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THE EFFECT OF BETA BLOCKERS ON THE CLINICAL COURSE AND HEMODYNAMICS IN PATIENTS WITH DILATED CARDIOMYOPATHIES

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ABSTRACT

Dilated cardiomyopathy (DCM) is the most common (60% of all cardiomyopathies) and occurs in all countries of the world with a frequency of 5 - 8 cases per 100,000 population, in particular, 36 cases per 100,000 population are registered in the USA. DCM is a myocardial disease characterized by dilatation of the heart chambers, impaired contractile function, and progressive chronic heart failure (CHF). The criterion for disease is a decrease in the left ventricular ejection fraction below 45% and an increase in the size of the left ventricular (LV) cavity in diastole more than 6 cm (2013 ACCF / AHA Guideline for the Management of Heart Failure).

Key words: *Dilated cardiomyopathy (DCM),*beta blockers,angiotensin-converting enzyme,Carvedilol

INTRODUCTION

Dilated cardiomyopathy (DCM) is the most common (60% of all cardiomyopathies) and occurs in all countries of the world with a frequency of 5 - 8 cases per 100,000 population, in particular, 36 cases per 100,000 population are registered in the USA. DCM is a myocardial disease characterized by dilatation of the heart chambers, impaired contractile function, and progressive chronic heart failure (CHF). The criterion for disease is a decrease in the left ventricular ejection fraction below 45% and an increase in the size of the left ventricular (LV) cavity in diastole more than 6 cm (2013 ACCF / AHA Guideline for the Management of Heart Failure). The significant prevalence of CHF syndrome leads to high mortality among cardiac patients and requires extremely high treatment costs. The mortality rate is between 25% and 30% per year. Within 5 years after the diagnosis is established, 60-75% of patients with DCM die (Yu.M. Alekseeva et al. 2014). About 22 million people worldwide suffer from CHF syndrome, about 6.5 million people - in Europe, with an annual incidence of 580 thousand cases and an annual death rate of 300 thousand cases. In the USA, the total number of CHF patients is 5 million people (2.3% among the US population over 20 years old), with an annual incidence of 550 thousand cases and an annual mortality rate of more than 57 thousand cases. The main problem in the treatment of patients with CHF is the need for frequent hospitalizations associated with decompensation. So, over the past 25 years of the last century, the number of hospitalizations associated with CHF has increased 3 times. Due to the significant diffuse damage to the myocardium, its contractile ability decreases. A decrease in cardiac output leads to an increase in the residual blood volume in the ventricles, which leads to the development of CHF. In 60% of patients, parietal thrombi are formed in the ventricular cavities in the late stages of the disease, followed by the development of embolism in the small or large circle of blood circulation. DCM is accompanied, to a certain extent, by myocardial hypertrophy, which, however, does not reach a significant value and does not compensate for the violation of the systolic function of the ventricles.

Despite the increasing survival rates achieved with the help of new pharmaceuticals, the five-year mortality rate in patients diagnosed with HF is 50% (Mazur N.A., 2009), and most of the deaths occur suddenly and unpredictably. The main clinical syndromes of DCM are:

- CHF or asymptomatic left ventricular dysfunction. At first, signs of left and then right ventricular failure appear, which indicate a more serious prognosis. Signs of biventricular heart failure are observed at the time of diagnosis in 1/3 of patients.

- Arrhythmic syndrome - in almost 100% of patients. Any disturbances in rhythm and conduction are possible (sinus tachycardia, extrasystole, atrial fibrillation, atrioventricular blockade of 1 and 2 degrees, bundle branch blocks).

- Thromboembolic syndrome. With autopsy, left ventricular thrombi are found in 50% of patients.

- Painful cardiac syndrome - in 10 0% of patients. Patients develop prolonged pain in the left side of the chest and behind the sternum, often without a clear connection with physical activity. Pain reflects subendocardial ischemia associated with increased myocardial oxygen demand.

- Relative insufficiency of the mitral and tricuspid valves.

At the heart of all these clinical syndromes in the modern sense is the dyssynchrony of the heart, this is the dissociation of the contractions of its chambers and myocardial segments, due to impulse conduction disorders, which leads to a decrease in the pumping function of the heart and an increase in energy consumption by the myocardium. The main drugs for the treatment of heart failure are angiotensin-converting enzyme (ACE) inhibitors, beta-blockers (BB), diuretics, aldosterone antagonists, cardiac glycosides, angiotensin II receptor antagonists. The emergence and development of the theory of neuro-hormonal pathogenesis of heart failure has provided a rationale for the use of two groups of drugs that have great prospects due to their effect on the pathogenesis of ACE inhibitors and beta-blockers. Among the neuroendocrine changes observed in HF, stimulation of the adrenergic system occupies an important place. The study of BB revealed intra-group differences in drugs (selectivity, hydro / lipophilicity, presence / absence of internal sympathomimetic and membrane-stabilizing activity), which determined their different clinical efficacy in HF. Currently, only four drugs from the BB group are recommended for use in heart failure - bisoprolol, metoprolol succinate, nebivolol, carvedilol. Beta-blockers improve heart function, reduce the direct toxic effect of norepinephrine, reduce heart rate by lengthening diastole, and have an antiarrhythmic effect. Carvedilol, belongs to the third generation of adrenergic blockers, it acts on beta and alpha adrenergic receptors. Carvedilol reduces the preload on the heart, inhibits neurohormonal vasoconstrictive activation, has a long-term antihypertensive and antianginal effect, does not have its own sympathomimetic activity, inhibits the proliferation of smooth muscle cells, has antioxidant properties, which ensures its cardioprotective effect. The drug increases the ejection fraction, increases the functional class of heart failure.

THE AIM OF THIS STUDY

To reveal the effect of beta blockers on the clinical course and hemodynamics in patients with dilated cardiomyopathies ”.

To achieve the goal, the following research objectives were set:

1. Standardization of diagnostic approaches of dilated cardiomyopathy ECG, echocardiography, and determination of the functional class of heart failure.

2. To determine in terms of 6 and 12 months after the start of carvedilol therapy the number of patients (%) who improved their functional class of CHF and quality of life in the long term.

2. To study the dynamics of the duration of hospitalization and survival in patients with dilated cardiomyopathy;

3. To assess the dynamics of the risk of: the first hospitalization in patients with CHF with a wide QRS complex, sudden cardiac death of patients, taking into account the data of the functional status and blood coagulation system.

4. To evaluate the increase in ejection fraction and improvement in the quality of life of patients as a result of therapy with carvedilol, a selective aldosterone antagonist — eplerenone (layelon), and the use of a new oral anticoagulant rivaroxoban.

MATERIAL AND METHODS

This work will be based on the results of examination and treatment of 60 patients with clinical and instrumental signs of DCM, 3 with the simultaneous use of a new oral anticoagulant - rivaroxoban. All patients will receive conservative basic therapy with ACE inhibitors, β-blockers, glycosides, aldosterone antagonists.

At the first stage of the work, data from a survey of 60 patients with DCM associated with CHF will be analyzed. An assessment will also be made of the effect of the antcoagulant rivaroxaban on the processes of preventing thrombosis of the heart cavities, and on the correction and prevention of cardiac arrhythmias in patients with DCM, against the background of the ongoing standard conservative therapy of CHF.

Standard diagnostic methods will be performed, including complete blood count, urine analysis, biochemical blood tests: blood glucose, alanine aminotransferase, aspartate aminotransferase, creatinine, total cholesterol and its fractions: low and high density lipoproteins, triglycerides, blood coagulation system.

An electrocardiographic study will be performed to assess the amplitude-interval characteristics of each lead, rhythm and conduction disturbances, and measure the width of the QRS complex.

Echocardiographic examination of patients will allow determining the function of the left ventricle by measuring the end diastolic volume (EDV), end systolic volume (ESV) and ejection fraction (EF) based on the Simpson algorithm, the degree and volume of mitral regurgitation. Echocardiography will also reveal dilatation of the heart chambers, hypokinesis of the myocardial walls, insufficient (relative) atrioventricular valves, signs of circulatory failure, as well as assess LV systolic and diastolic function.

There will also be a 6-minute walk test and echocardiography (EchoCG) with measurement of the left ventricular ejection fraction in the dynamics of CRT.

RESEARCH RESULTS AND DISCUSSION

The efficacy of BB carvedilol in the complex treatment of patients with left ventricular systolic dysfunction with DCM will be studied in the immediate and long-term follow-up.

An approach to differentiated treatment of arrhythmic syndrome depending on the diagnostic parameters of LV diastolic and systolic dysfunction in patients with DCM will be proposed.

The parameters of LV systolic-diastolic dysfunction will be formed and substantiated, which may serve as criteria for the need to include rivaroxoban and a selective aldosterone antagonist - eplerenone in the complex therapy for the treatment of arrhythmic syndrome in patients with DCM.

The collected data on the improvement of the functional status, a decrease in the number of days of hospitalization for decompensation of heart failure, assessed by counting bed-days, 6, 12 months after the optimal drug therapy for DCM and severe heart failure, will reveal the effect and recommend it in practice. An ongoing positive response to combination therapy will improve the annual survival rate of patients.

CONCLUSION

The obtained data on the improvement of the functional status, a decrease in the number of days of hospitalization for decompensation of heart failure, assessed by counting bed-days, 6, 12 months after the optimal drug therapy for DCM and severe heart failure, will reveal the effect and recommend it in practice. An ongoing positive response to combination therapy will improve the annual survival rate of patients. The proposed method of DCM treatment will significantly improve the clinical and functional status of patients with congestive heart failure who initially have ventricular dyssynchrony. A significant decrease in the functional class of CHF, an increase in EF and an improvement in the quality of life will be demonstrated.

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