COMPARATIVE EVALUATION OF THE EFFECTIVENESS OF SPIRINOLACTONE AND EPLERENONE IN PATIENTS WITH DIFFERENT LEFT VENTRICULAR EJECTION FRACTION IN CHRONIC HEART FAILURE.

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ABSTRACT

In the article, the scientific literature confirming the effect of spirinolactone and eplerenone, belonging to the group of mineralocorticoid receptor antagonists, on the quality of life, the number of hospitalizations, the outcome of the disease, and the length of life of patients with chronic heart failure was studied, and the effects of these two drugs were comparatively evaluated.

Introduction. Chronic heart failure (CHF) is a pathophysiological condition in which the heart cannot meet the needs of tissue exchange due to impaired pumping function. According to the results of scientific research conducted in recent years, at least 26 million people are currently suffering from chronic heart failure [2]. The consequences of this disease are serious, and the average life expectancy of patients with SYY functional class (FC) III-IV is 3-8 years[13]. Despite the advances in modern medicine in the field of treatment and prevention, mortality and morbidity from this disease is still high. Statistical observations show that the number of patients with CHF will increase by 46% by 2030[2]. Prevention of such a negative growth creates the need for more in-depth research in the field of medicine.

The purpose of the study. Analysis and comparative evaluation of scientific studies on the effectiveness of spirinolactone and eplerenone in patients with different left ventricular ejection fraction in chronic heart failure.

The main part. CHF is a set of symptoms resulting from decompensated myocardial dysfunction, manifested by an increase in the volume of intercellular fluid, a decrease in perfusion of organs and tissues. The pathophysiological basis of this syndrome is that the heart cannot meet the metabolic needs of the body due to impaired pumping function. CHF has been treated for many years in two main directions: to eliminate the symptoms of the disease and to improve the quality of life of patients. Clinical symptoms of CHF are manifested by impaired blood pumping function of the left ventricle. New treatment guidelines are based on the degree of left ventricular ejection fraction impairment. The classification representing this indicator is as follows:

1. Reduced ejection fraction <40%;
2. Blood ejection fraction is between 41%-49%;

3. Ejection fraction preserved >50%[1].

Today, among several groups of drugs that have been proven to be effective in the treatment of CHF, attention has been paid to studying the effects of mineralocorticoid receptor antagonists (MRA) such as spironolactone and eplerenone. The main reason for this is the positive effect on the quality and length of life of these patients when the drugs of this group are used in the treatment of patients with CHF [6].

One of the factors underlying the mechanism of CHF development is aldosterone, a hormone secreted from the glomerular part of the adrenal gland, which ensures sodium reabsorption and potassium excretion in the renal tubules. Aldosterone secretion decreases renal perfusion, which in turn leads to synthesis of angiotensin II and activation of adrenocorticotropic hormone. The effect of aldosterone is caused by its binding to mineralocorticoid receptors in the endothelium of kidney tubules. Renine-angiotensin-aldosterone system (RAAS) and sympathoadrenal system are activated as a protective reaction in patients with CHF in the initial period, compensatingly eliminating hemodynamic disturbances[10]. In addition, activation of these compensatory mechanisms manifests itself in pathological processes. Direction of elevated aldosterone levels in serum of patients with CHF. Its concentration is responsible for recovery of negative clinical conditions, formation, retention of a lot of sodium and water in the body, endothelial dysfunction, hypertrophy of the left ventricle and fibrotic changes in the myocardium [5]. It can be seen that the concentration of aldosterone and angiotensin II in the blood has taken the state of death. Based on three mechanisms, the American College of Cardiology/American Heart Association (NYHA) guidelines for the management of heart disease recommend the use of MRA in patients with a left ventricular ejection fraction of 35% or less. In this case, the patient's indications should be examined: NYHA class II-IV symptoms, glomerular filtration rate >30 ml/min/1.73 m2 and serum potassium <5.0 mEq/L[18]. Myocardial remodeling is one of the main causes of the traumatic consequences observed in CHF. In the process of reconstruction, complex changes in the size, volume, cellular composition and functional state of the myocardium occur, resulting in hemodynamic and non-hemodynamic processes [15]. In addition, restructuring can lead to left ventricular systolic and diastolic dysfunction, heart palpitations, and atrial fibrillation [15]. Aldosterone plays a pathogenic role in the restructuring process. Intracardiac aldosterone secretion increases in patients with CHF. Intracardiac and plasma aldosterone correlates with the N-terminal end of procollagen III, a biochemical marker of myocardial fibrosis. This is the basis for describing aldosterone as a stimulator of the fibrosis process. Therefore, administration of MRA reverses the fibrosis process by correcting intracardiac aldosterone secretion[12]. Another cardiovascular effect of aldosterone is to modulate cardiac sympathetic nerve activity, which restores cardiac contractility (and cardiac response). Aldosterone helps rebuild the structure by checking the adergic effect, which leads to the heart[4]. In another study, hypersynthesis of the N-terminal fragment of procollagen III was detected after acute myocardial infarction with spironolactone. Spirinolactone, when used with AO'F inhibitors, has been shown to induce remodeling of the left ventricular myocardium after myocardial infarction. Similar products—myocardial physis contraction and reconstituted eplerenone—have also been observed in patients receiving angiotensin II receptor antagonists (ARA) [14]. Myocardial

fibrosis is known to be a source of ventricular arrhythmias. When spironolactone was given to a group of patients with ventricular arrhythmias, it was observed that the frequency of arrhythmias decreased[17]. MRA is performed nationally in patients with myocardial infarction, but also in the acute period of myocardial infarction. Eplerenone has been shown to improve outcomes in patients with ST-elevation acute myocardial infarction [16]. In the treatment of CHF, it may be necessary to use the drug due to the correction of long additional MRA examination defects. This prompted the selective creation of MRA. In 2011, eplerenone, a drug belonging to the MRA group, was recommended for the treatment of UTI. [9] According to the results of the EPHESUS randomized placebo-controlled study, in which the administration of eplerenone for 3 to 14 days in 6632 patients with acute myocardial infarction resulted in clinical manifestations of SYY FS I-IV. 15% of patients have a history of SII, and 7% of cases have already been hospitalized with SII. Patients receiving other potassium-sparing diuretics, patients with a plasma creatinine level of more than 220 μmol/l or a potassium level of more than 5.0 mmol/l were not included in the study. The majority of participants received optimal medical treatment for CHF, including beta-blockers (75%), diuretics (60%), aspirin (88%), and statins (47%). 45 patients underwent reperfusion therapy or revascularization. Eplerenone was administered at an average dose of 42.6 mg/day. Taking eplerenone resulted in a 15% qualitative reduction in overall mortality [8].

In one of the studies comparing the effectiveness of eplerenone and spironolactone, it was observed that the left ventricular ejection fraction increased by 6.2% after a 6-month course of treatment, and by 4.1% in the group treated with spironolactone[11]. In patients treated with spironolactone, gynecomastia was observed in 10.4%, dizziness in 11.4%, and mastalgia in 5.7%, while in patients treated with eplerenone, dizziness was observed in 3.9% of patients, and none of the examined patients had gynecomastia and mastalgia. [7].

Summary. The reviewed scientific literature indicates that the use of MRA in the treatment of patients with CHF reduces aldosterone-induced adverse effects such as excessive sodium and water retention, endothelial dysfunction, left ventricular hypertrophy, and fibrotic changes in the myocardium. by eliminating it, it has a positive effect on improving the quality of life of patients, reducing the number of re-hospitalizations and prolonging life. It is known from the comparative studies of the effectiveness of spirinolactone and eplerenone that the effectiveness of both drugs in the course of CHF and in the elimination of its symptoms does not differ. Nevertheless, the fact that eplerenone is a selective drug compared to spirinolactone prevents its side effects from appearing and makes it a preferable drug compared to spirinolactone.

References:

1. 2022 AHA/ACC/HFSA Heart Failure Guideline: Key Perspectives, Heidenreich PA, Bozkurt B, Aguilar D, et al. J Am Coll Cardiol. 2022 May, 79 (17) e263–e421.
2. Gianluigi savarese and Lars H Lund, Department of Medicine, Cardiology Unit, Karolinska Institutet, FoU Tema Hjarta och Karl, S1:02, 17176 Stockholm, Sweden. E: 2017, Radcliffe Cardiology.
3. González A, Ravassa S, López B, Moreno MU, Beaumont J, José GS, et al. Myocardial Remodeling in Hypertension. Hypertension (Dallas, Tex: 1979). 2018;72:549–58.
4. Khan, M.H., Gerson, M.C. Use of mineralocorticoid receptor antagonist in ST elevation myocardial infarction. J. Nucl. Cardiol. 29, 2336–2339 (2022).

5. King M, Kingery J, Casey B. Diagnosis and evaluation of heart failure. Am fam Physician. 2020 Jun 15;85(12):1161-8.
6. Kirichenko A.A. Cardioprotective effect of eplere- none. Consilium Medicum. 2018;20 (1): 15–20. Russian (Кириченко А. А. Кардиопротективные эффекты эплеренона. Consilium Medicum. 2018;20 (1): 15–20). DOI: 10.26442/2075.
7. Komajda M, Isnard R, Cohen-Solal A, et al. Effect of spirinolactone in patients with heart failure with preserved ejection fraction: the EDIFY randomized placebo-controlled trial. Eur J Heart Fail. 2017; 19:1495–1503.
8. Kovesdy C.P., Matsushita K., Sang Y. et al. CKD Prognosis Consortium. Serum potassium and adverse outcomes across the range of kidney function: a CKD Prognosis Consortium meta-analysis. Eur Heart J. 2018;39:1535–42. DOI: 10.1093.
9. Maryam Nabati MD Person Envelope Sasan Tabiban MD Afshin Khani MD Jamshid Yazdani MD Hamideh. The Effects of Spironolactone and Eplerenone on Left Ventricular Function Using Echocardiography in Symptomatic Patients With New-Onset Systolic Heart Failure: A Comparative Randomised Controlled Trial. Sep, 2021.
10. Matthew S. Durstenfeld, Stuart D. Katz, Hannah Park&Saul Blecker, 2019; Mineralocorticoid receptor antagonist use after hospitalization of patients with heart failure and post-discharge outcomes: a single-center retrospective cohort study.
11. Md. Noornabikhon Dokar, Khurshed Ahmed, Mohammad Ashraf Hossain Comparison between Spironolactone and Eplerenone on LV Systolic Function in Patients with Chronic Heart Failure.2, July 2020
12. Monticone S, D’Ascenzo F, Moretti C, Williams TA, Veglio F, Gaita F, et al. Cardiovascular events and target organ damage in primary aldosteronism compared with essential hypertension: a systematic review and meta-analysis. The lancet. Lancet Diabet Endocrinol. 2018;6:41–50.
13. Polyakov D. S., Fomin I. V., Belenkov Yu. N., Mareev V. Yu., Ageev F.T., Artemyeva E.G. et al. Chronic heart failure in the Russian Federation: what has changed over 20 years of follow-up? Results of the EPOCH-CHF study. Cardiology. 2021;61 (4): 4–14. Russian (Поляков Д.С., Фомин И.В., Беленков Ю.Н., Мареев В.Ю., Агеев Ф.Т., Артемьева Е.Г. и др. Хроническая сердечная недостаточность в Российской Федерации: что изменилось за 20 лет наблюдения? Результаты исследова- ния ЭПОХА–ХСН. Кардиология. 2021;61
14. Toda K, Kasama S, Toyama T, Kasahara M, Kurabayashi M. Effects of mineralocorticoid receptor antagonist eplerenone on cardiac sympathetic nerve activity and left ventricular remodeling after reperfusion therapy in patients with first ST-segment elevation myocardial infarction. J Nucl Cardiol 2021.
15. Tsai, CH., Pan, CT., Chang, YY. et al. Left ventricular remodeling and dysfunction in primary aldosteronism. J Hum Hypertens 35, 131–147 (2021).
16. Zhang M, Zhu P, Wang Y, Wu J, Yu Y, Wu X, et al. Bilateral sympathetic stellate ganglionectomy attenuates myocardial remodelling and fibrosis in a rat model of chronic volume overload. J Cell Mol Med 2019;23:1001-13.
17. Zhou M, Liu Y, Xiong L, Quan D, He Y, Tang Y, et al. Cardiac sympathetic afferent denervation protects against ventricular arrhythmias by modulating cardiac sympathetic nerve activity during acute myocardial infarction. Med Sci Monit 2019;25:1984-93.

18. Коваленко Е.В., Маркова Л.И., Белая О.Л. Антагонисты минералокортикоидных рецепторов в лечении больных с хронической сердечной недостаточностью: доказанная эффективность и перспективные возмож- ности. Международный журнал сердца и сосудистых заболеваний. 2022; 10 (34): 33–43.