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ABSTRACT

of the dissertation for the degree of Philosophy

EARLY DIAGNOSIS OF CARDIAC ARRHYTHMIAS AND THE EFFECTIVENESS OF ANTIARRHYTHMIC TREATMENT IN PATİENTS WITH CHRONIC DESTRUCTIVE PULMONARY TUBERCULOSIS

Speciality: 3228.01– Phthisiatry

Branch of science: Medicine

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The work was performed at the Department of Pulmonary Diseases of the Azerbaijan Medical University, located under the Tuberculosis Dispensary No. 4, and at the Department of the Scientific-Research Institute of Cardiology named after J.Abdullayev.

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GENERAL DESCRIPTION OF THE WORK

Relevance of the topic. Currently, the fight against tuberculosis is one of the most important problems of health care. Drug resistance of tuberculosis mycobacteria reduces the success of chemotherapy in these patients, leads to the emergence of chronic destructive forms and complications from various organs.

One such complication is pulmonary-heart failure. In the initial stages of pulmonary-heart failure, disturbances in the rhythm and conduction of the heart are also found in most cases. Hypoxemia, dystrophic changes of the myocardium, toxic effect of inflammation of the bronchial tree on the myocardium can be indicated as the main pathogenetic factors of the occurrence of arrhythmias and blockages. In widespread forms of pulmonary tuberculosis, it leads to a violation of the cardiovascular system. Chronic pulmonary heart disease (CPHD) takes the leading place among the cardiovascular pathologies that occur during tuberculosis. Chronic pulmonary heart disease consists of right ventricular hypertrophy with subsequent dilatation, precapillary pulmonary hypertension, impaired gas exchange due to lung damage, small and large vessel damage, and chest deformity.

The international community has set a goal of ending the tuberculosis epidemic by 2030. The main task of this ambitious goal is to reduce the death due to tuberculosis by 90% and the incidence of tuberculosis by 80%. Currently, 1.7 billion people in the world are reported to be suffering from the latent form of tuberculosis[1].

According to the World Health Organization's 2021 Global Report, 9.9 million people were infected with tuberculosis in 2020, of which 1.3 million died. This made up 13% of the total number of infected people. Wider prevalence of this disease has been recorded in Southeast Asia, Europe, Africa and the Western Pacific. In these

[1] Harries, A.D. The Growing Importance of Tuberculosis Preventive Therapy and How Research and Innovation Can Enhance Its Implementation on the Ground / A.D. Harries, A.M.V. Kumar, S. Satyanarayana [et al.] // Tropical Medicine and Infectious Disease, – 2020. 5 (2), – p. 1-17

areas, the ratio of men and women infected with tuberculosis was 1.7:1[2].

Damage to the cardiovascular system during pulmonary tuberculosis increases the risk of a poor prognosis of the disease. Thus, the mortality rate among patients suffering from tuberculous pericarditis was recorded to be 40%. As a result of tuberculosis, the ventilation function and hemodynamics of the lungs weaken, tissue hypoxia deepens. In persons with pulmonary tuberculosis, uneven ventilation occurs from the initial stages of the disease, alveolar hypoxia is consistently noted, which leads to spasm of the vessels supplying the poorly ventilated areas of the lungs. Secondary arterial hypertension is formed, which increases the load on the right sides of the heart and the oxygen demand of the myocardium, the ejection fraction (EF) decreases, and ventricular ischemia deepens[3].

As a result, pulmonary hypertension (increased resistance in pulmonary vessels as a result of vascular spasm against the background of alveolar hypoxia, acidosis and hypercapnia); hypertrophy of the right and left branches of the heart (development of the pulmonary heart); heart failure and changes in electrical stability of cardiomyocytes are noted. Under this term, right ventricular hypertrophy and dilatation secondary to lung diseases are understood[4].

Usually, this situation is caused by the deep morphological changes that lead to the violation of ventilation and respiratory failure, accompanied by a decrease in the partial pressure of oxygen in the alveolar air[5].

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[2] Adefuye, M.A. Tuberculosis and Cardiovascular Complications: An Overview / M.A. Adefuye, N. Manjunatha, V. Ganduri [et al.] // Cureus. – 2022. 14 (8), – p. 1-9

[3] Борисов, С.Е. Эффективность и безопасность режима химиотерапии, включающего препарат SQ109, у больных туберкулезом легких с множественной лекарственной устойчивостью возбудителя / С.Е. Борисов, Е.М. Богородская, Г.В. Волченков [и др.] // – Москва: Туберкулез и болезни легких, – 2018. № 3, – 6-18.

[4] Blanco, I. Updated Perspectives on Pulmonary Hypertension in COPD / I. Blanco, O. Tura-Ceide, V.I. Peinado [et al.] // International Journal of Chronic Obstruction of Pulmonar Diseases, – 2020. 15, – p. 1315-1324.

[5] Matthay, M.A. Acute respiratory distress syndrome / M.A. Matthay, R.L. Zemans, G.A. Zimmerman [et al.] // Nature Reviews Disease Primers, – 2019. 5 (1), – p. 1-22

Damage to the cardiovascular system during pulmonary tuberculosis manifests itself as tuberculosis aortitis, systemic damage to arteries, and thromboembolic cases. In addition, pericarditis, myocarditis, endocarditis, coronary artery damage, left ventricular aneurysms and atrial fibrosis are also common in these patients. Based on the researches, it was known that tuberculosis is the main risk factor of thromboembolic complications. The reason for this is explained by disruption of coagulation mechanisms and dysfunction of the endothelium. In addition, chronic hypoxia that occurs during tuberculosis creates the basis for venous thromboembolism[6].

In addition, it can be noted that drugs used in lung diseases (theophylline and its analogues, β-receptor agonists and others) have an arrhythmogenic effect even in therapeutic doses[7]. At the same time, additional arrhythmogenic effect is more common, especially in patients accompanied by pathology of the cardiovascular system. Anaerobic glycolysis, essential for life, occurs under conditions of marked hypoxia, which is noted in all chronic lung diseases, and under these conditions, it is considered the only and main source of ATF[8]. Anaerobic glycolysis is characterized by the release of lactate from the cell and the accumulation of H+ ions in the intracellular environment. The indicated processes lead to acidosis, disruption of the permeability of the cell membrane, enzymes move from the intracellular environment to the blood. NA+/K+ - ATF-aza, membrane pump transmission system of Ca2+ATF-aza is disturbed. Na+ and Ca2+ accumulate in the cytoplasm, loss of intracellular K+ ions is observed[9].

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[6] Плоткин, Д.В. Распространенность внутрибольничных венозных тромбоэмболических осложнений у пациентов с туберкулезом, впервые выявленным или рецидивом: данные Московского городского регистра (многоцентровое исследование) / Плоткин Д.В., Титомер А.И., Лобастов К.В. [и др.] // – Москва: Туберкулез и болезни легких, – 2024. № 1, – с. 12-19

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[8] Page, R.L. Cause or Exacerbate Heart Failure / R.L. Page, C.L. O'Bryant, D. Cheng [et al.] // Circulation, – 2016. 134, – p. 32–69

[9] Koziel, A. Hypoxia and aerobic metabolism adaptations of human endothelial cells / A. Koziel, W. Jarmuszkiewicz // Pflügers Archiv, – 2017. 469 (5-6), – p. 815-827

In parallel, mitochondrial damage, membrane breakdown leading to cell death, activation of lysosomal enzymes, phospholipids are observed[10].

Against the background of alveolar and coronary hypoxia, cellular pathology occurs as a result of a violation of the electric stability of the myocardium and the occurrence of arrhythmias.

Thus, an analysis of literature data shows that, most likely, when chronic lung diseases are exacerbated, various clinical manifestations of ischemic heart disease develop, as well as severe heart rhythm disturbances. The wide spread of chronic forms of pulmonary tuberculosis accompanied by drug-resistant destruction in our Republic and the frequent occurrence of heart rhythm disorders in the majority of such patients, the fact that despite the success in their treatment, the mortality rate is in the forefront due to the high and actuality of this study, are grounds for conducting this study.

It has also been proven in the modern phthisiatric science that the functional indicators of the heart and respiratory organs change mainly due to the influence of 2 factors. Of these, tuberculosis intoxication and the degree of spread of tuberculosis in the lungs play a big role.

Taking this into account, the study of changes in heart and respiratory activity in this direction is of great importance in phthisiology.

Object and subject of research:

Patients with chronic pulmonary tuberculosis accompanied by destruction and early detection of heart rhythm disturbances in this group of patients.

Purpose of the study is to prevent, detect at early stages, and develop more effective complex treatment methods for heart rhythm disorders that are dependent on functional classes (FC) in chronic destructive forms of pulmonary tuberculosis

The tasks of the research:

[10] Kherd, A.A. Changes in erythrocyte ATPase activity under different pathological conditions / A.A. Kherd, N. Helmi, K.S. Balamash [et al.] // African Health Sciences, – 2017. 17 (4), – p. 1204-1210.

1. Study of heart rhythm and conduction disorders, investigate the functional state of the heart and assessing central hemodynamics in individuals diagnosed with chronic destructive pulmonary tuberculosis.

2. Study of external respiratory function in patients with chronic destructive pulmonary tuberculosis.

3. Explore of interrelationship of the functional state of the heart, central hemodynamics, external respiratory function in patients with chronic destructive pulmonary tuberculosis.

4. Long-term monitoring of patients with chronic destructive pulmonary tuberculosis and application of optimal complex treatment.

Provisions of the dissertation submitted for defense:

- Study of the interrelationship of the functional state of the heart, central hemodynamics, external respiratory function in patients with chronic destructive pulmonary tuberculosis.

- Investigation of heart rhythm and conduction disorders in patients with chronic destructive pulmonary tuberculosis.

- Evaluation of antiarrhythmic potential of cardioselective β1-adrenoblocker Egilok (metoprolol) and Ethacyzine in the complex treatment of patients with chronic destructive pulmonary tuberculosis.

Scientific novelty of the work:

For the first time in patients with chronic destructive pulmonary tuberculosis

- Depending on the functional class, the functional state of the heart, central hemodynamics, external respiratory function were studied and their interaction with each other was studied.

- Disturbances of heart rhythm and conduction depending on FC have been studied.

- The antiarrhythmic capabilities of cardioselective β1-adrenoblocker Egilok (metoprolol) and class I C antiarrhythmic drug Ethacyzine in complex treatment were evaluated.

Practical significance: In patients with chronic destructive pulmonary tuberculosis, functional changes in the lungs and

cardiovascular system, disturbances in heart rhythm and conduction, which occur in most cases in the initial stages of pulmonary-cardiac failure, dangerous ventricular tachycardia, are among the important criteria leading to sudden death and syncopal conditions. Practitioner-doctors working in anti-tuberculosis facilities are advised to study dysrhythmogenesis in patients with chronic destructive pulmonary tuberculosis. As a component of the treatment of such patients, the use of cardioselective β1-adrenoblocker Egilok (metoprolol) and Ethacyzine as a drug that reduces the risk of fatal arrhythmia during both supraventricular and ventricular heart rhythm disturbances has an important practical significance.

Approval of research work: The initial discussion of the dissertation work was conducted at the Department of Phthisiology of the Azerbaijan Medical University (Protocol No. 03; dated 17.11.2018).

The scientific seminar of the dissertation work was held at the scientific seminar of the BFD 4.17 Dissertation Council at the Azerbaijan Medical University. (Protocol No. 01; dated 01.03.2024).

The scientific results of the research have been discussed and presented at the Scientific and practical conference dedicated to the 70th anniversary of A.A. Akhundbeyli (Baku, 2008), at the International scientific conference dedicated to the 80th anniversary of AMU (Baku, 2010), at the III Republican Scientific and Practical Conference on Tuberculosis and Lung Diseases and I national respiratory congress (Baku, 2010), at the Scientific-practical conference dedicated to the 70th anniversary of Doctor of Medical Sciences, professor B. M. Ashurov (Baku, 2013), at the VI Scientific-practical conference on tuberculosis and lung diseases (Baku, 2013), at the International symposium dedicated to the 90th anniversary of national leader Heydar Aliyev (Baku, 2013), Republican scientific conference dedicated to the 75th anniversary of the birth of N.N. Aliyev and the 50th anniversary of his scientific and practical activity on the topic "Actual problems of medical prevention in the 21st century: achievements and prospects" (Baku, 2015), XXV International Scientific and Practical Conference,

Modern Medicine New Approaches and Actual Studies (Moscow, 2019), International scientific-practical congress dedicated to the 90th anniversary of Azerbaijan Medical University on the topic "Actual problems of medicine-2020" (Baku, 2020), International congress dedicated to the 100th anniversary of the birth of Tamerlan Aziz oglu Aliyev (Baku, 2021), IV İnternational Ankara Multidisciplinary Studies Congress, (Ankara, 2022), Karabakh 3rd International Congress of Applied Sciences "Year of Shusha-2022" (Baku, 2022)

Application of the research: The results of the research have been applied at the Anti-tuberculosis dispensaries N 4 in the city of Baku, and the Department of Pulmonary Diseases of the Azerbaijan Medical University.

The organization in which the dissertation work was carried out. Dissertation work was performed at the Department of Pulmonary Diseases of the Azerbaijan Medical University, Anti-Tuberculosis Dispensary No. 4 and the Scientific Research Institute of Cardiology named after J. Abdullayev.

Published scientific works. 32 scientific works were published on the results of the research. Of these, 12 are scientific articles (3 of which are abroad, 2 without co-author, 10 with co-author), 7 are theses (1 abroad), 4 are congress materials (2 are abroad), and 7 are conference materials (2 abroad, and 5 in our republic).

Scope and structure of the dissertation work. The dissertation consists of 151 pages of computer text (195,470 characters), introduction (13,327 characters), Chapter I "Literature review" (49,624 characters), Chapter II "Materials and Methods" (22,371 characters), Chapter III (24,046 characters), Chapter IV (20,431 characters), Chapter V (27,567 characters), conclusions (36,003 characters), results (1,504 characters), practical recommendations (597 characters) and a bibliography, including 152 sources (of which 13 domestic, 139 - foreign). The work is illustrated with 3 pictures, 6 graphics and 28 tables.

MATERIALS AND METHODS OF THE RESEARCH

Under our control, at the Department of Pulmonary Diseases of Azerbaijan Medical University, located on the basis of the Anti-Tuberculosis dispensary No. 4, there were 80 patients with chronic pulmonary tuberculosis accompanied by destruction in inpatient and outpatient treatment. All patients were divided into three functional classes (FC) according to the course of the disease: I FC – 14 (17.5±4.2%) patients; II FC – 30 (37.5±5.4%) patients; III FC – 36 (45.0±5.6%) patients **(**Figure 1).

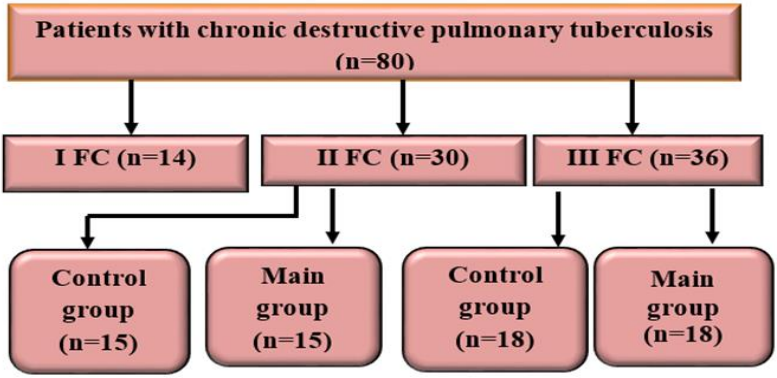


Figure 1. Design of the study

Most of the patients were aged between 31 and 50. 63 (78.8%) of them were men and 17 (21.3%) were women. 93% of patients are married and have children of different ages from 1 to 3 years old. Some of the patients (29 – 36.3±5.4%) belong to the poor class. The living conditions of 46 (57.5±5.5%) patients were satisfactory, and the living conditions of 14 (17.5±4.2%) patients did not meet sanitary and hygienic requirements. The duration of the chronic destructive process in patients was 1-5 years and more. 64 of the patients (80±4.5%) have been suffering from tuberculosis for 1-5 years, and 16 (20.0±4.5%) for more than 5 years.

From the anamnesis, it is known that 39 (48.8±5.6%) of the male patients have different degrees of smoking experience. Smoking index was 31.2±1.3. Abuse of alcoholic beverages was observed in 12 men (15.0±4.0%). 4 of the men (5.0±2.4%) abused drugs at different times of their lives. No harmful habits were recorded among female patients.

When patients entered the clinic, they presented complaints characteristic of respiratory diseases. The main complaint among patients was cough, which was observed in 73 out of 80 patients (91.3±3.2%). It should be noted that the character of the cough was different. Cough without sputum was observed in 14 (17.5±4.2%) patients, which indicates stabilization of the main disease from a clinical and radiological point of view. In 59 (73.8±4.9%) patients who secreted purulent and mucous sputum, different degrees of endobronchitis were recorded. Grade I-II bilateral diffuse mucoid and muco-purulent endobronchitis was observed in 34 (42.5±5.5%) patients, II-III grade diffuse purulent endobronchitis was observed in 22 (27.5±5.0%) patients. In 3 (3.8±2.1%) patients, local unilateral damage of large bronchi was detected. In addition, in 5 (6.3±2.7%) patients, specific local damage such as edema, hypertrophy, and infiltration of the mucous membrane of the large bronchi was observed, which we evaluated as a complication of a specific process in the lungs in the form of bronchial exudative-infiltrative tuberculosis.

Dyspnea observed in 56 (70±5.1%) patients is one of the important and significant complaints corresponding to the degree of spread of the specific process in the lung parenchyma. Dyspnea during physical exertion was observed in 36 (45.0±5.6%) patients, which usually occurs in patients with I-II degree respiratory failure. Dyspnea at rest was present in 20 (25.0±4.8%) patients, which proves that they have severe respiratory failure. One of the more common complaints was bleeding and hemoptysis observed in 33 (41.3±5.5%) patients. Chest pains were observed in 19 (23.8±4.8%) patients, signs of intoxication such as increased body temperature, decreased appetite, weight loss, insomnia, night sweats, general weakness, psycho-emotional lability were observed in 64 (80.0±4.5%) patients.

Examination methods.

In the examined patients, the estimation of external respiratory function (ERF) was performed using the spirography method with the "Jaeger" (Germany) device.

Patients were divided into 3 groups according to the degree of disorder of external respiratory function: noticeable disorders (79%-60% decrease in the forced expiratory volume in 1 second (FEV1) – 25(31.5%)); significant disorders (39%-40% decrease in FEV1 – 21(26.3%)); acute disorders (39% decrease in FEV1-34(42.2%))

The sputum and bronchial lavage were subjected to microscopy by the Sil-Nielsen method, at the same time cultivation was carried out in Levenstein-Jensen solid nutrient medium (DHT), the sensitivity to anti-tuberculosis drugs was determined by BacTek MGIT and GeneXpert MTB/RIF.

Electrocardiography was performed on the "Chanel ECG unit ECG-9801" device. In addition, ECG and daily monitoring (ECG-pro-Holter) were performed.

In radiography, Ikons (Germany) apparatus was used.

Echocardiographic examination on the "Copyright General Electric Co. 2003-Vivid3" device to evaluate the indicators of intracardiac and pulmonary hemodynamics, and Doppler echocardiogram was performed in impulse mode.

Treatment method. Patients included in the study were prescribed cardioselective β1-adrenoblocker Egilok (metoprolol) and Ethacyzin. The starting dose of Egilok is 25 mg per day. If bradycardia (less than 60 beats per minute), hypotonia (less than 100/65 in men, less than 95/60 in women) and bronchial permeability did not deteriorate, the dose of the drug was increased to 50 mg per day. Ethacyzin was prescribed to research subjects in a dose of 50 mg 3 times a day.

Statistical analysis. All numerical indicators obtained in the course of the research were statistically analyzed taking into account modern recommendations. Statistical analysis was carried out in EXCEL-2010 and SPSS-20 programs using variation, discriminant, and dispersion analysis methods.

RESULTS OF THE RESEARCH

Heart rhythm disorders. According to the ECG indicators, heart rhythm disturbances were found in 41 (51.3±5.6%) of the examined patients. Sinus tachycardia was recorded in 9 patients (11.3±3.5%). However, in 5 patients (6.3±2.7%) the pulse frequency did not correspond to the increase in body temperature and was observed even in the absence of fever.

Sinus tachycardia with a pulse rate of more than 90 beats per minute was recorded in 7 patients (8.8±3.2%). I want to note that tachycardia in these patients was not accompanied by heart palpitations, which we attribute to patients' habituation to tachycardia. However, the heart rate increases significantly during waking up and walking, and the heart rate is also subjectively recorded by the patients.

Sinus arrhythmia was observed in 4 patients (5.0±2.4%). Extrasystolic arrhythmias were detected in 16 (20.0%±4.5) patients, of which 10 (12.5±3.7%) had supraventricular extrasystoles (SVES), 6 (7.5±2.9%) had ventricular extrasystoles (VES) were recorded. Sinus bradycardia was detected in 8 (10.0±3.4%) patients with chronic destructive pulmonary tuberculosis.

Disorders of cardiac conduction. 21 (26.3±4.9%) patients had cardiac conduction disorders. In the electrocardiogram of almost half of the patients, it is clearly visible that the violation of intraventricular conduction of the heart is noted. In our opinion, the cause of such a violation of cardiac conduction is a chronic destructive form of pulmonary tuberculosis accompanied by hypertrophy of the right branches of the heart. In addition, the long-term undulating course of the chronic specific process in the lungs leads to neurogenic disorders, organic changes in the myocardium and the conduction system of the heart. Among these patients, blockade of the right leg of a bundle of His was recorded in 7 (8.8±3.2%) people. It should be noted that the blockade of the right leg did not lead to severe hemodynamic disorders. In the electrocardiogram of 3 (3.8±2.1%) patients with blockade of the left leg of the bundle of Hiss, a shift of the electrical axis of the heart to the left was detected. In 3 of these patients (3.8±2.1%), cardiac conduction disorders were observed in the anterior leg of the bundleof

Hiss. Atrioventricular conduction delay was observed in 1 patient (1.3±1.2%), which we associate with the direct effect of tuberculosis intoxication on the conduction system of the heart or extracardiac nerves. A pathological prolongation of the PQ interval was recorded in the electrocardiogram of this patient. Sinus node weakness syndrome was recorded in 2 (2.5±1.7%) patients with chronic pulmonary tuberculosis accompanied by destruction. The cause of this type of cardiac conduction disturbance is considered to be the effect of a long-term specific process on the heart muscle. In all cases, this syndrome appeared as palpitations, paroxysms appearing unexpectedly and quickly disappearing, so tachycardia was never recorded. Disturbance of intraatrial conduction was observed in 8 (10.0±3.4%) patients, whose electrocardiograms showed changes in the shape of the P-wave, splitting and crossing, expansion up to 0.12 seconds. Intraventricular conduction disturbance was recorded in 10 (12.5±3.7%), atrioventricular (AV) conduction delay in 1 (1.3±1.2%), sinus node weakness in 2 (2.5±1.7%) cases. Thus, in patients with chronic destructive pulmonary tuberculosis, an isolated violation of the conduction system of the heart was found in 26.3±4.9% (patients) cases and was related to the influence of tuberculosis intoxication, as well as a specific process directly on the heart and the conduction system of the heart.

Daily monitoring of heart rhythm and conduction disturbances by the Holter method. Holter ECG monitoring was applied to all patients on the first day of admission to the hospital for 24 hours. Cardiac glycosides, antiarrhythmic drugs, sympatholytics were not used during the monitoring period. According to the results of ECG monitoring by the Holter method, heart rhythm and conduction disorders were detected in all examined patients. Our attention was drawn to the fact that 70% of heart rhythm disturbances are permanent and observed for more than 12 hours during daily monitoring. As a result of Holter monitoring, various types of arrhythmias, cardiac conduction disturbances and their combinations were detected. Supraventricular disorders were more frequently recorded, which constituted 71.3±5.1% (57 patients). In most cases, these were ventricular extrasystoles, which presented as rare monotopic supraventricular extrasystoles in 29 (36.3%±5.4) patients.

Supraventricular tachycardia was observed in 12 (15.0±4.0%), ventricular disorders in 38 (47.5±5.6%), cardiac conduction disorders in 15 (18.8±4.4%) patients. In addition to the above, 44 (55.0±5.6%) patients had both of heart rhythm and conduction disturbances.

At this time, the combination of supraventricular extrasystole and ventricular extrasystole was observed in more cases - 27.5±5.0%. The second most frequent combination of monotopic supraventricular extrasystole and rare polytopic ventricular extrasystole was found in 12 (15.0±4.0%) patients. The combination of sustained supraventricular extrasystole and ventricular extrasystole was observed in 6 (7.5±2.9%) patients with marked respiratory failure but without signs of blood circulatory failuri (BCF). In 5 (6.3±2.7%) patients, hypertrophy of the right side of the heart, accompanied by a combination of supraventricular extrasystole and ventricular extrasystole confirmed by echocardiography, and complete intraventricular blockade, along with symptoms of hypoxia, was detected.

Functional disorders of central hemodynamics, external respiratory and heart in patients with chronic destructive pulmonary tuberculosis and their relationship. When analyzing external respiratory function (ERF) and heart echocardiographic parameters in patients with chronic destructive pulmonary tuberculosis, the interaction between them was determined. This relationship allows patients to be divided into 3 functional classes (FC). The criteria used to distinguish it to a certain FC are the following: various degrees of respiratory failure, changes in spirographic and echocardiographic parameters, and the presence of pulmonary hypertension. 14 (17.5±4.2%) patients with predominant pulmonary symptoms in the absence of cardiac dysfunction were assigned to I FC. 30 (37.5±5.4%) patients were characterized by signs of pulmonary tuberculosis in II FC and impaired external respiratory function, 36 (45,0±5,6%) patients were characterized by symptoms of pulmonary tuberculosis in III FC, along with impaired external respiratory function, hypertrophy, and dilatation of the right ventricle.

When studying external respiratory function (ERF), indicators such as vital capacity of the lungs (VC), forced vital capacity of the lungs (FVC), forced expiratory volume in the first second (FEV1),

Tiffno index, forced expiratory flow (FEF) 25, 50, 75 registered. In all patients belonging to functional class I, indicators of external respiratory function were within the norm.

Moderate bronchial obstruction (FEV1=56.8±1.2%)was determined in patients belonging to functional class II. FEF 75, 50, 25 indicate moderate changes and localization of bronchial obstruction (46.7±1.4%, 42.5±1.5%, and 38.4±2.1%, respectively). During the determination of the Tiffno index, we recorded a downward trend (66.8±2.4%) of this indicator. A decrease in VC and FVC indicators was recorded in patients belonging to III FC. Severe obstruction was observed in these patients, which was confirmed by low FEV1 (45.2±1.6%). A decrease in the Tiffno index was also recorded in these patients and was 52.7±2.0%.

During echocardiography, the following parameters were focused on: right ventricular end-systolic size (RVESS), interventricular septum thickness (İVST), left ventricular end-systolic size (LVESS), left ventricular end-diastolic size (LVEDS), right ventricular wall thickness thickness (RVWT), ejection fraction (EF), systolic pressure on the pulmonary artery (PASP). In patients belonging to functional class I, these indicators were on average close to the norm.

In patients belonging to the II functional class, there is a decrease in EF (59.0±0.5%) and slight pulmonary hypertension (29.6±0.8 mm Hg). Of particular importance is the marked reduction of left ventricular EF in patients belonging to functional class III, which was 52.9±0.9%. During the course of the study, we detected weak pulmonary hypertension, that is, we did not find a very high indicator of PASP in patients belonging to III FC (31.4±0.6 mmHg).

The results of daily monitoring by Holter method in patients with chronic destructive pulmonary tuberculosis belonging to functional class I showed supraventricular disturbances in 8 (57.1±13.2%) of these patients, ventricular disturbances in 2 (14.3±9.4%), 1 patient (7.1±6.9%) had conduction disorders, 3 patients (21.4±11.0) had combined disorders. In functional class II, supraventricular disorders was observed in 26 (86.7±6.2%) patients, supraventricular tachycardia - in 5 (16.7±6.8%) patients, ventricular disorders - in 16 (53.3±9.1%) patients, cardiac conduction violation - in 5 (16.7±6.8%) patients, combined

violations - in 18 (60.0±8.9%) patients. Supraventricular disorders, ventricular disorders, and conduction disorders are more common during the day in patients belonging to the III functional class, as well as combined disorders. Supraventricular disorders were recorded in 23 (63.9±8.0%) patients, supraventricular tachycardia - in 7 (19.4±6.6%) patients, ventricular disorders - in 20 (55.6±8.3%) patients, conduction disorders - in 9 (25.0±7.2%) patients, combined disorders - in 23 (63.9±8.0%) patients.

Comparative assessment of ERF and central hemodynamic indicators depending on the functional class.

The results of echocardiographic examination depending on FC in patients with chronic destructive pulmonary tuberculosis are reflected in table 1.

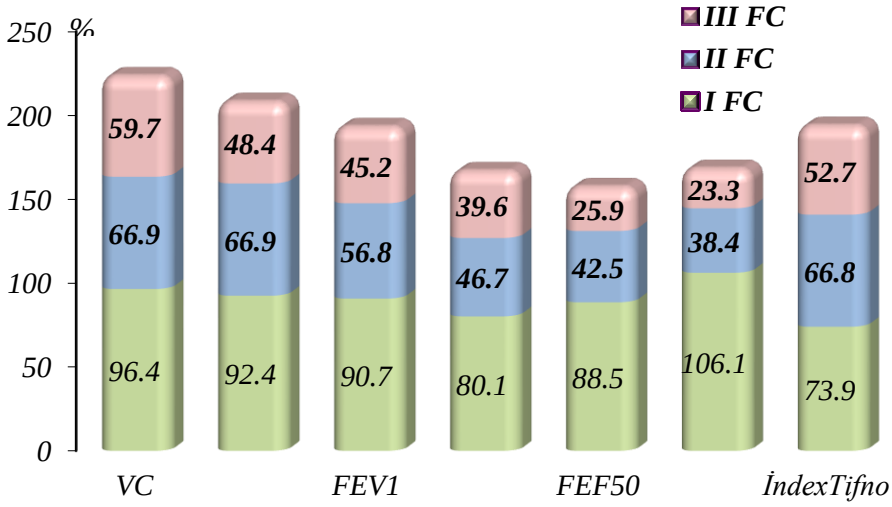
Table 1

Results of echocardiographic examinations in patients with chronic destructive pulmonary tuberculosis depending on FC

EchoCG parameters	I FC (n=14)	II FC (n=30)	III FC (n=36)	p (Kruskal-Wallis)
EF, %	63,9±1,0 (59 – 70)	59,0±0,5 (55 – 66)	52,9±0,9 (45 – 64)	< 0,001
PASP, mm Hg	26,1±0,6 (11,5 – 18,2)	29,6±0,8 (22 – 36)	31,4±6,6 (23 – 37)	< 0,001
LVWT, mm	4,11±0,22 (2,9 – 5,5)	4,43±0,15 (3,2 – 5,8)	5,68±0,16 (3,4 – 6,9)	< 0,001
LVESS, mm	30,6±1,5 (21 – 39)	32,3±0,8 (24 – 45)	35,3±0,7 (28 – 47)	0,013
LVEDS, mm	45,3±0,9 (39 – 52)	50,5±1,0 (41 – 59)	50,8±1,3 (40 – 64)	0,036
RVESS, mm	21,9±1,3 (15 – 31)	31,4±0,6 (24 – 40)	35,8±0,7 (29 – 45)	< 0,001
IST, mm	8,2±0,3 (6,8 – 10,2)	11,5±0,3 (8 – 15)	12,5±0,4 (8 – 17)	< 0,001

As can be seen from the table, the thickness of the anterior wall of the right ventricle was within the norm in patients belonging to I and II FC, but this indicator fluctuated in the upper limits of the norm in patients belonging to II FC. It was these two criteria that were decisive in assigning patients to a certain FC. Right ventricular hypertrophy and dilatation started to increase markedly towards III FC. The thickness of the interventricular septum (IVS) was within the norm only in patients belonging to the I FC, its hypertrophy increased from the II to the III FC, the difference between the classes was statistically honest. The left ventricular end-diastolic diameter (LV EDD) indicator was normal on average. At the same time, a marked decrease in left ventricular EF from I FC to III FC was recorded. In patients with chronic destructive pulmonary tuberculosis, a significant increase in pulmonary artery systolic pressure (PASP) from I FC to III FC was recorded.

A comparative assessment of the diversity of ERF and central hemodynamic parameters depending on the functional class in patients with chronic destructive pulmonary tuberculosis is shown in graphic 1.



Graphic 1. ERF indicators in patients with chronic destructive pulmonary tuberculosis depending on FC

In patients with chronic destructive pulmonary tuberculosis, according to the functional class, as the pathological process worsens, we have recorded a tendency for the indicators of the external respiratory function to decrease, and even for acute noticeable disturbances.

We observed a significant decrease in VC and FVC from functional class I to functional class III (I FC – 96.4±0.5%, II FC – 66.9±1.4%, III FC – 59.7±1.6%, $p<0.001$, I FC – 92.4±0.8, II FC-66.9±1.3%, III FC – 48.4±1.5%, $p<0.001$). Also, a significant decrease of the FEV1 indicator from functional class I to functional class III was recorded (90.7±1.0%, 56.8±1.2%, 45.2±1.6%, $p<0.001$). In addition, a statistically significant decrease of the Tiffno index from functional class I to functional class III was observed (73.9±1.9%, 66.8±2.4%, 52.7±2.0%, respectively, $p <0.001$).

As it can be seen, from I FC to III FC, all the ERF parameters were recorded to decrease significantly.

24-hour ECG monitoring in FC-dependent patients with CDLTB. During ECG monitoring by the Holter method in patients with chronic destructive pulmonary tuberculosis depending on FC, it was determined that the degree of dysrhythmogenesis increases as FC increases. Only rare monotopic supraventricular and ventricular extrasystoles were found in patients belonging to I FC. Supraventricular extrasystoles prevailed in this group of patients. An increase in the number of supraventricular extrasystoles and high-grade frequent monotopic ventricular extrasystoles was recorded in patients belonging to II FC, but prognostically favorable arrhythmias dominated. In III FC, we recorded supraventricular and ventricular extrasystoles with the same percentage, and the frequency of occurrence of high and low gradation ventricular extrasystoles was the same. The frequency of supraventricular tachycardia is also increased. More intraventricular monofascicular blocks were recorded, which was associated with increased hypoxia and metabolic disturbances. From I FC to III FC, the number of patients with various arrhythmias and blockages increased.

Thus, from the results of our research, it can be concluded that during Holter monitoring, various types of disturbances of heart rhythm and conduction are detected 2 times more often than during conventional ECG. We determined that the degree of dysrhythmogenesis increases as the functional class increases: I FC - 85.7%, II FC - 90.0%, III FC - 100.0%. Only rare monotopic supraventricular and ventricular extrasystoles were found in patients belonging to FC I. Supraventricular extrasystoles prevailed. An increase in the number of supraventricular extrasystoles and high-grade dense monotopic ventricular extrasystoles was recorded in patients belonging to functional class II, but prognostically favorable arrhythmias dominated. In the III functional class, we recorded supraventricular and ventricular extrasystoles with the same percentage (69.4±7.7%- and 55.6±8.3%) and the frequency of high and low gradation ventricular extrasystoles was the same. The frequency of supraventricular tachycardia is also increased. More intraventricular monofascicular blockades (19.4±6.6%) were recorded by us, which is associated with increased hypoxia and metabolic disturbances. From functional class I to functional class III, the number of patients with various arrhythmias and blockages increased (21.4±11.0%, 60.0±8.9% and 63.9±8.0%).

Effectiveness of the treatment of patients with chronic destructive pulmonary tuberculosis. In the study, the effect of cardioselective β1-adrenoblocker Egilok (metoprolol) and Ethacyzine on the clinical status of patients with chronic destructive pulmonary tuberculosis, indicators of central hemodynamics and external respiratory function was studied. The reason we refer to them during the selection of drugs is that the application of β-blockers by several researchers is effective in both supraventricular and ventricular type heart rhythm disorders and has a preventive antifibrillation effect. The starting dose of Egilok is 25 mg per day. In the absence of bradycardia (less than 60 beats per minute), hypotonia (less than 100/65 in men, less than 95/60 in women) and deterioration of bronchial permeability, the dose of the drug was increased to 50 mg per day. Ethacyzine was prescribed at a dose of 50 mg 3 times a day.

Egilok and Ethacyzine in the indicated dose were assigned to 15 patients of II FC and 18 patients of III FC. Patients from the control group were not prescribed this drug.

Complaints and clinical status of both patients who received β-blockers as part of the treatment and included in the control group were evaluated before the start of the treatment and at the last visit to the doctor.

When evaluating the dynamics of complaints and clinical symptoms of patients with chronic destructive pulmonary tuberculosis belonging to the II-III FC against the background of treatment, we must admit that there was a significant clinical effect when taking Egilok (metoprolol) and Ethacyzin. It should also be noted that the positive effect of β-blockers has been recorded in terms of cardiovascular pathology.

Parameters of Holter monitoring. In the analysis of heart rhythm disturbances detected in patients belonging to II FC receiving Egilok and Ethacyzine, the effectiveness of treatment in patients with supraventricular extrasystole was 100%.

There was no change in the number of patients with ventricular extrasystole in the control group. Similar dynamics of rhythm disorders against the background of treatment were recorded in patients belonging to III FC.

Thus, in our study, high antiarrhythmic activity specific to the pharmacological class of Egilok (metoprolol) and Ethacyzin was demonstrated, which was manifested in both ventricular and supraventricular arrhythmias occurring in patients with chronic destructive pulmonary tuberculosis.

Central hemodynamic parameters. Based on the data obtained from EchoCG, during the study of the parameters of central hemodynamics, it was found that at the end of the observation period in both groups of patients belonging to the II FC, the systolic pressure on the pulmonary artery (PASP) decreased, more so in the main group, and it was higher. the decrease was in the main group (13.5%, $p0<0.01$), the difference between the groups was not significant. Nonsignificant increase in ejection fraction was recorded in both the control group and the main group. During the treatment,

the size of heart cavities and heart chambers changed nonsignificantly.

The similar dynamics were observed in patients with CDLTB belonging to III FC: a decrease in pulmonary hypertension in the form of a decrease in PASP was recorded in both groups, but this decrease was more pronounced in the treatment with Egilok and Ethacyzine. Thus, PASP decreased by 8.1% ($p0<0.01$) in the control group, and by 16.1% ($p0<0.001$) in the main group.

Thus, the inclusion of selective β-blocker Egilok (metoprolol) and Ethacyzin in the treatment scheme of patients with chronic pulmonary tuberculosis accompanied by destruction had a positive effect on central hemodynamics, in addition to the antiarrhythmic effect. This was manifested by the decrease in the level of pulmonary hypertension, the factor that promotes the development and progression of chronic lung-heart failure in patients from that category. Pulmonary hypertension, as it is known, acts as the main driving factor in the development and exacerbation of chronic pulmonary heart failure in patients of that category.

External respiratory parameters. Considering the long-term effect of β-blockers on bronchial β2-adrenoreceptors and the potentiation of bronchospasm, they have contraindications. As a result of the emergence of a new generation of β-adrenoblockers, which have a minimal effect on β2-adrenoreceptors, it was possible to prescribe them to patients with bronchial obstruction syndrome. In both groups of patients belonging to II FC, significant deterioration of ERF parameters was not recorded.

There was no significant difference between patients in the main group receiving Egilok (metoprolol) and Ethacyzin and those in the control group. In both groups, there was a trend of limitation of restrictive changes in the lungs and improvement of bronchial permeability against the background of treatment. Obstructive and restrictive disorders of lung ventilation were more prominent in patients belonging to the III functional class, indicators of external respiratory function did not worsen in both the main and control groups against the background of treatment.

On the contrary, most of the indicators improved: FEF $_{50}$ increased by 11.2% ($p<0.05$) in the control group, and by 11.9% ($p<0.05$) when receiving Egilok and Ethacyzine.

Of course, the improvement of some ERF indicators detected by us on the background of treatment was not related to the pharmacological effectiveness of the β-blocker, but to the conduct of broncholytic treatment during the observation period, as well as the constant and strict control over the regularity and adequacy of the treatment.

Thus, in our study, high antiarrhythmic activity of Egilok and Ethacyzin was demonstrated in relation to both ventricular and supraventricular arrhythmias in patients with CDLTB. In patients belonging to II and III FC group, during the use of Egilok and Ethacyzin, deterioration of bronchial permeability and worsening of restrictive disorders were not observed, which can be explained by the cardioselectivity of the drug.

CONCLUSIONS

1. Based on the results of echocardiography and daily ECG monitoring, various types of heart rhythm and conduction disorders were found in all patients with chronic destructive pulmonary tuberculosis. So, in accordance with the increase in the clinical-functional class, the percentage of dysrhythmogenesis increases, EF significantly decreases, PASP increases. [1,3,7,9,10,12,16,22,24,27].

2. According to the indicators of external respiratory functions, all patients belonging to I FC were within the norm, moderate bronchial obstruction and a tendency to decrease Tiffno index were noted in patients belonging to II FC, a decrease in VC and FVC indicators was noted in patients belonging to III FC [6,11,13,14,17,19,20,23,26,32].

3. When studying the functional state of the heart, central hemodynamics, external respiratory function in patients with chronic pulmonary tuberculosis accompanied by destruction, we have determined the interaction that allows us to divide them into 3 FC.These are criteria for a FC: the presence of various degrees of

respiratory failure, changes in spirography and echocardiography indicators, pulmonary hypertension [2,4,5,8,18,21,25].

4. The inclusion of selective β-adrenoblocker Egilok and Ethacyzin in the treatment scheme of patients with chronic pulmonary tuberculosis accompanied by destruction had a satisfactory effect on central hemodynamics in addition to the antiarrhythmic effect. Thus, EF increased by 7.6% and PASP decreased by 13.5% in II FC patients receiving egilok and ethacyzin. EF increased by 6.4% and PASP decreased by 10.1% in III FC patients receiving Egilok and Ethacyzin [15,28,29,30,31].

PRACTICAL RECOMMENDATIONS

1. Patients with chronic destructive pulmonary tuberculosis are more prone to cardiac rhythm and conduction disorders, especially those in higher functional classes. As a result, it is essential to extensively employ daily ECG monitoring in such cases.
2. The classification of patients based on specific functional classes enables a more accurate study of dysrhythmogenesis, correlating it with clinical and instrumental indicators.
3. It is advisable to use superselective β-adrenoblockers such as Egilok and Ethacyzine to regulate and normalize the frequency of cardiac contractions in cases of frequent, polytopic, and couplet supraventricular and ventricular extrasystoles, as well as during tachysystolic-type atrial fibrillation.

Published scientific works on the topic of the research:

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LIST OF ABBREVIATIONS USED

ATF	- adenosine triphosphate
ATF-ase	- adenosine triphosphatase
AV	- atrioventricular
BCF	- blood circulatory failure
CPHD	- chronic pulmonary heart
CDPTB	- chronic destructive pulmonary tuberculosis
ECG	- electrocardiogram
Echo-CG	- echocardiography
EF	- ejection fraction
ERF	- external respiratory function
FC	- functional class
FEF_{25}	- forced expiratory flow at 25% of the pulmonary volume
FEF_{50}	- forced expiratory flow at 50% of the pulmonary volume
FEF_{75}	- forced expiratory flow at 75% of the pulmonary volume
FEV_1	- forced expiratory volume in 1 second (FEV1)
FVC	- forced vital capacity
LVESS	- left ventricular end-systolic size
LVEDS	- left ventricular end-diastolic size
LVWT	- left ventricular wall thickness
MTB	- Mycobacterium tuberculosis
PASP	- pulmonary arterial systolic pressure
SVES	- supraventricular extrasystole
VC	- vital capacity
VES	- ventricular extrasystole

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