THE EFFECT OF ASSOCIATED CHRONIC OBSTRUCTIVE PULMONARY DISEASE ON THE INDICATORS OF PRECURSOR OF TYPE B NATURAURETIC PEPTIDE AND PROADRENOMEDULLIN AMONG PATIENTS WITH ISCHEMIC CARDIOMYOPATHY

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ABSTRACT — The study showed that a statistically significant increase of NT-proBNP levels (779,36 [473; 2193] pg/ml) and MR-proADM (1,72 [1,56; 1,98] nmol/l) relative to the control values (69.90 [48.96; 91.00] pg / ml and 0,49 [0,18; 0,58] nmol/l, respectively) is common for the patients with ischemic cardiomyopathy. The presence of concomitant chronic obstructive pulmonary disease among the patients is associated with more pronounced increase in the level of NT-proBNP (872,37 [510; 2355] pg/ml) and MR-proADM (1,97 [1,75; 2,19] nmol/l) compared with a group of patients with isolated ischemic cardiomyopathy. This can be considered as one of the compensation links for this comorbid combination.

KEYWORDS — ischemic cardiomyopathy, chronic obstructive pulmonary disease, proadrenomedullin, precursor of type B natriuretic peptide, chronic heart failure (CHF).

The study of the features of pathogenetic mechanisms, clinical picture, diagnosis and treatment of various somatic diseases when they are combined remains one of the urgent problems of medicine. To a large extent, this refers to coronary heart disease and chronic obstructive pulmonary disease (COPD), which is currently defined as comorbid [1, 2]. They are the leading chronic diseases among patients of older age groups and occupy leading position among the causes of incapacity, disability and premature death [3, 4].

The aim of the study

Is to evaluate the effect of concomitant chronic obstructive pulmonary disease on the precursor levels of type B natriuretic peptide and proadronedullin among patients with ischemic cardiomyopathy.

MATERIALS AND METHODS

A one-time (transverse) observational study included 172 men who, in accordance with the purpose of the study, were divided into two groups: 130 patients with ischemic cardiomyopathy (ICMP) and 42 patients with ICMP and chronic obstructive pulmonary disease (ICMP + COPD). Exclusion criteria from the study: age over 65 years, acute and malignant diseases, mental disorders. The control group consisted of 30 somatically healthy men, the average age was 52.76 [40; 59]. Clinical characteristics of patients are presented in Table 1.

Chronic ischemic heart disease diagnosis: ICMP was made on the basis of clinical recommendations "Diagnosis and treatment of chronic coronary heart disease" by the Ministry of Health of the Russian Federation (2013) and formulated according to the International Classification of Diseases (X revision) [5]. The COPD diagnosis was made according to the recommendations provided by the "Global strategy for the diagnosis, treatment and prevention of chronic obstructive pulmonary disease" program (GOLD, 2018) [6].

To determine the level of proadrenomedullin (MR-proADM) in serum samples, the test system "BRANMSMR-proADMKRYPTOR" (Germany), the level of the precursor of the natriuretic peptide type B (NT-proBNP) - test system "BiomedicNT-proBNP" (Austria) was used.

The study was done in accordance to the standards of good clinical practice (GoodClinicalPractice) and the principles of the Declaration of Helsinki and was approved by the Regional Independent Ethics Committee (protocol № 11 dated November 6, 2014). All patients received complete information about the study and gave informed consent to voluntary participation in it.

Table 1. *Clinical characteristics of patients in groups*

Indicator	ICMP n = 130	ICMP + COPD n = 42
Age, years	55,57 [43; 63]	54,81 [41; 63]
Body mass index, kg/m2	31,65 [22,96; 45,92]	31,3 [28,04; 49,73]
The duration of symptoms of coronary artery disease, years	4,98 [2; 13]	5,14 [3; 12]
Duration of CHF symptoms, years	2,84 [1; 6]	2,76 [1; 5]
Functional class CHF (NYHA)		
2, n (%)	21 (16%)	6 (14%)
3, n (%)	88 (68%)	28 (67%)
4, n (%)	21 (16%)	8 (19%)
6-minute walk test, m	169 [38; 368]	158 [41; 349]
Scale of assessment of the clinical condition, points	9,19 [4; 15]	9,46 [5; 14]
The duration of arterial hypertension in history, years	14,17 [3; 25]	13,34 [2; 25]
Systolic blood pressure, mm hg. art.	98,51 [80; 130]	95,38 [80; 125]
Diastolic blood pressure, mm hg. art.	65,83 [60; 80]	67,28 [60; 80]
Smoking at the time of the study, n (%) / history of smoking, n (%)	82 (63%) / 8 (6%)	37 (88%) / 5 (12%)
Smoking Man Index (pack/year)	24,35[12; 32]	36,46 [22; 48] p*<0,001

Note: *p * — statistically significant differences in the group of patients with ICMP.*

Statistical data processing was done using the program "Statistica 12.0" (StatSoft, Inc., USA). The values of the median (Me) and percentiles (5% and 95%) were calculated for each studied indicator. Statistically significant differences between the studied parameters were considered at p<0,05.

RESULTS

As shown in table 2, the data in the studied groups, the indicators of the levels of NT-proBNP and MR-proADM were statistically significantly higher than in the control group. At the same time they were statistically significantly higher in the ICMP + COPD group than in the group with isolated ICMP.

Table 2. *NT-proBNP and MR-proADM levels in the studied groups*

Indicator	Control	ICMP n = 130	ICMP + COPD n = 42
NT-proBNP, pg/ml	69,90 [48,96; 91,00]	779,36 [473; 2193] p1<0,001	872,37 [510; 2355] p1<0,001, p2=0,042
MR-proADM, nmol/l	0,49 [0,18; 0,58]	1,72 [1,56; 1,98] p1<0,001	1,97 [1,75;2,19] p1<0,001, p2=0,046

p1 — the level of statistical significance of differences with the control group,
p2 — the level of statistical significance of differences with the group of patients with ICMP.

The detected high levels of NT-proBNP in the ICMP group are explained by pronounced structural and functional dysfunction of the left ventricle with ICMP, since this peptide is known to be secreted by cardiomyocytes in response to an increase in left ventricular wall tension, an increase in ventricular volume and pressure, and a complex of its physiological effects aimed at reducing the hemodynamic load on the myocardium. COPD among the patients with ICMP apparently contributes to increased hypoxemia, oxidative stress and cytokine imbalance, which has an additional negative impact on the state of cardiomyocytes among the patients with ICMP. In addition, COPD leads to more pronounced structural changes in the heart (hypertrophy and dilatation of the right heart, development of pulmonary hypertension), which increases the mechanical stretching of cardiomyocytes and increases the expression of NT-proBNP [7, 8, 9].

The revealed change in the MR-proADM level with ICMP is consistent with the data of other researchers, indicating its increase in various forms of IHD. Hypoxia and cytokine release are indicated as a

possible reason for this increase, which cause increased secretion of MR-proADM by vascular cells as a compensatory agent involved in neoangiogenesis, which suppresses collagen synthesis and has antioxidant, inotropic effects and increases myocardial contractility. The presence of ICMP among the patients with COPD increases hypoxia and hypoxemia, which leads to increased stimulation of the production of MR-proADM. In addition considering the antibacterial, bronchodilatory and immunoregulatory effects of MR-proADM, it can be assumed that changes in the respiratory tract with COPD are also an additional stimulus for its development [10, 11, 12].

CONCLUSION

Patients with ICMP are characterized by increased levels of NT-proBNP and MR-proADM relative to control values. The presence of concomitant COPD is associated with more pronounced increase in the level of NT-proBNP and MR-proADM, compared with the group of patients with isolated ICMP, which can be considered as one of the compensation links for this comorbid combination.

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