American Journal of Medicine and Medical Sciences 2022, 12(10): 1044-1046
DOI: 10.5923/j.ajmms.20221210.07

Recommendations for Diagnostics and Treatment of Pulmonary Arterial Hypertension

Khajiyev S. O., Fayzullayev B. R., Ruzmetova F. A.

Department of Internal Diseases and Dermatovenerological Diseases, Urgench Branch of Tashkent Medical Academy, Urgench, Uzbekistan

Abstract The article presents the results of a study of the emotional status, attitude to the disease and the quality of life of patients with pulmonary arterial hypertension. It has been shown that the quality of life of patients is significantly reduced, but to the greatest extent - in patients with pulmonary arterial hypertension. At the same time, patients with pulmonary arterial hypertension, despite the existing physical limitations, more successfully than patients with atrial fibrillation, adapt to the situation of the disease, which is due to the peculiarities of the course of the disease and its social consequences.

Keywords Pulmonary hypertension, Cor pulmonale, Endothelin-1

1. Introduction

Pulmonary hypertension (PH) is an increase in mean pressure in the pulmonary artery (PA) of more than 25 mm Hg. Art. at rest or more than 30 mm Hg. Art. with physical stress. PH is also diagnosed if the systolic pressure in the PA, measured by Doppler imaging, exceeds 40 mm Hg. PH can occur in various diseases, as a result of their progression or reflecting the activity of being damaged by pulmonary tissue or vascular disease. [1]

Primary pulmonary hypertension. Idiopathic pulmonary hypertension is characterized by an increase in pressure predominantly in the precapillary vascular bed. Its risk factors have not been identified. Familial cases of PH are described, the frequency of which among all patients with primary PH (PPH) is about 7%. A significant increase in the prevalence of PLH in the 1960-1970s is associated with the use of appetite suppressants (anorectic drugs of central action).

The role of aminorex was established most reliably, since the prohibition of the sale of the drug led to a decrease in the frequency of PLH. A repeated increase in the prevalence of PLH was recorded with the use of anorectic fenfluramine and its derivatives, as well as phentermine. With the use of these anorectics, the risk of PLH increases more than 10 times, and with constant use for 3 months or more - 23 times. An increase in the frequency of PLH occurs in HIV-infected patients, as well as in patients with chronic diffuse liver diseases with portal hypertension. A lethal outcome was described in a pregnant woman with PLH, combined with multiple focal liver hyperplasia and portal hypertension. A survey of families whose members suffered from PLH revealed gene mutations leading to the development of the disease.

Received: Sep. 15, 2022; Accepted: Oct. 7, 2022; Published: Oct. 14, 2022
Published online at http://journal.sapub.org/ajmms

2. Materials and Methods

Endothelial dysfunction plays a leading role in the pathogenesis of PLH. With PLH, the production of thromboxane significantly increases with a simultaneous decrease in the formation of prostacyclin, which is at least partially associated with the inhibition of prostacyclin synthase in the small branches of PA. It was shown that induction of prostacyclin synthase expression prevents the formation of PH in animals. Currently, it is generally accepted that the central link in the pathogenesis of PPH is endothelial dysfunction, characterized by dysregulation of vascular tone (tendency to vasospasm), activation of endothelium-dependent cells, followed by hemostatic Most of the changes in endothelial function during PLH are recorded only in the vessels of the pulmonary circulation. No specific PLH laboratory markers have been found. In many patients, hyperuricemia is revealed, which correlates with the severity of the impairment of the pulmonary vascular bed and indicates a high risk of death.

The formation of impaired contractility of the right ventricle reflects an increased plasma concentration of B-type natriuretic peptide (as in the case of left ventricular heart failure), which also serves as an unfavorable serum level of normal prognostic blood pressure and an endogenous prognostic recognition. All named laboratory parameters in patients with PLH are recommended to be assessed at baseline and during treatment with prostaglandins. For the clinical assessment of patients with PLH, the New York Heart Association (NYHA)

classification and 6-minute walk test, generally accepted for chronic left ventricular heart failure, are used. The prognosis of a patient with PLH is assessed on the basis of the results of clinical, laboratory and instrumental examination. [2,3,4]

The most common and reliable method of screening for PH is transstrocal echocardiography (EchoCG), which determines the systolic pressure in the PA, equivalent to the systolic pressure in the right ventricle. The approximate range of its normal values is 25–35 mm Hg. Art. This indicator grows with increasing age and body mass index. The data of transstracic echocardiography, as a rule, correlate with the parameters determined during diagnostic catheterization of the right parts of the heart. With transstracic echocardiography in some patients, it is possible to establish the cause of the increase in pressure in the small circle of blood circulation (for example, revealing a defect of the mitral and aortic valve, myocardial damage). Thus, transstracic echocardiography is the preferred non-invasive method for the diagnosis of PH and dynamic observation of patients, including assessing the response to treatment. PH in chronic obstructive pulmonary diseases PH of varying severity complicates the course of obstructive pulmonary diseases in more than half of the patients.

The severity of hemodynamic disorders in LA and, as a consequence, the formation of heart failure is determined by nosological features. PH can itself lead to death in patients with chronic obstructive pulmonary disease (COPD), ahead of the onset of respiratory failure. The survival rate of patients with COPD with PH is almost 2 times lower than that of patients with normal pressure in PA (36% versus 62%). At the same time, the magnitude of pressure in the LA has a greater influence on the prognosis than the severity of hypoxemia and hypercapnia. [5,6,7]

The treatment of PH in COPD is not radically different from other PH options. When prescribing inhaled bronchodilators, it is advisable to use selective drugs to reduce cardiotoxic effects. In addition, technologies that increase the respiratory fraction of drugs have the advantage of being more effective due to more accurate dosing and more efficient delivery of drugs to the distal airways.

3. Result and Discussion

PH for interstitial lung diseases. The pathogenesis of PH in ILD remains the subject of intense research. Along with the well-known reduction of the vascular bed, associated with a decrease in the lumen and, subsequently, in the number of vessels due to progressive fibrous transformation of the lung tissue, the mechanisms of PH, similar to the signs of endothelial dysfunction in PLH, have been deciphered. A significant decrease in the expression of the main mediator of vasodilation - endothelial NO-synthase - with a simultaneous increase in the production of endothelin-1 was established.

In addition, the activity of the vascular endothelial growth factor increases, which in itself contributes to the remodeling of the pulmonary vascular bed. [8,9,10] In COPD, the combustion products of tobacco are named as the leading factors of endothelial dysfunction. A significant decrease in the expression of endothelial NO-synthase in smokers has been demonstrated. In idiopathic pulmonary fibrosis, a reliable inhibition of the production of nitrogen oxide is observed in comparison with patients with ILD in the framework of SCTD or patients with exogenous allergic alveolitis. The lowest intensity of NO production was noted at the stage of “honeycomb lung”, when the plasma concentration of NO was significantly lower than in earlier stages of this disease.

The consequence of endothelial dysfunction, aggravating PH in ILD, can be considered the activation of procoagulant systems, the concentration of markers of which (thrombin-antithrombin complex and platelet factor 4) is maximal in active interstitial volume % of lung tissue). PH in IPL is also accompanied by excessive synthesis of histamine, the effects of which are directed not only to the vascular wall, but also induce fibrosis and proliferation in the lungs. PH in SCTD Pulmonary hypertension is observed in various SCTD - systemic scleroderma, systemic lupus erythematosus, a little less often - with dermatomyositis, rheumatoid arthritis and SHEGREN disease. Often, the formation of PH reflects the evolution of lung collapse (progressive interstitial fibrosis and / or alveolitis), which is characteristic of SCTD. The pathogenesis of PH in SCTD is determined by progressive interstitial fibrosis, which is observed in at least 70% of patients. [10,11]

Treatment of PH Treatment of most PH options remains more difficult and less effective than treatment of chronic left ventricular heart failure. The number of effective drugs for PH is relatively small, and controlled studies evaluating their effectiveness and safety are few. Calcium antagonists are considered first-line drugs for the treatment of various types of PH, although their use is based on relatively small clinical trials. We can talk about the benefits of long-term use of these drugs in high doses, the largest amount of data has been accumulated in relation to nifedipine and diltiazem. Treatment is recommended to start with small dosestitration should be very careful, especially if an acute test with vasodilators was not initially performed.

One of the most effective classes of drugs that are used to treat PH are currently considered to be synthetic analogs of prostacyclin (prostaglandin drugs). Basically, in clinical trials of these drugs, patients with PH or PH caused by SCTD took part. The use of epoprostenol significantly improves exercise tolerance and, in some studies, the survival rate of PH patients. In most forms of PH, a significant increase in patient survival has been shown when taking warfarin. Monitoring the effectiveness of therapy when using the drug should be carried out taking into account the international normalized relationship, maintaining it at the level of 2-3. With PH, therapeutic effects on the microvasculature of the lungs are especially relevant.

Drugs that reduce platelet aggregation and cause vasodilation (acetylsalicylic acid, pentoxifylline, dihydroergocriptine, etc.) prevent the formation of

microthrombi, and, consequently, remodeling of pulmonary vascular remodeling in pulmonary vascular remodeling. These drugs are widely used in angioneurology. [10,12] Indications for oxygen therapy in PH are determined primarily by the severity of hypoxemia, which is caused by chronic lung disease and is accompanied by an increase in pressure in the pulmonary circulation. In PH, which develops in the absence of chronic lung disease, oxygen therapy does not seem to allow an increase in exercise tolerance and life expectancy of patients (demonstrated for Eisenmenger syndrome).

4. Conclusions

In this way, PH treatment continues to present many challenges. The combined use of drugs, taking into account their organoprotective properties in conditions of progressive heart failure, will prevent complications and thereby improve the long-term prognosis of patients. In recent years, based on a number of experimental and clinical studies, phosphodiesterase type 5 (IFDE-5) inhibitors are considered as the most important approach to the pathogenetic therapy of PAH. IFDE-5 improve pulmonary hemodynamic parameters, reduce the severity of pulmonary vascular remodeling, improve the functionality of PAH patients for the treatment of PAH patients with functional class II – IV – FC.

REFERENCES

[1] Lip GYH, Banerjee A, Boriani G, Chiang CE, Fargo R, Freedman B, Lane DA, Ruff CT, Turakhia M, Werring D, Patel S, Moores L. Antithrombotic Therapy for Atrial Fibrillation: CHEST Guideline and Expert Panel Report. // Chest. 2018 Nov; 154(5): 1121-1201.

[2] McLaughlin VV, Gaine SP, Howard LS, Leuchte HH, Mathier MA, Mehta S, Palazzini M, Park MH, Tapson VF, Sitbon O. Treatment goals of pulmonary hypertension. //J Am Coll Cardiol. 2013 Dec 24; 62(25 Suppl): D73-81.

[3] Medi C, Kalman JM, Ling LH, Teh AW, Lee G, Lee G, Spence SJ, Kaye DM, Kistler PM. Atrial electrical and structural remodeling associated with longstanding pulmonary hypertension and right ventricular hypertrophy in humans. // J Cardiovasc Electrophysiol. 2012 Jun; 23(6): 614-20.

[4] Mujović N, Dobrev D, Marinković M, Russo V, Potpara TS. The role of amiodarone in contemporary management of complex cardiac arrhythmias. // Pharmacol Res. 2020 Jan; 151: 104521.

[5] Olsson KM, Nickel NP, Tongers J, Hoeper MM. Atrial flutter and fibrillation in patients with pulmonary hypertension. // Int J Cardiol. 2013 Sep 1; 167(5): 2300-5.

[6] Peña J. M., Macfadyen J., Glynn R.J., Ridker P.M. High-sensitivity C-reactive protein, statin therapy, and risks of atrial fibrillation: an exploratory analysis of the JUPITER trial. // Eur Heart J 2012; 33: 531- 7.

[7] Reddy SA, Nethercott SL, Khialani BV, Grace AA, Martin CA. Management of arrhythmias in pulmonary hypertension. // J Interv Card Electrophysiol. 2021 Apr 5.

[8] Rottlaender D, Motloch LJ, Schmidt D, Reda S, Larbig R, Wolny M, Dumitrescu D, Rosenkranz S, Erdmann E, Hoppe UC. Clinical impact of atrial fibrillation in patients with pulmonary hypertension. // PLoS One. 2012; 7(3): e33902.

[9] Rottlaender D, Motloch LJ, Schmidt D, Reda S, Larbig R, Wolny M, Dumitrescu D, Rosenkranz S, Erdmann E, Hoppe UC. Clinical impact of atrial fibrillation in patients with pulmonary hypertension. // PLoS One. 2012; 7(3): e33902.

[10] Wen L, Sun ML, An P, Jiang X, Sun K, Zheng L, Liu QQ, Wang L, Zhao QH, He J, Jing ZC. Frequency of supraventricular arrhythmias in patients with idiopathic pulmonary arterial hypertension. // Am J Cardiol. 2014 Nov 1; 114(9): 1420-5.

[11] Yo CH, Lee SH, Chang SS et al. Value of high-sensitivity C-reactive protein assays in predicting atrial fibrillation recurrence: a systematic review and meta-analysis.// BMJ 2014; 20: 4.

[12] Zhang YQ, Zhang FL, Wang WW, Chen XH, Chen JH, Chen LL. The correlation of pulmonary arterial hypertension with late recurrence of paroxysmal atrial fibrillation after catheter ablation. // J Thorac Dis. 2018 May; 10(5): 2789-2794.