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IMMUNOBIOCHEMICAL MARKERS OF THE DEVELOPMENT OF PULMONARY HYPERTENSION IN PATIENTS WITH CHRONIC DISEASES OF THE BRONCHOPULMONARY SYSTEM

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ABSTRACT

In light of the high prevalence of chronic nonspecific lung diseases and their significant impact on disability rates, one of the key healthcare challenges is the prevention, accurate diagnosis, and effective treatment of patients with such respiratory diseases. It is unequivocally important to pay attention to cross-disciplinary research and continue studying this issue, as it represents a serious medical and social problem that significantly limits the quality of life of patients. Exploring new mechanisms offers a promising path for developing innovative approaches to diagnosing and treating the combination of bronchial asthma and chronic obstructive pulmonary disease. It is important to note that only systematic clinical and functional monitoring of patients allows for an accurate diagnosis of chronic diseases. In our country, as well as worldwide, there is a growing trend of comorbid diseases of the bronchopulmonary and cardiovascular systems. The combination of bronchial asthma and COPD increases the risk of complications in the vascular bed of the small circulation, which, in turn, places this issue among the most urgent.

Key words: BA, COPD, ACO, EN1, NT-proBNP, CRP, fibrinogen.

INTRODUCTION

In light of the high prevalence of chronic nonspecific lung diseases and their significant impact on disability, one of the key healthcare challenges is the prevention, accurate diagnosis and effective treatment of patients with such respiratory diseases. It is definitely important to pay attention to cross-disciplinary research and continue to study this issue, since it represents a serious medical and social problem that significantly limits the quality of life of patients [1,5,15]. The

study of new mechanisms represents a promising path for development in the field of innovative approaches to the diagnosis and treatment of the combination of bronchial asthma and chronic obstructive pulmonary disease. It is important to note that only systematic clinical and functional monitoring of patients allows an accurate diagnosis of chronic diseases to be established.

In our country, as well as throughout the world, the trend of comorbid diseases of the bronchopulmonary and cardiovascular systems is growing. [2,8,14]. The combination of bronchial asthma and COPD increases the risk of complications in the vascular bed of the pulmonary circulation, which in turn makes this problem one of the most pressing. [3,7,12].

A fundamentally important question in modern practical medicine is the connection between the formation of a layer of chronic diseases, such as BA/COPD and hypertension/CHD, with processes occurring in the cardiorespiratory system or with shifts in the immune system. According to many authors, the cause of the overlap or overlap of bronchial asthma and chronic obstructive pulmonary disease and the development of vascular complications are various immune disorders that cause a decrease in the body's resistance to microbial infection [4,6,11].

Purpose of the study: to study the role of brain natriuretric peptide and endothelin 1 in the development of PH in patients with bronchial asthma, COPD and the crossover of BA and COPD.

Materials and research methods: To complete the work in the period from 2021-2023. 187 patients were examined with chronic diseases of the lower respiratory tract. Clinical material was collected at the Bukhara Regional Multidisciplinary Medical Center and in the Bukhara branch of the Republican Scientific and Practical Center for Emergency Medical Care. Of 187 patients, 95 patients with pulmonary hypertension (PH) were selected to study immunobiochemical markers. The first group included 17 patients with BA, the second - 35 patients with COPD, and the third - 43 patients with PBA. The concentrations of CRP, fibrinogen, NT-proBNP and EN1 were determined in blood serum by ELISA according to the attached instructions. We used the "ELISA" test kit (Germany).

Statistical data processing and creation of graphic images were carried out using MS Excel 16 software. Data reliability was assessed using the reliability criterion (t).

Results of the study and discussion:

The average age of patients with bronchial asthma was 43.3 ± 1.49, patients with COPD - 44.6 ± 1.54, patients with PBA - 42.9 ± 1.38. Age at the time of

examination did not reveal any significant differences in patients with a combination of asthma and COPD. (Fig. 1.)

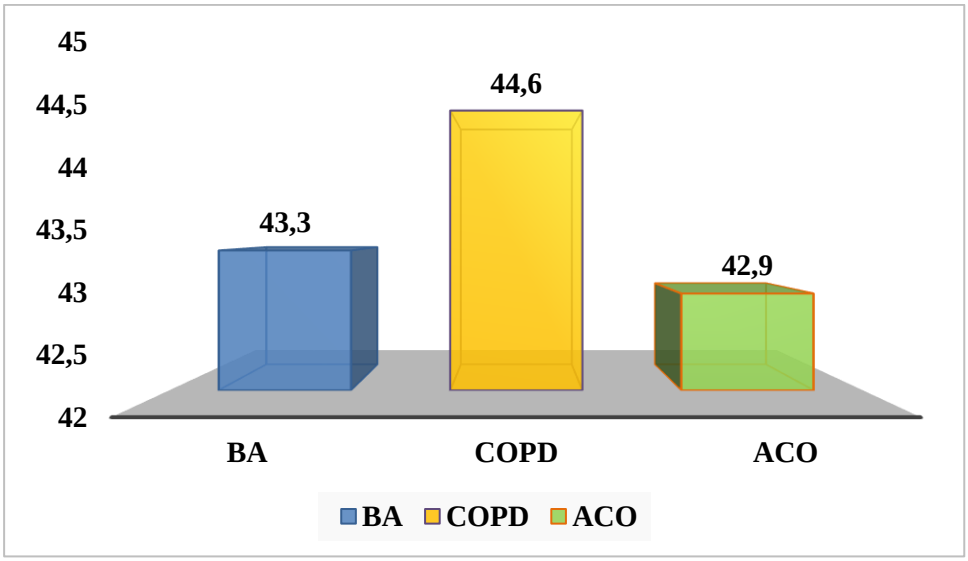

Figure 1. Distribution of groups by age (%), P≤0.05

Analysis of gender revealed that women prevailed in all groups, especially in the group with bronchial asthma.

The earliest onset of the disease was observed in bronchial asthma at a young age (21.3 ± 1.14).

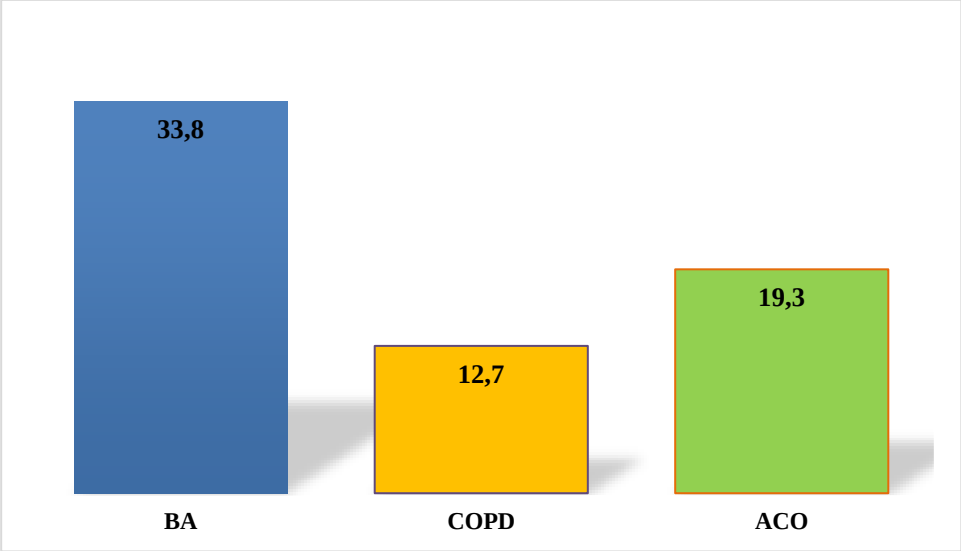

Fig.2. Distribution of groups by disease duration, P≤0.05

Isolated COPD was characterized by a shorter duration (12.7 ± 2.74) of the disease compared to PBA (19.3 ± 2.31) and bronchial asthma (33.8 ± 3.11) (Fig. 2).

40.8% of patients with PBA had a burdened allergic history and all patients with isolated BA, while in patients with COPD there were no signs of severe atopy.

The main complaint of patients with the pathology under study was cough of various types in 100% (187).

Shortness of breath was detected on average in 71.1% (n=133), but was observed to a greater extent in the PBAH group; signs of intoxication (pallor, cyanosis of the nasolabial triangle, weakness, sweating, decreased appetite were observed) were observed to a greater extent in the PBAH group as well as chest pain. (Fig.3)

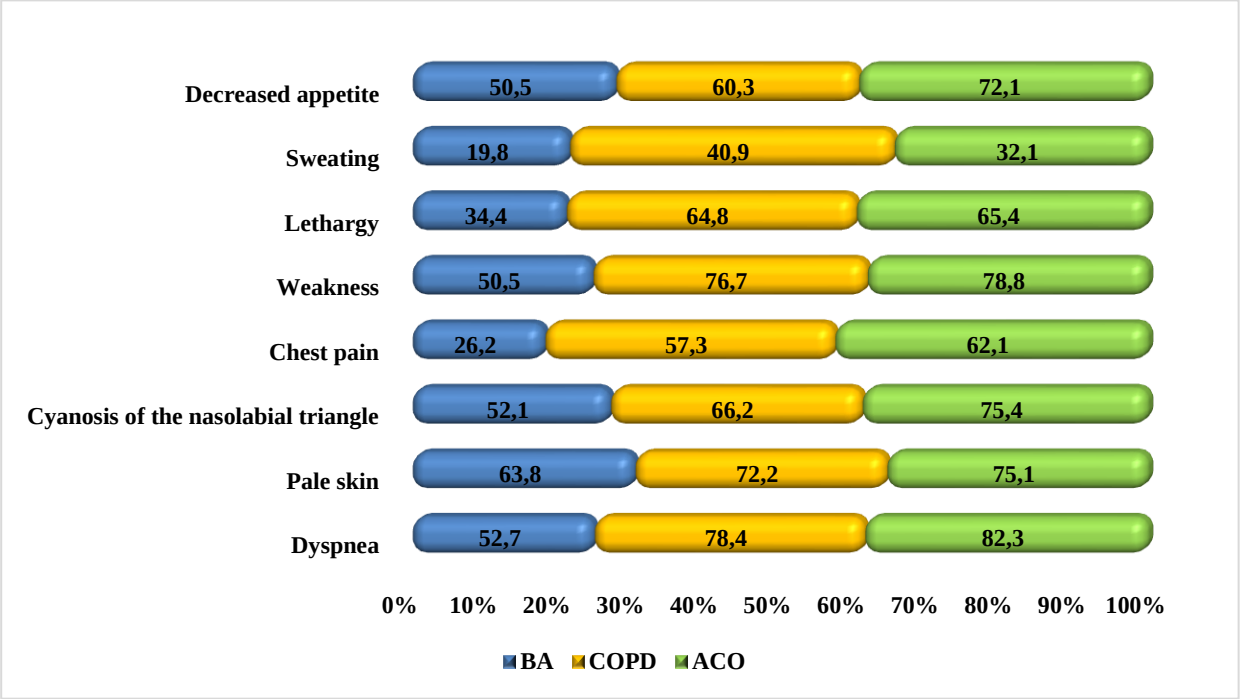

Fig.3. Main complaints of patients (%), P≤0.05

Analysis of somatic diseases revealed that in patients with COPD and PAH, hypertension was more common (90.2% and 82.1%, respectively). A history of coronary heart disease in the group of patients with COPD was 65.6%, which was significantly higher than in the group of bronchial asthma (32.2%). Diseases of the gastrointestinal tract (GERD, chronic gastritis, gastric ulcer and diseases of the hepatobiliary system) were detected in 50.7% of patients with PBA, which is significantly more often than in the group with isolated COPD (34.4%) and BA (20. 3%). The incidence of ENT diseases (allergic rhinitis, chronic tonsillitis and sinusitis) was higher in the isolated BA group (61.0%), possibly due to the presence of an allergic component in this group. Endocrine diseases and anemia were detected more in the group with COPD. (Fig. 4.)

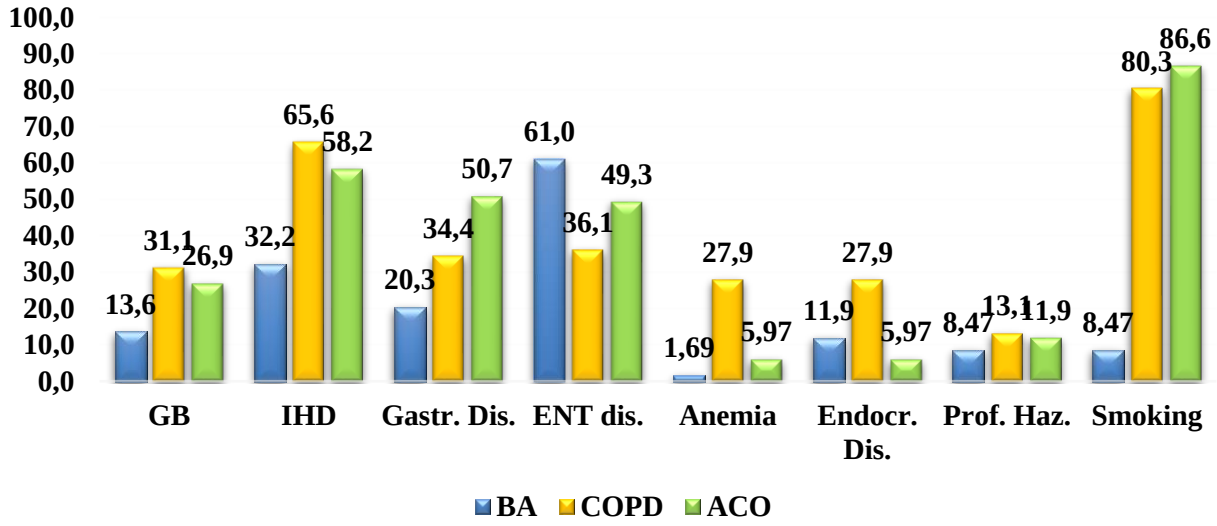

Fig.4. Concomitant pathology in patients with asthma, COPD and PBA, (%)

Tobacco smoking is also one of the main risk factors for the development of PBA. Most of the patients we examined, especially in the group with PBA (86.6%) and COPD (80.3%), had a long history of smoking. Among patients with asthma, only three patients had a smoking history of less than 1 pack/year.

Pulmonary hypertension (PH) is a pathological condition characterized by increased pressure in the pulmonary arteries, which can develop in various diseases, including bronchial asthma (BA), chronic obstructive pulmonary disease (COPD) and cross-sectional asthma and COPD (BACO). Inflammatory markers and biomarkers, such as C-reactive protein (CRP), fibrinogen, NT-proBNP and endothelin-1 (EN1), play an important role in the development and progression of PH. In this subchapter, we examined the significance of these markers in PH in patients with asthma, COPD and PBA.

C-reactive protein (CRP) is a marker of systemic inflammation and plays an important role in the pathogenesis of bronchopulmonary diseases [5,9,13]. Our study found that CRP levels were elevated in all three groups. In particular, the average values of CRP were: control - 4.25±0.11 mg/l, asthma - 11.9±0.64 mg/l, COPD - 7.76±0.44 mg/l, PBA - 9 .82±0.46 mg/l, which is 2.8 times higher in the group with BA, 1.8 times higher in the group with COPD and 2.3 times higher in the group with PBA compared with the control group (P<0 .05).

Fibrinogen is an important plasma protein that plays a key role in the blood clotting process and is a marker of inflammation. Increased fibrinogen levels are associated with an increased risk of cardiovascular disease[6,12]. Its increase is also associated with the risk of developing PH. In our study, the fibrinogen level values were as follows: control - 1.93±0.06 g/l, asthma - 2.43±0.14 g/l, COPD - 3.97±0.09 g/l, PBA - 3.25±0.08 g/l. (Fig. 5.)

The greatest increase in fibrinogen levels is observed in patients with COPD, indicating a more pronounced inflammatory process and hypercoagulability in this group. In patients with PBA, fibrinogen levels are also significantly elevated, confirming the severity of the overlap between these diseases.

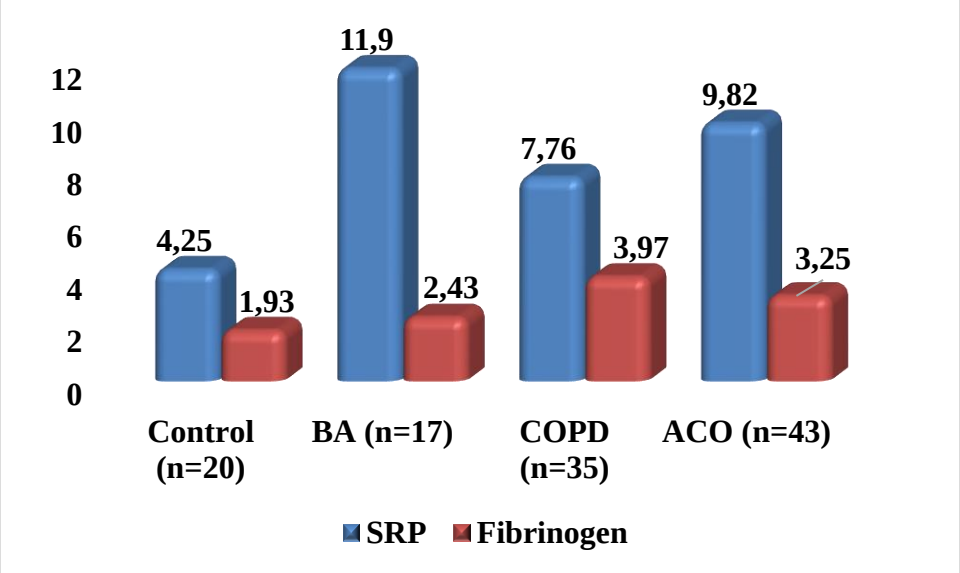

Fig.5. Levels of CRP and fibrinogen in those examined (mg/l, g/l)

N-terminal fragment of brain natriuretic peptide (NT-proBNP) is an important biomarker used for the diagnosis and monitoring of heart failure and pulmonary hypertension (PH). NT-proBNP is released by ventricular cardiomyocytes in response to stretch and stress on the heart wall, which may be caused by volume overload or increased pressure. The main actions of NT-proBNP include increasing the excretion of sodium and water by the kidneys, dilating blood vessels, and preventing thickening of the heart walls. These effects are aimed at reducing circulating blood volume and pressure, which makes the heart work easier and reduces pressure in the pulmonary arteries. [1,7, 11]. In this connection, the next stage of our study was to study the level of NT-proBNP. NT-proBNP parameters in the control group - 113.6±6.13 pg/ml, in the group with BA - 526.3±6.68 pg/ml, in the group with COPD - 1206.8±9.43 pg/ml , PBAC - 1103.7±8.39 pg/ml, which is 4.6 times, 10.6 times and 9.7 times higher, respectively ($P<0.05$) compared to the control group (Fig. 6).

A study of NT-proBNP levels in patients with pulmonary hypertension associated with asthma, chronic obstructive pulmonary disease, and their combination demonstrates a significant increase in this biomarker, indicating high right ventricular workload. The most pronounced increase in NT-proBNP levels is observed in patients with COPD, then in those with combined PBA, and the least in patients with bronchial asthma. This highlights the importance of using NT-

proBNP to diagnose and monitor pulmonary hypertension in these patients and to assess the severity of the condition and prognosis.

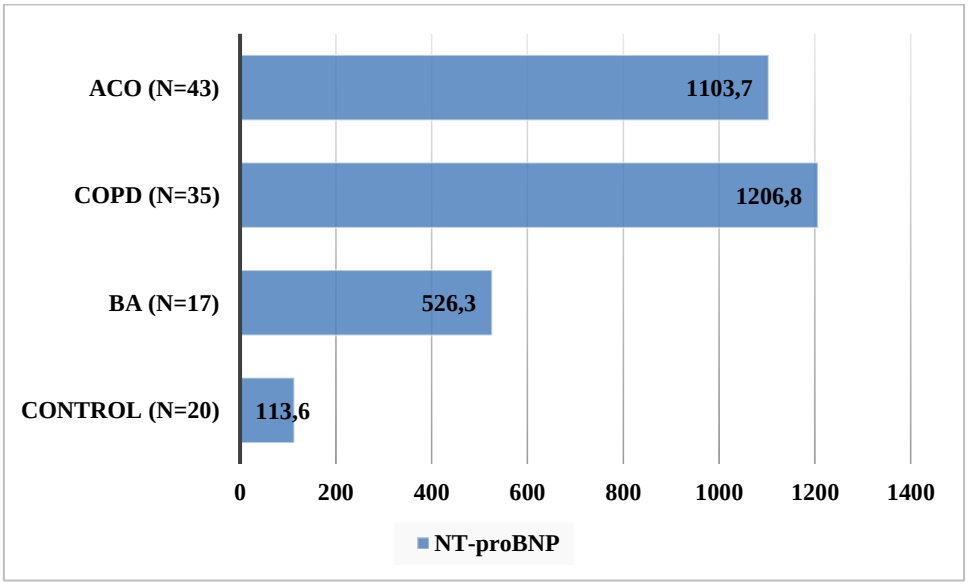

Fig.6. NT-proBNP level in those examined (pg/ml)

Endothelin-1 (EN1) is a vasoconstrictor peptide that plays an important role in the pathogenesis of PH. It is synthesized by vascular endothelial cells and has various biological effects, including vasoconstriction, smooth muscle cell proliferation, and inflammation [3,8,14].

A comparative analysis of EN1 levels among patients from three groups showed the following results: the average values of EN1 levels in patients with BA were 1.41±0.07 pg/ml, which indicates a moderate increase compared to the control group (0.83±0.06 pg/ml); 3.81±0.09 pg/ml was in the group of patients with COPD and 3.07±0.08 pg/ml in the group with PBA, which is significantly higher compared to the control group (Fig. 7) and indicates a more pronounced vascular remodeling and inflammation.

The increased level of EN1 in the studied groups is associated with the presence of hypoxia, vasoconstriction phenomena, i.e. narrowing of the pulmonary arteries and vascular remodeling. Chronic targeting leads to proliferation and hypertrophy of vascular smooth muscle cells, which contributes to thickening of arterial walls and increased resistance to blood flow. Developing inflammation stimulates the production of cytokines, which aggravates vascular damage and leads to the development of PH.

These data highlight the importance of EN1 as a marker of PH and its significance in assessing disease severity and prognosis in patients with asthma, COPD and PAD. They also highlight the need to develop targeted therapies aimed at reducing EN1 production and attenuating its effects to improve the condition of patients with PH.

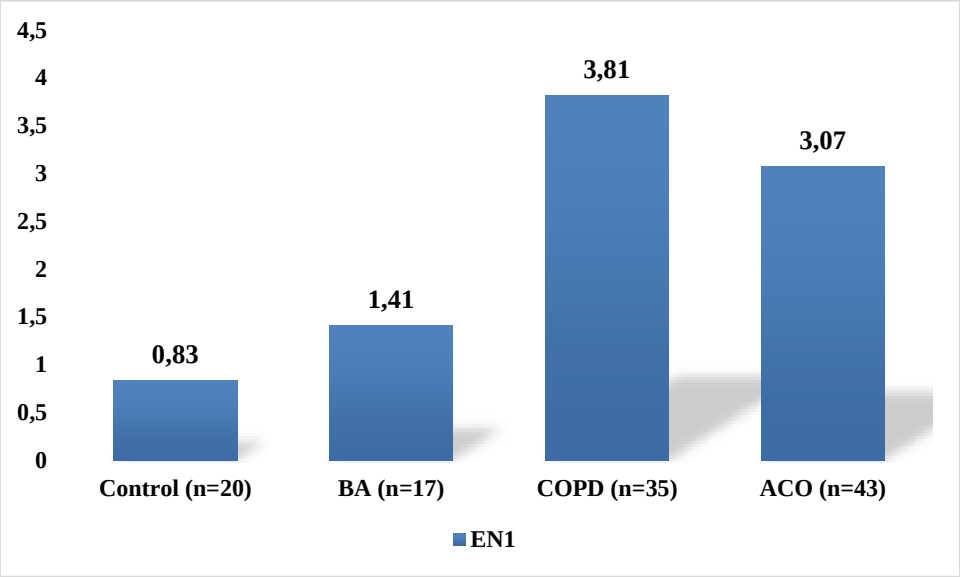

Fig.7. Endothelin-1 level among those examined (pg/ml)

Thus, the results showed that patients with asthma, COPD and PAH with PH exhibited significant changes in the levels of CRP, fibrinogen, NT-proBNP and EN1 compared to the control group. An increase in these biochemical markers indicates the presence of chronic inflammation, which leads to vascular remodeling and increased vascular resistance, and also indicates a load on the right side of the heart and the development of chronic cor pulmonale (CHP). Together, these markers can be used to prevent the progression of pulmonary hypertension, the development of chronic pulmonary heart disease and other associated complications.

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