

The importance of early detection of complications in Bronchial asthma

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Abstract: Bronchial asthma, commonly referred to as asthma, is a chronic inflammatory disease of the airways characterized by episodes of wheezing, shortness of breath, chest tightness, and coughing. These symptoms occur due to a combination of airway inflammation, bronchospasm, and mucus production. Asthma can affect individuals of all ages, and its severity can range from mild to life-threatening.

Keywords: bronchial asthma, chronic heart failure, treatment, pro-BNP, endothelium

Background. Studies by the European Society of Cardiology show that among hospitalised and outpatients, all-cause mortality rates are 17% and 7%, respectively, and hospital admissions are 44% and 32%, respectively [3,4]. Most deaths in patients with CHF (both hospitalised and outpatients) are related to cardiovascular causes, which are associated with sudden cardiac death (primary cardiac arrest) and worsening of the course of CHF. Different levels of CHF have been identified in hospitalised patients with complications of bronchial asthma and have caused difficulties in treatment. Therefore, the development of therapeutic strategies for the treatment of pathology complicated by bronchial asthma with CHF is particularly relevant [1,2,5].

The number of patients with bronchial asthma has increased significantly in recent years. In all countries, BA is a major cause of disability and death, resulting in economic and social losses that increase every year. Bronchial asthma mortality is the fourth highest in the world in the age group over 45 years. By 2030, bronchial asthma is expected to become the third leading cause of death. The main category of patients is people of working age (40 to 67 years) [6,7].

The data on diagnosis, modern methods of treatment, as well as the author's approach to the scientific solution of this problem are analysed. The above cases

show the relevance of the problem of internal diseases and encourage the study of issues of practical importance [8,9].

Materials and Methods. Based on the aim of the study, the anamnesis and age history of the patients were studied in three comparative groups. The first initial group consisted of 110 patients with CHF and bronchial asthma stage II-III according to the results of the study: 34 women (30.9%) and 76 men (69.09%). In the second control group 50 patients with CHF were examined, including 21 women (42%), 29 men (58%) and 30 healthy people in the third control group, including 15 men (50%) and 15 women (50%).

This study is based on the results of examination of 110 patients of the main group with CHF and bronchial asthma stage II-III: 34 women (30.9%), 76 men (69.09%). In the second control group 50 patients with CHF were examined, including 21 women (42%), 29 men (58%), 30 healthy people in the third control group, including 15 men (50%) and 15 people. 50%).

From 2019 to 2021, patients who came to the therapeutic room of the admission department were examined in the first therapeutic department.

Based on the aim of the study, anamnesis and age history of the patients were studied in two comparative groups.

The first (main) group consisted of 60 patients under 50 years of age (20 females, 33.33%; 40 males, 66.66%). There were 50 patients over 50 years of age (14 women 28%; 36 men 72%).

The second (control) group consisted of 30 patients under 50 years of age (12 females 40%; 18 males 60%). There were 20 patients over 50 years of age (9 women 45%; 11 men 55%).

The first group of patients under 50 years of age was 21-50 years old, with a mean age of 36.8 ± 0.7 years; the age of patients over 50 years old was 51-76 years old, with a mean age of 61.0 ± 0.6 years. compact.

The second group of patients younger than 50 years old was 20-50 years old, mean age 35.6 ± 0.6 years, patients older than 50 years old was 51-70 years old, mean age 56.0 ± 0.7 years. years. compact.

Table 1

Clinical features of patients of the main group

Indicators		Average age	Minimum age	Maximum age
Age		48.9	21	76
		Number of patients	% of the total number of patients in the group	
Floor	Men	76	69.09%	
	Women	34	30.9%	
Body mass index kg/m2		27.8 (25.2; 29.7)		
CHF	NYHA I FC	20	18.18%	
	NYHA II FC	38	34.54%	
	NYHA III FC	52	47.27%	

Average number of hospitalizations per year		3	
BRONCHIAL ASTHMA	I degree	23	20.9%
	II degree	53	48.18%
	III degree	34	30.9%
Smoking duration		32 [28; 36]	
Emphysema		41	37.27%
Pulmonary hypertension (EchoCG)	I degree	38	34.54
	II degree	9	8.18
	III degree	3	2.72

The table shows the distribution of patients in the main group by sex, age, body mass index, level of CVD and bronchial asthma by functional classes. The main group included 110 patients with FCH and OCD, with a mean age of 48 years, and the majority of patients in the group were 76 (69.09%) males and 34 (30.09%) females. The incidence of CHF FC in the study patients was CHF I FC 20 (18.18%), NYHA II FC 38 (34.54%) and NYHA III FC 52 (47.27) respectively. The mean duration of smoking was 32 years. Of the main group of patients, 23 had degree I, 53 had degree II, and 34 had degree III. Forty-one patients had emphysema. Echocardiography revealed degree I pulmonary hypertension in 38 patients, degree II in 9 patients and degree III in 3 patients.

Results. The first main group examined 110 patients with bronchial asthma complicated by chronic heart failure. The first control group consisted of 50 patients with CHF and the second control group consisted of 30 healthy subjects. The use of static methods to assess differences necessitated the creation of groups according to sex, age, duration and severity of the disease.

At the initial stage of the study, a cross-sectional analysis of all patient groups was performed to determine the characteristics of CHF in treated patients with bronchial asthma complicated by chronic heart failure.

The main correlations were characteristic for CHF: proBNP ($r = -0.73$), CHF Clinical Status Assessment Scale (CSAS) ($r = 0.71$), 6-minute walk test, LV EF and LVEF, and EQ-5D-5L questionnaire - there was a correlation.

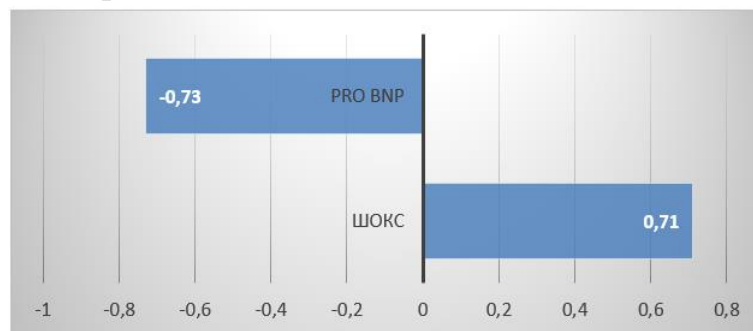


Figure 1. Pro-BNP relationships.

Interestingly, the correlation between the BODE proBNP index and the EQ-5D-5L health assessment questionnaire, which characterises the ICU, is of great interest, and it is important to determine proBNP in the ICU. We present the results of

correlation analysis of left ventricular post-systolic and post-diastolic parameters with functional tests, reflecting the interdependence of parameters characterising the functional class of CHF. LV EF ($r = 0.93$) showed moderate and strong direct correlation between the main tests.

Patients admitted to the hospital presented complaints inherent to both CHS and bronchial asthma: palpitations on physical and psychoemotional stress, unpleasant sensations behind the sternum, dyspnoea, constant intake of short-acting b2-agonists, peripheral edema, general weakness, rapid breathing. Taking into account the necessity of differential diagnostics of dyspnoea symptoms in bronchial asthma and CHF, NT-proBNP level in blood was determined in all patients.

NT-proBNP level was determined to determine the functional class of CHF. These results are described in Table 2.

Table 2

NT-proBNP levels in the CHF group

1 group		
(n=110)	EF>40% (n=76)	EF<40% (n=34)
2755 [1260; 3781]	1068 [1025-2062]	1793 [1010-2358]
P<0.01		
2nd group		
(n=50)	EF>40% (n=28)	EF<40% (n=22)
2593 [978; 3714]	1028 [979-1699]	1401 [1065-1789]
P<0.01		

Significant increases in the levels of fibrinogen and proinflammatory cytokines were observed in both groups during the analysis for signs of inflammation. Moreover, these changes were more pronounced in group 1, indicating a more pronounced systemic inflammatory response in bronchial asthma patients. All inflammatory symptoms were slightly higher in the 2nd main subgroup, but significant differences were noted only for fibrinogen and IL-6. Elevated levels of pro-inflammatory cytokines were also found, but significant differences were noted in both groups only for IL - 8, indicating a lack of anti-inflammatory potential (Table 3).

Cytokine activity was significantly increased in patients with bronchial asthma complicated by CHF and a comparable group with CHF, in contrast to the group with healthy subjects. Significant decrease of IL-6 and 8 levels in patients in the main group was noted against the background of treatment with inhaled corticosteroids, which at the end of treatment did not differ from that in the group of healthy people. Thus, it is possible to fix the balance of the system of proinflammatory cytokines.

Table 3

Immunological analysis results

Control groups	Fibrinogen	SRB	IL - 6	IL - 8
1 - group (110)	5.48±1.4	53.3±17.41	135.0±20.81	225.0±20.8

2 - group (50)	4.35±1.5	38.3±10.81	59.1±11.41	63.2±10.5
3 - group (30)	2.57±0.3	2.8±0.5	2.4±0.5	28.4±8.4
Norma	2-4 mg/l	0-5 mg/l	7 pg/ml	0-62 pg/ml

The average NT-proBNP level at the time of inclusion in the study in group 1 was 2755 [1260; 3781], 2 groups - 2593 [978; 3714]. These values show no significant difference in NT-proBNP levels between the two groups ($p > 0.05$). Patients with LVEF less than 40% had significantly higher NT-proBNP levels in the intragroup analysis, which was associated with severity of CHF ($p < 0.05$).

Table 4

Results of the 6-minute walk test and SHOKS

Indicators	(n=110)	(n=50)	(n=30)	R
6 minute walk (meter)	226.0[232.0; 374.0]	254.0[225.0; 410.0]	600 [500; 600]	<0.001
SHOKS	10 [6; 10]	9 [5; 9]	0	<0.001

The above data show that patients of both main groups had approximately the same exercise tolerance at the initial stage. The results of these functional tests show that the symptoms of CHF were predominant in both groups. No significant statistical differences were found between groups ($p < 0.05$), although the mean distance was greater in correlation with the 6-minute walk test in group 2. Thus, the assessment of the functional class of CHF was based on laboratory parameters, data obtained from the patient’s history, and functional tests that complemented each other and showed similar results. This is a test with six-minute walking and on the SHOCS scale - assessment of the clinical condition of a patient with CHF.

At the stages of the study, echoCG was used to assess cardiac activity of all patients and to determine central haemodynamics. Comparative analysis of haemodynamics in the studied groups showed reliable changes in both groups. Dilatation of the left atrium and left ventricle, increase in the posterior wall of the left ventricle, increase in the thickness of the interventricular septum were observed. However, high left ventricular and pulmonary artery pressures were in both groups of CHF. These changes were associated with the severity of the condition of the patients with CHF and bronchial asthma. The echocardiographic findings complement previous laboratory and functional examination methods and represent the distribution of patients with chronic heart failure by functional class, as well as the severity associated with the presence of pulmonary hypertension. Table 5 presents the main echocardiographic parameters of patients in this group.

Table 5

Comparative analysis of hemodynamics

Indicators	1 - group (110)	2 - group (50)	p
LV EDV cm	5.7 [5.4-5.9]	5.4 [5.0-5.9]	>0.05
LV ESV cm	4.3 [3.6-5.25]	4.0 [3.7-4.3]	> 0.05
LVEF %	45.25 [38.5-52.0]	48 [42.0-54.0]	> 0.05
TZS LV diast, cm	1.1 [1.0-1.2]	1.2 [1.1-1.3]	>0.05
LV TMJ, cm	1.1 [1.0-1.2]	1.2 [1.1-1.3]	> 0.05

LP	4.5 [4.0-5.0]	4.5 [3.8-5.2]	> 0.05
pancreas	3.1 [2.9-3.3]	3.0 [2.9-3.1]	> 0.05
PP	4.4 [4.1-4.7]	4.3 [4.0-4.6]	> 0.05
Aircraft pressure	40.9 [39.6-46.1]	32.0 [26.0-44.0]	<0.05

Table 5 shows that both group 1 and group 2 patients had high CSR and CRP. These results suggest that, bronchial asthma being complicated by chronic heart failure, these two diseases may aggravate each other's condition. All patients underwent spirometry to assess the functional status of the respiratory system.

The following results were obtained when evaluating the results of spirometry in the studied groups of patients with bronchial asthma. In the first group, restrictive disorder was not statistically significant ($p > 0.05$). The value of OFV1 indicates impaired bronchial patency. Pharmacological test with fenoterol at a dose of 400 mg in both groups showed a negative result in the bulk of patients in the first group, indicating irreversible airway obstruction.

Thus, in patients with bronchial asthma there is a progressive decrease in all indicators of bronchial permeability. Disturbance of bronchial permeability leads to increased respiratory insufficiency, which, in turn, causes complications from the cardiovascular system and quickly leads patients to decompensation.

From these results it can be seen that in the study of external respiratory function in patients with CHF in the first and second groups, significant differences were found. The level of obstruction is much higher in the first group of patients, which is confirmed by the fact that patients in this group already have bronchial asthma. In addition, patients in both groups gave negative results on bronchodilator test.

All patients in group 1 and group 2 had their pro-BNP levels determined. Were found in groups 1 and 2, high levels of this enzyme and were not statistically different. The level of pro-BNO in the main group with bronchial asthma and CHF and in the second group with CHF it was high, indicating the presence of heart failure in both groups. Some additions to the standards of diagnostics and treatment are required to solve the problem of CHF with bronchial asthma phenotype.

Patients were assessed for NT-proBNP, 6-minute walk test, SCS questionnaire, echocardiography and spirometry, EQ-5D-5l and SGRQ, and BODE score.

Determination of proBNP levels after 6 months of therapy showed the following results.

Table 6

ProBNP levels after 6 months of therapy

1 - group (110)			
Indicators	(n=110)	FV>40%(n=76)	FV<40%(n=34)
At the initial stage of inspections	2755 [1260; 3781]	1068 [1025-2062]	1793 [1010-2358]
In 6 months	1564 [1200-3863]	1035 [1020-3050]	1079 [1018-1140]
p	$_{1-2}>0.05$	$_{1-2}>0.05$	$_{1-2}>0.05$
2 - group (50)			

Indicators	(n=50)	FV>40%(n=28)	FV<40%(n=22)
At the initial stage of inspections	2593 [978; 3714]	1028 [979-1699]	1401 [1065-1789]
In 6 months	1239 [978; 1500]	1037 [902-1712]	1045 [1015-2083]
P	3-4<0.05	3-4<0.05	3-4<0.05
	2-4<0.05	2-4<0.05	2-4<0.05

When analyzing the results obtained, no significant differences in the dynamics of NT-proBNP levels were identified in the main and first control groups. There was an increase in the NT-proBNP parameter when assessing the main group in patients with CHF>40% and CHF<40%, but there was no statistical difference. This result does not show significant positive clinical results in a stable CHF clinic. After 6 months in the first control group i.e. in patients only with CHF, significant positive dynamics are observed. The significance of the differences was also important when assessing this indicator in the group with CHF > 40% (p < 0.05), but the average NT-proBNP values were approximately the same. There was a more pronounced decrease in the NT-proBNP value by 40% in the group with CHF <40%. Therapy with the addition of ARNI in groups of patients with CHF and with BA and CHF had a greater effect on patients with a less favorable prognosis.

Distribution of groups into subgroups with CHF >40% and CHF <40%. The dynamics of the condition of such patients are completely different, and clinical assessment should be carried out with more accurate data. The data presented showed that the mean NT-proBNP levels in groups 1 and 2 were 2755 pg/ml and 2593 pg/ml, respectively. In patients with CHF <40%, divided into the second group according to CHF criteria, this figure was 1239 pg/ml after 1564 months of therapy, which radically changed the approach to this category of patients. The dynamics of NT-proBNP levels helps the doctor in choosing treatment tactics and especially in assessing its effectiveness. Details are shown in Figures 2 and 3.

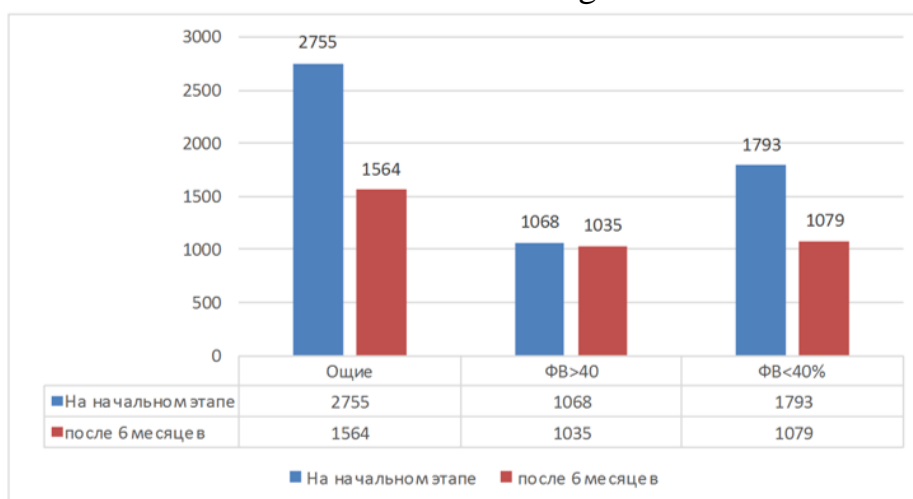


Figure 2. Dynamics of proBNP level of group 1 pg/ml

In the histogram in Figure 3, the graph shows a significant decrease in brain natriuretic peptide levels in patients treated with ARNI and an if-receptor blocker in

combination in patients with ejection fraction <40%. At the time of the study, the average proBNP value was 2593 [1028-1401], and within 6 months the decrease in this parameter was almost 40% and reached 1293 [1037-1045]. The results obtained are undeniable and demonstrate the effectiveness of therapy with ARNI and if-receptor inhibitors in patients with high functional classes of CHF and low EF.

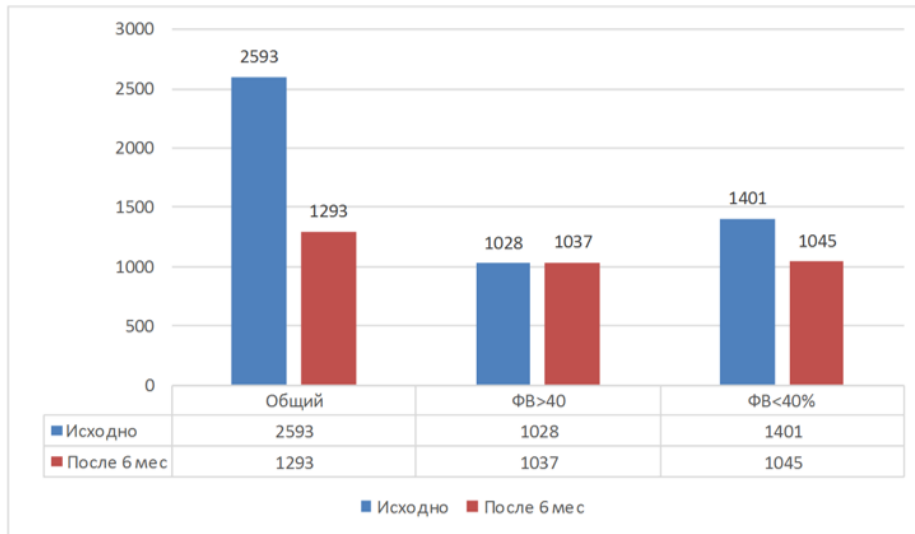


Figure 3. Dynamics of proBNP levels in group 2 pg/ml

The valsartan/sacubitril complex showed better results than ACE inhibitor treatment. Significant laboratory dynamics in the form of a decrease in NT-proBNP levels were observed in patients with CHF <40%, which affects the pathogenetic mechanisms associated with the formation and development of CHF. The results obtained significantly influenced the increase in exercise tolerance in patients with chronic obstructive pulmonary disease complicated by chronic heart failure. Narrowing of the RA cavity and a decrease in PA pressure indicate not only regression of bronchial asthma, but also regression of CHF. The use of IF channel inhibitors in the treatment of obese patients with chronic obstructive pulmonary disease complicated by chronic heart failure reduces broncho-obstructive syndrome in these patients and significantly reduces the number of attacks.

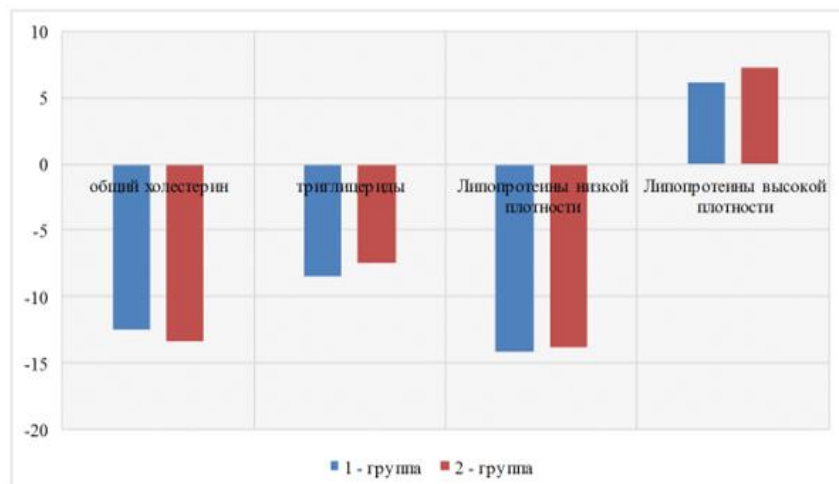


Figure 4. Lipid spectrum

In 75 (80%) patients, blood lipid parameters such as plasma cholesterol, triglycerides, very low-density lipoproteins, a significant increase in low-density lipoproteins, and a decrease in high-density lipoproteins were initially impaired.

After six months of treatment, non-significant positive dynamics were observed in both groups. A slight decrease in total cholesterol and its atherogenic fractions was shown, which led to a decrease in the atherogenic index by 14.9% and by 17.4% in the first and second groups (Fig. 4). The use of statins in the treatment of obese patients with chronic obstructive pulmonary disease complicated by chronic heart failure has a metabolically neutral effect. Blockers of the neurohormonal RAAS system help improve the lipid profile due to their vasoprotective, antioxidant effects and synergy, which, in turn, helps improve vascular permeability and thus reduce the clinical manifestations of heart failure.

Levels of fibrinogen and proinflammatory cytokines decreased in both groups after treatment. In addition, the changes were greater in both groups (Table 5).

In patients with chronic obstructive pulmonary disease complicated by chronic heart failure during long-term therapy, cytokine activity was significantly reduced. Thus, it is possible to fix the balance of the proinflammatory cytokine system during remission of bronchial asthma.

Table 7

Immunological analysis results

Control groups	Fibrinogen	CRO	IL - 6	IL - 8
1 - group (110)	4.8±1.4	32.2±15.1	62.0±20.81	48.0±9.2
2 - group (50)	4.2±1.4	15.3±10.81	9.1±1.41	30.2±3.1
3 - group (30)	2.52±0.3	2.8±0.5	8.4±2.5	25.4±8.4

The dynamics of the 6-minute walking test and the scale for assessing the clinical condition after 6 months are presented in Table 8.

Table 8

6 Minute Walk Test and SHOKS

1 - group (110)			
6 Minute Walk Test			
Indicators	(n=110)	CHF>40% (n=76)	CHF<40% (n=34)
In 6 months	226.0[232.0; 374.0]	300.0 [220.0-420.0]	245.0 [240.0-250.0]
P	1-2 <0.05	1-2 <0.05	1-2 <0.05
SHOKS			
Indicators	(n=50)	CHF>40% (n=28)	CHF<40% (n=22)
6 months	10 [6; 10]	5 [4; 6]	7.5 [7; 8]*
P	3-4 <0.05	3-4 <0.05	3-4 <0.05
2 - group (50)			
6 Minute Walk Test			
Indicators	(n=50)	CHF>40% (n=28)	CHF<40% (n=22)
In 6 months	254.0[225.0; 310.0]	220.0[180.0-280.0]	210.0[120.0-240.0]
P	5-6 <0.05	5-6 <0.05	5-6 <0.05
	2-6 >0.05		
SHOKS			

Indicators	(n=50)	CHF>40% (n=28)	CHF<40% (n=22)
In 6 months	9 [5; 9]	4 [3-5]	9 [7-9]
P	7-8 <0.05	7-8 <0.05	7-8 <0.05
	4-8 >0.05		

The inclusion of proBNP level determination in the diagnostic standards of patients with bronchial asthma also serves as an effective method for early detection and early treatment of chronic heart failure and prevention of its worsening.

CONCLUSION

1. Chronic obstructive pulmonary disease in obese patients, complicated by chronic heart failure, is characterized by the predominance of pathogenetic mechanisms of endothelial dysfunction, depending on the stage of bronchial asthma and the stage of CHF. The more severe the bronchial asthma, the higher the levels of pro-inflammatory cytokines, which indicate the severity of endothelial dysfunction. Also, the higher the stage of CHF, the higher the proBNP level.

2. The use of an if-receptor blocker in patients with stable CHF is characterized by an improvement in the quality of life based on the SGRQ and EQ-5D-5L questionnaires, as well as the SCS. An analysis of the effectiveness of if-receptor blocker therapy on endothelial function, markers of cytokine inflammation, NUP level, and hemostatic system showed a significant improvement in all parameters in patients with bronchial asthma complicated by CHF.

3. When using ARNI, pro-BNP levels can be used not only to assess CHF, but also for the prognosis of patients with bronchial asthma complicated by CHF, since there is a strong correlation with both parameters of the disease. Pro-BNP levels decreased with long-term ARNI therapy in both groups.

4. During long-term therapy of obese patients with bronchial asthma complicated by CHF, the use of ARNI led to a decrease in pro-BNP levels. Patients with reduced ejection fraction (EF<40%) entered the stage with intermediate EF (EF>40%). The inclusion of an if-receptor blocker in the complex treatment of patients with stable CHF did not lead to a deterioration of bronchial obstruction in patients with chronic obstructive pulmonary disease with obesity, complicated by chronic heart failure with sinus rhythm.

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