

EVALUATION OF A NATRIURETIC PEPTIDE TO OPTIMIZE THE MANAGEMENT OF COMORBID PATIENTS WITH THYROTOXICOSIS AND HEART FAILURE

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ABSTRACT

Objective: to determine the threshold level of natriuretic peptide to optimize the diagnosis of heart failure in comorbid patients with thyrotoxicosis, to evaluate the dynamics of the indicator against the background of therapy. **Materials and methods:** 111 patients aged 58.3 ± 5.6 years were divided into 4 groups: the main group — 25 patients with coronary heart disease (CHD), chronic heart failure (CHF) and thyrotoxicosis; the first comparison group — 30 patients with CHD and CHF, without thyrotoxicosis; the second group — 30 patients with thyrotoxicosis without CHF; The third group consisted of 26 patients with thyrotoxicosis and coronary heart disease without signs of CHF. Thyroid function and the level of the N-terminal fragment of the precursor of the cerebral natriuretic peptide (NT-proBNP) were evaluated initially and after 6 months of treatment for thyrotoxicosis, coronary heart disease and CHF. Using ROC analysis, the threshold level of NTproBNP for the diagnosis of CHF in comorbid patients was calculated. **Results:** in patients of all groups, an increased concentration of NT-proBNP (more than 125 pg/ml) was determined, in the second group it was 225.5 (180.1; 376.1) pg/ml. Values NT-proBNP did not significantly differ in patients of the first and third groups. The highest level of NT-proBNP was determined in the main group — 712.1 (434.3; 893.9) pg/ml. The cut-off marker for CHF screening in patients with coronary heart disease and thyrotoxicosis was calculated at 556.4 pg/ml (sensitivity — 72%, specificity — 100%, accuracy — 87.2% ($p < 0.001$)). After 6 months of treatment, the level of NT-proBNP in the second comparison group decreased by 74% ($p < 0.0001$), reached a normal value (64.6 (42.2; 76.3)), decreased by 43% in the main group and amounted to 406.7 (309.1; 498.6) pg/ml. **Conclusions:** in patients of all groups, an increased concentration of NT-proBNP was detected, the highest in the group of patients with CHF on the background of coronary heart disease and thyrotoxicosis. A new threshold level of NT-proBNP has been determined, which

makes it possible to diagnose CHF in patients with a combination of coronary heart disease and thyrotoxicosis – 556.4 pg/ml.

Key words: natriuretic peptides, chronic heart failure, comorbid patients, coronary heart disease, thyrotoxicosis, threshold level.

INTRODUCTION

Chronic heart failure (CHF) remains an urgent public health problem, as it is the most severe, prognostically unfavorable complication of cardiovascular diseases (CVD). Despite the use of modern diagnostic methods, the development and introduction of new groups of drugs into practical medicine, the mortality rate in CHF remains high. Recent studies have shown that one of the common causes of the development and progression of CHF ischaemic heart disease (CHD) — in 69.7% of cases. It is known that in the pathology of the thyroid gland, accompanied by its hyperfunction, changes in the cardiovascular system (CVS) are observed, which, as a rule, are reversible when euthyroidism is achieved. At the same time, structural and functional remodeling of the heart, which develops when combined thyrotoxicosis and pre-existing CVD may be irreversible. In modern National and European guidelines for the diagnosis and treatment of CHF, special attention is paid to determining the level of natriuretic peptides (NUP) and the N-terminal fragment of its precursor (NT-proBNP) for early diagnosis of CHF, especially in the presence of a preserved and intermediate ejection fraction (LV) of the left ventricle (LV). As is known, NPAs, which are actively involved in the neurohumoral regulation of cardiovascular disease, are secreted in response to overload of the chambers of the heart with volume and pressure and have a sufficiently high sensitivity and specificity in the diagnosis of CHF. However, according to the literature, with hyperthyroidism without CVD, an increased level of NUP is also determined. Researchers' opinion on The reasons for the increase in this indicator are ambiguous, which arouses interest in studying the level of natriuretic peptides in patients with thyrotoxicosis in the presence of coronary heart disease and CHF, assessing the possibility of using this indicator for the diagnosis of CHF in comorbid patients. The aim of the study was to determine the threshold level of natriuretic peptide to optimize the diagnosis of heart failure in comorbid patients with thyrotoxicosis, to assess the dynamics of the indicator against the background of therapy.

MATERIALS AND METHODS OF RESEARCH

The study included 111 patients aged 45 to 65 years (average age — 58.3 ± 5.6 years). All patients were divided into 4 groups: The main group consisted of 25 patients with thyrotoxicosis, coronary heart disease and CHF II-III functional class (FC), average age — 59.23 ± 3.81 . The first comparison group consisted of 30 patients with coronary heart disease and CHF II—III FC, without thyroid pathology, average age —

±57.6 2.73. The second comparison group consisted of 30 patients with thyrotoxicosis without coronary heart disease, the average age was 45.4±3.51. The third comparison group consisted of 26 patients with thyrotoxicosis and coronary heart disease, without signs of CHF, the average age was 59.12±3.14. All participants were probably participants in the II—III stages of the competition. Diagnosis and treatment of coronary heart disease and CHF were carried out in accordance with modern recommendations. The analysis of clinical symptoms of CHF in patients of the main group and the first comparison group was performed using a scale for assessing the clinical condition (SHOCK, modification of Mareeva V. Yu., 2000), exercise tolerance was assessed by the results A 6-minute walking test (6MTH). As a result, the results of the analysis using thyrotoxicosis were obtained (the level of thyrotropic hormone (TSH) is less than 0.1mmol/l, the level of free thyronide (Ft3) is higher than 5.8 pmol/l, free fall (fT4) above 23.0 pmol/l), who in 100% of cases were diagnosed with diffuse toxic goiter - Graves' disease (the level of antibodies to the TSH receptor is above 1.5 U/l). Patients with thyrotoxicosis in the hospital were prescribed standard therapy with thyrostatics (thiamazole at a dose of 30-40 mg / day, followed by a dose reduction to a maintenance 5-10 mg / day). All studies were performed initially (before the appointment of thyrostatics) and after 6 months of therapy. The criteria for exclusion from the study were autoimmune thyroiditis, functional autonomy of the thyroid gland, iatrogenic thyrotoxicosis, hemodynamically significant heart defects (congenital, acquired), pericarditis, myocarditis, myocardial infarction or acute cerebrovascular accident less than 6 months old, severe pathology of the liver, kidneys, the presence of an electrocardiostimulator, inflammatory and infectious diseases, malignant neoplasms. The static processing of the obtained data was carried out using the Statistica 10.0 program (statsoft, USA). The main values are presented in absolute numbers (n) and percentages (%), which were compared by Pearson's criterion χ^2 . For quantitative variables whose distribution was different from normal, the values are presented as median and quartiles. When comparing more than two groups by quantitative and qualitative characteristics, the Kraskel-Wallis method of rank analysis of variations was used. When comparing the two groups on a quantitative basis, the following was used the Mann-Whitney criterion. Differences in statistical values were recognized as significant at a significance level of $p < 0.05$. ROC analysis (determination of the characteristic curve of the receiver operator) was used to determine the new value. The dynamic method determined the distribution path of the area under the curve (AUC or Area under the curve).

THE RESULTS AND THEIR DISCUSSION

Indicators of the hormonal spectrum of blood, heart rate (HR) did not significantly differ in patients of the main group, the second and third comparison groups, whereas waist circumference (OT), body mass index (BMI) in the group of

patients with thyrotoxicosis without CVD (the second comparison group) were significantly lower ($p < 0.05$) in compared with the indicators of the main group, the first and third comparison groups, which, apparently, is due to the younger age of patients and the lack of comorbidity. A comparative analysis of the clinical symptoms of CHF did not reveal significant differences in the indicators of SHOCK in patients of the main and first comparison groups (7.08 and 6.61 points, respectively, $p = 0.3$), whereas the distance traveled in 6 minutes in the main group turned out to be 1.2 times smaller (253.96 ± 16.88 and 300.32 ± 19.12 m, respectively ($p = 0.01$)). Assessing the systolic function of the left ventricle, it should be noted that the values of the ejection fraction in patients of the second and third comparison groups were within the normal range (67% and 56%, respectively). In patients of the first comparison group, with coronary heart disease and CHF, the left ventricular ejection fraction (LVEF) was significantly lower, than in the second and third comparison groups ($p < 0.001$), and corresponded to an intermediate type of heart failure — 47,0 % (40,0; 48,0) [1,2,4]. At the same time, patients with CHF on the background of coronary heart disease and thyrotoxicosis (main group) were diagnosed with the lowest LVEF — 40.0% (37.0; 42.0), compared with the corresponding indicator in the comparison groups ($p < 0.001$).

Much attention was paid to the development of the NT-proBNP concept. It should be emphasized that an increased level of this indicator was detected in patients of all groups (Fig. 1). Thus, in Whether with thyrotoxicosis from CVD (the second group of manufacturers), the value of the NT sample was 2.04 times higher than the threshold level (125 pg/ml) recommended for diagnosis. In patients with coronary heart disease and CHF (the first comparison group) and in patients with coronary heart disease and thyrotoxicosis without clinically pronounced CHF (the third comparison group), the level of NT probability increased by 28.8% (i.e. by 1.28 times, $r_1 = 0.017$) and by 35.2% (i.e. by 1.35 times, $r_2 = 0.008$), respectively, a similar indicator in patients with thyrotoxicosis without CVD (the second comparison group). It was the integration of NT-proBNP in the partners of the first and third comparison groups that was 2.18 and 2.06 times lower than in the main group ($p < 0.0001$), but the indicators did not differ significantly between each other ($p = 0.88$). The highest level NT is the probation period received from a large social group, compared with the corresponding indicators in the comparison groups ($p < 0.0001$). In accordance with the task, a new basic value of NT-proBNP was determined, which allows us to study the organic nature of man, taking into account his individual characteristics. thyrotoxicosis. When determining the threshold value, based on the values of sensitivity and specificity, the construction of a characteristic curve was used (ROC-curve) with my ROC-analysis. As a result, the dividing point of separation, or the cut-off moment, was calculated. First of all, we determined the value of the disconnect parameter for a group of subscribers with thyrotoxicosis without CVD — 402.83 pg/ml (diagnostic sensitivity — 100%,

specificity — 93.3%, diagnostic accuracy — 95.6% ($p < 0.001$). According to the obtained result, NT-proBNP values of more than 402.83 pg/ml suggest the presence of CHF in 100 % of patients with thyrotoxicosis, and the level of NT-proBNP below the specified threshold value, CHF is excluded in 93.3% of patients with thyroid diseases occurring with its hyperfunction.

The analysis of the severity of clinical symptoms of CHF did not reveal significant differences in patients of the main group (with coronary heart disease, thyrotoxicosis and CHF) and the first comparison group (with coronary heart disease and CHF without thyroid pathology). However, significantly lower exercise tolerance was found in patients with CHF of ischemic genesis and thyrotoxicosis (main group). Thus, the average distance traveled in the main group turned out to be 15.4% less than in the first comparison group ($p = 0.01$), which is apparently due to the presence of concomitant thyrotoxicosis syndrome in patients of the main group. It should be noted that patients of all study groups showed elevated levels of NT-proBNP, including those with thyrotoxicosis without CVD (comparison group 2). The data obtained are consistent with the results of foreign and domestic researchers who noted an increase in the concentration of NT-proBNP in individuals with high levels of thyroid hormones and low TSH. It should be emphasized that in our work in patients of the second comparison group (with manifest thyrotoxicosis without CVD) all the obtained NT-proBNP values turned out to be below the calculated threshold (cut-off), which confirms absence of CHF in patients of this group. In a comparative analysis of the results of NT-proBNP in patients with coronary heart disease and CHF (group 1) and patients with There was no statistically significant difference between coronary heart disease and thyrotoxicosis without CHF (the third group), which allows us to think about a comparable effect on the level of natriuretic peptides of both LV volume and/or pressure overload in CHF and hyperproduction of thyroid hormones. The highest concentration of NT-proBNP detected in patients of the main group is probably due to the presence of comorbidity — CHF and thyrotoxicosis. The data obtained confirm the controversial judgments available in the literature about the diagnostic value of determining the level of NT-proBNP for the detection of CHF in conditions of hyperthyroidism, which motivated the revision and search for a new threshold level of the marker. The paper calculates a new diagnostic level of NT-proBNP for CHF screening in comorbid patients with coronary heart disease and thyrotoxicosis. According to the result, the level of NT-proBNP above 556.4 pg/ml in 72% of cases will indicate the presence of CHF in patients with thyrotoxicosis and coronary heart disease, and the values are lower 556.4 pg/ml will eliminate CHF in 100 % of patients Coronary heart disease and thyrotoxicosis.

Analyzing the dynamics of NT-proBNP levels during therapy, it should be noted that in conditions of achieved euthyroidism in patients with thyrotoxicosis without

CVD, there was a marked decrease in NT-proBNP levels to normal values (less than 125 pg/ml). At the same time, in the main group of patients, despite a significant decrease in the concentration of this indicator, its level still exceeded the threshold (125 pg/ml) and remained the highest in comparison with the initial results in patients of the first, second and third groups comparisons ($p_1=0.02$; $p_2=0.001$; $p_3=0.04$, respectively), which is obviously due to more pronounced morpho-functional changes in the heart in patients with Coronary heart disease and CHF on the background of hyperthyroidism. A comparative assessment of the NT-proBNP index in patients of the main group after 6 months of therapy with a calculated new threshold value for the diagnosis of CHF is noteworthy. The level of NT-proBNP in patients with CHF of ischemic genesis and thyrotoxicosis against the background of achieving drug-induced euthyroidism and optimal therapy of HF, after 6 months was 406.73 pg/ml. The result obtained was below the calculated threshold value (556.4 pg/ml) for patients in this group, which is probably due to compensation for thyrotoxicosis and a decrease in the severity of HF during therapy.

CONCLUSIONS:

1. An increased concentration of NT-proBNP was detected in patients of all study groups. The highest level of NT-proBNP was observed in the group of patients with CHF on the background of coronary heart disease and hyperthyroidism, due to the combined effect of volumetric load on the heart and thyrotoxicosis.
2. A new threshold value of NT-proBNP —556.4 pg/ml has been determined, which will allow the diagnosis of CHF in patients with a combination of coronary heart disease and thyrotoxicosis.
3. Against the background of achieving drug-induced euthyroidism in patients with diffuse toxic goiter without CVD, there was a marked decrease in the level of NT-proBNP with reaching a value of less than 125 pg/ml .
4. In conditions of comorbidity in patients of the main group, there was a significant decrease in the concentration of NT-proBNP below the calculated threshold level indicates stable compensation for thyrotoxicosis and effective treatment of CHF.

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