the bronchial wall, the lung parenchyma, and the pulmonary vessels and leads to the formation of the main manifestations of COPD: emphysema, remodeling of the airways, including per bronchial fibrosis.

Activated inflammatory cells (neutrophils, macrophages) secrete a large number of free radicals that have a powerful damaging effect. Smoking is an exogenous source of oxidants (oxygen, ozone, peroxides, and hydro peroxides). The pulmonary antioxidant defense consists of enzyme (superoxide dismutase and glutathione) and non-enzyme (vitamin E, C, beta-carotene, uric acid, flavonoids, bilirubin) systems. Oxidants have a direct toxic effect on the structural components of the lungs (DNA, lipids, proteins, connective tissue); enhance the synthesis of mucus glycol conjugates by epithelial cells, damage mucociliary transport, fibroblasts; stimulate the formation of thromboxanes; reduce the activity of surfactant; promote endothelial dysfunction. Oxidants inactivate protease inhibitors, which contributes to the destruction of alveolar walls and extracellular membranes by elastics, which stimulates the synthesis of pro-inflammatory interleukins. Thus, the imbalance between oxidants and antioxidants is important in the pathogenesis of COPD.

Persistent inflammation in COPD is associated with a number of systemic manifestations that affect patient survival and the development of co morbidities. Systemic manifestations of COPD include cachexia, loss of skeletal muscle, and increased risk of cardiovascular disease, anemia, osteoporosis, and depression. There is an increase in the risk of cardiovascular disease, correlated with an increase in the level of C-reactive protein and lepton. The mediator of some systemic effects may be an increase in the concentrations of proinflammatory cytokines and free oxygen radicals.

Currently, the state of the endothelium in chronic obstructive pulmonary disease is widely studied. In COPD, inflammation is a persistent process and leads to a permanent adverse effect on the endothelium. Risk factors for endothelial damage include: hypercholesterolemia; hyperhomo cysteinemia (GHZ); elevated levels of cytokines (IL-1β, TNF-α, IL-8). When the vascular endothelium is exposed to various aggressive factors, its activation occurs, the initial effect of which is protective. With prolonged exposure to negative factors, there are 3 stages of endothelial activation: 1) initial activation of synthetic intracellular processes in the endothelium; 2) secondary disruption of the sequence and balance of these processes; 3) depletion of cells and their destruction.

Endothelial dysfunction is accompanied by a decrease in vasodilator and an increase in vasoconstrictor processes, activation of the cytokine system, increased platelet aggregation and adhesion, accelerated free radical oxidation, impaired vascular wall thrombosis, and a predominance of proliferative processes. The central components of endothelial function are: nitric oxide, angiotensin II, and endothelin-1.

One of the most powerful vasoconstrictors – angiotensin II, is formed as a result of activation of the renin-angiotensin system. Currently, the role of the renin-angiotensin-aldosterone system (RAAS) in the pathogenesis of COPD and the formation of pulmonary hypertension and chronic pulmonary heart disease (CHL) has been proven.

In patients with chronic obstructive pulmonary disease, endothelial dysfunction is already detected at stages I and II of the disease. In the initial stages of the disease, there is an increase in the concentration of such markers of endothelial damage as C-reactive protein and will brand factor.

Insulin resistance is a disturbed biological response of the peripheral tissues of the body to the effects of exogenous or endogenous insulin. Thus, the prevalence of IR in people aged 40 to 79 years in Italy is: 10 % - in people without metabolic disorders, 58 % - in people with arterial hypertension, 63 % - in people with hyperuricemia, 84 % - in people with hypertriglyceridemia, 88 % - in people with low levels of high-density lipoprotein cholesterol and 84 % - in people with DM 2.

It is known that tumor necrosis factor-α (TNF-α) reduces insulin sensitivity at the level of adipose and muscle tissues, however, research is still ongoing to clarify the mechanism of IR development in this case. Developing independently of each other, insulin resistance and dysfunction of the pancreatic beta cells combine at some stage and contribute to the development of hyperglycemia and related glucose toxicity.

Studies in recent years have enabled to discover local components of the RAAS in adipose tissue and pancreas. The role of this system in the development of visceral obesity and diabetes mellitus has been proven. The diabetic genie role of RAAS is determined by the effect of angiotensin II on both mechanisms of the development of diabetes mellitus: insulin secretion and insulin resistance. It is the activation of the tissue components of RAAS that leads to the development of complications of diabetes mellitus. Thus, the activation of the renin-angiotensin system is accompanied by a decrease in vascular thrombosis resistance, which contributes to an increase in the predisposition to thrombotic complications.

The main role in the pathogenesis of vascular complications in DM 2 is played by endothelial dysfunction. Hyperglycemia, insulin resistance, an increase in free fatty acids, oxidative stress and other metabolic changes associated with diabetes mellitus lead to the development of endothelial dysfunction and, as a result, to the development and progression of atherosclerosis. The vascular endothelium is a complex endocrine organ that regulates the tone and permeability of blood vessels, the balance in the systems of homeostasis and fibrinolysis, the formation of foci of inflammation, the processes of their restoration and repair through the synthesis of many mediators. Many researchers note the relationship between the state of the endothelium of the vascular wall and the course of various diseases.

Currently, the co morbid pathology of COPD and diabetes mellitus is being actively studied. Thus, when these diseases are combined, structural and functional changes in the endothelial cells of the alveolar capillaries are observed. Endothelial dysfunction develops faster due to the mutual negative influence. Chronic hyperglycemia supports pathological processes in the endothelium, which leads to early severe complications of DM and accelerates the progression of COPD. Also, persistent systemic inflammation introduces a number of aggravating endothelial changes.

All these factors negatively affect the condition of patients with chronic obstructive pulmonary disease in combination with diabetes mellitus, leading to early disability of such patients and an increase in mortality.

Thus, systemic inflammation in COPD contributes to metabolic imbalance in the body, the development of insulin resistance, and DM2, which indicates a significant role of COPD in the pathogenesis of type 2 diabetes. In DM2, the secretion of pro-inflammatory cytokines is also stimulated, oxidative stress and endothelial dysfunction develop, which support persistent inflammation in the respiratory tract and contribute to the progression of COPD and diabetes mellitus and the development of complications. There is a "vicious circle" of the burdened mutual influence of COPD and type 2 diabetes. Knowledge of the etiopathogenetic aspects of co morbid pathology will allow a personalized approach to the treatment of patients with COPD and type 2 diabetes.

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