Modern Methods Of Treatment Of Pulmonary Hypertension

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ABSTRACT

Pulmonary hypertension (PH) is a disease characterized by increased pressure in the pulmonary vessels. In most cases, PH develops as a secondary condition, but there are also idiopathic forms. If symptoms suggestive of PH or other organic pathologies appear, all patients are recommended to undergo echocardiography (EchoCG) of the heart. The probability of PH is estimated by the peak velocity of tricuspid regurgitation on EchoCG and characteristic signs of the disease. EchoCG allows for the prompt detection of PH and referral of the patient to a specialized or regional center for further examination and treatment.The main task of such centers is to determine the PH group (according to the classification), evaluate its hemodynamic parameters and decide on the need for specific therapy. Patients who contact these centers must undergo a complete examination. For accurate diagnosis of PH, invasive catheterization of the right heart is required, which is available only in specialized medical institutions. This procedure also allows for assessing the possibility of prescribing calcium channel blockers and increasing the effectiveness of the vasoreactive test. If the vasoreactivity test is negative, the patient is prescribed specific therapy. Treatment components are selected individually and can only be prescribed by experts in specialized centers. Given the high cost of LH therapy, the emergence of high-quality generics can significantly reduce treatment costs while maintaining comparable effectiveness. In a new drug from the class of endothelin receptor antagonists was registered in Russia - Bozenex (bosentan), which has proven its bioequivalence to the original drug.

Keywords: Pulmonary hypertension, pulmonary arterial hypertension, treatment of pulmonary hypertension, specific therapy, bosentan, Bosenex.

Pulmonary hypertension (PH) is a disease associated with increased pressure in the pulmonary vessels. In most cases, it is secondary, but idiopathic forms of PH also occur. Idiopathic (primary) PH is characterized by the absence of any known causes of the disease. It occurs in 1-2 cases per 1 million population. 6% of such patients will have a familial form of PH. And although the incidence of PH in various diseases requires clarification, it is known that, for example, in scleroderma it ranges from 2 to 35%, in portal hypertension - 2-4%, in HIV - 0.1-0.6%. With PH, the pulmonary vessels are in spasm for a long time, their walls are hypertrophied, which ultimately leads to their fibrosis and a decrease in the vascular bed.

It is this mechanism that underlies the development of right ventricular overload and its failure. The main symptoms of PH are shortness of breath, weakness, a feeling of discomfort in the chest and fainting. The diagnosis of this disease is quite simple - measuring the average pressure in the pulmonary artery. In 2004, the upper limit of this indicator at rest was defined as 25 mm Hg, and under load - 30 mm Hg. If the average pressure in the pulmonary artery is higher than these values, an examination is necessary to identify the cause of PH and decide on the treatment of the disease. However, in the last decade, the paradigm of PH has changed, at the 6th International Symposium on PH, the definition and classification of the disease, as well as approaches to its therapy, were updated. Pulmonary hypertension (PH) is a disease in which there is an increase in pressure in the pulmonary vessels. In most cases, PH develops as a secondary condition, but there are also idiopathic forms of the disease. Idiopathic, or primary, PH is characterized by the absence of obvious causes and is extremely rare - approximately 1-2 people per 1 million population. At the same time, about 6% of such patients have a familial form of PH. The prevalence of pulmonary hypertension varies in different diseases: for example, in scleroderma it is from 2 to 35%, in portal hypertension - 2-4%, and in HIV infection - 0.1-0.6%.With pulmonary hypertension, there is a long-term spasm of the pulmonary vessels, accompanied by thickening of their walls, which ultimately leads to fibrosis and narrowing of the vascular bed. These changes cause overload of the right ventricle of the heart and the development of its failure. The main symptoms of pulmonary hypertension are shortness of breath, weakness, discomfort in the chest and fainting. Diagnosis of the disease is based on measuring the average pressure in the pulmonary artery. In 2004, the normal limits were established: at rest, this indicator should not exceed 25 mm Hg, and during physical exertion - 30 mm Hg. If the pressure exceeds these values, additional examination is required to determine the cause of pulmonary hypertension and select the appropriate therapy.In recent years, approaches to understanding PH have undergone significant changes. At the 6th International Symposium on Pulmonary Hypertension, the definition, classification, and treatment of this disease were revised.

The role of outpatient services in the diagnosis of pulmonary hypertension (PH)

The symptoms of PH are not specific and may include shortness of breath during physical exertion, weakness, dizziness of varying severity, fainting, and in some cases, cough. Some patients also have signs of progressive right ventricular failure, such as edema, ascites, a feeling of bloating, and rapid satiety during meals.

An important stage in the diagnosis of PH is a thorough collection of anamnesis.

It is necessary to find out whether the patient has had cases of thromboembolism, whether anticoagulant therapy has been previously administered and how long it lasted, whether there is a history of heart defects, systemic connective tissue diseases, and also to clarify the drug and family history.

Examination of the patient also plays a key role in the diagnosis of PH. Cardiac auscultation often reveals an accentuated second heart sound over the pulmonary artery, dilated cardiac borders, and signs of right ventricular failure, such as jugular vein distension, positive venous pulse, enlarged liver and/or spleen, edema, systolic tricuspid regurgitation murmur, or pulmonary artery murmur.

If PH or other organic cardiac pathologies are suspected, echocardiography (EchoCG) is recommended for all patients. The probability of PH is estimated based on the peak velocity of tricuspid regurgitation and characteristic echocardiographic signs of the disease (see Table 1) [3]. EchoCG allows for the prompt detection of PH and referral of the patient to an expert or regional center for further examination and treatment. In some cases, patients present to the outpatient service with echocardiography results indicating the presence of PH. Such patients should also be referred to specialized centers to clarify the type of PH and determine further treatment tactics.

The role of regional centers and PH offices

Rephrase it to me The main task of regional centers is to determine the pulmonary hypertension group (according to the classification), its hemodynamic parameters, and to decide on the appointment of specific therapy. Patients who contact these centers should be further examined. Most often in the population, pulmonary hypertension occurs due to pathology of the left heart and lung pathology. This determines the diagnostic search.All patients should undergo echocardiography according to a special protocol, electrocardiogram (ECG), chest X-ray, complete blood count, biochemical blood test, determination of blood gases, NT-proBNP (natriuretic peptide) level, spirometry (if not previously done in the outpatient clinic), 6-minute walk test; according to indications — cardiorespiratory exercise test, computed tomography, coronary angiography, etc.If the patient is diagnosed with left heart disease or lung disease in the absence of severe right ventricular dysfunction and pronounced pulmonary hypertension, he should be recommended periodic echocardiography monitoring (usually every 6-12 months or if the condition worsens) and treatment of the underlying disease should be started. It should be remembered that the patient may have a mixed etiology of pulmonary hypertension, therefore, if the severity of the underlying disease and right ventricular dysfunction do not correspond, the patient should be referred to the Federal Expert Center. If the patient is suspected of having CTEPH, he needs ventilation-perfusion lung scintigraphy. If such equipment is not available, the possibility of referring him to MSCT angiography (multislice computed tomography), which is available in most regional centers, should be considered. Also, if indicated, such patients are tested for coagulopathy [1]. If systemic connective tissue diseases are suspected, primarily systemic sclerosis, it is necessary to test for antinuclear and anticentromere antibodies, as well as antibodies to Scl-70 (topoisomerase I) [1]. According to the hemodynamic definition, PH can be precapillary, isolated postcapillary, and combined pre- and postcapillary (Table 2) [2]. Its diagnosis requires invasive catheterization of the right heart, which is available in expert or large regional medical centers. In order to assess the possibility of prescribing calcium channel blockers to patients during this procedure, a vasoreactivity test is also performed [2]. After diagnosis of the PH group, all patients need to determine the risk of adverse outcomes within the next 12 months (Table 3). It is recommended to determine the patient's risk at each visit to the doctor. It should be noted that this algorithm was developed based on data obtained in studies of patients with idiopathic PAH and has not been validated for other forms of PH.

Therapy PH

Treatment of patients with pulmonary hypertension (PH) includes not only the prescription of specific therapy, but also a set of additional measures aimed at improving the prognosis and quality of life. An important aspect is the individual selection of the level of physical activity for patients with PH. Physical activity should not cause severe shortness of breath, dizziness, fainting, or chest pain [4]. All patients with pulmonary arterial hypertension (PAH) are recommended to be vaccinated against influenza and pneumococcal infection. During air travel, given the high risk of vasoconstriction due to hypoxia, it is necessary to ensure access to oxygen. Women with PAH are advised to avoid pregnancy due to the high risk of complications [5].Supportive therapy also plays an important role in the treatment of patients with PH. It is aimed at eliminating the symptoms of heart failure and improving the prognosis. With any degree of anemia, hemoglobin levels must be corrected, since patients with PH are extremely sensitive to its decrease. In cases of erythrocytosis with a hematocrit above 65% (in the presence of symptoms such as headaches or impaired concentration) caused by prolonged hypoxia, phlebotomy may be considered. In other situations, this procedure should be avoided [1].Long-term oxygen therapy is indicated when oxygen saturation drops below 90%. It is especially effective in patients with pulmonary hypertension caused by lung diseases. However,

in patients with Eisenmenger syndrome, oxygen therapy does not have a significant effect on hematological parameters, quality of life, and survival [6].In case of decompensation of right ventricular failure, patients are prescribed diuretic therapy in accordance with recommendations for the treatment of chronic heart failure (CHF). It is necessary to regularly monitor renal function and electrolyte levels to timely adjust the dose of diuretics.Angiotensin-converting enzyme inhibitors (ACEI) and beta-blockers, as studies show, are ineffective in patients with PAH and therefore are not used. Moreover, their use even in low doses can lead to hypotension and worsening of right ventricular failure [.Oral anticoagulants (OAC) can be prescribed to some patients with PH. For example, in idiopathic PAH, they significantly improve survival (odds ratio 0.79, 95% confidence interval 0.66–0.94). OAC are also indicated in chronic thromboembolic PH (CTEPH), hereditary PAH, and PAH associated with the use of anorectic drugs. However, in other forms of PH, such as PAH associated with systemic connective tissue diseases, portopulmonary hypertension, or congenital heart defects (CHD), the risk of bleeding may be increased, which requires an individual approach to the prescription of these drugs .Cardiac glycosides can be useful in patients with PAH with reduced myocardial contractility. Intravenous digoxin in such patients results in a modest increase in cardiac output. Also, cardiac glycosides can be used to control heart rate (HR) in patients with atrial fibrillation or flutter. Inotropic drugs such as dopamine can be effective in patients with PH, as well as in left ventricular failure. If antiarrhythmic drugs are necessary, especially in atrial fibrillation or flutter, preference should be given to drugs without a negative inotropic effect, such as amiodarone.

Specific therapy for PH

Selection of specific therapy for patients with pulmonary hypertension (PH) is carried out in expert centers. After discharge, the patient must contact a regional center or a specialized office for patients with PH, where a medical commission will confirm the need to continue specific therapy. The commission's conclusion and relevant medical documents are sent to the regional Ministry of Health, where a decision is made to provide the patient with the necessary drugs. Monitoring the effectiveness and safety of specific therapy is carried out not only by the expert center, but also by regional institutions. Complex issues related to patient management can be resolved using telemedicine technologies, which ensures continuity and quality of medical care.Given the high cost of PH therapy, the emergence of high-quality generics can significantly reduce treatment costs while maintaining comparable effectiveness. One of the confirmations of the good clinical effectiveness of drugs is the data from clinical cases

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