

**CORONARY HEART DISEASE: EVALUATION OF EFFECTIVENESS**

**TELMISARTAN AND ENALAPRIL IN TREATMENT**

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**ABSTRACT:** The aim of the study was to study the effect of enalapril and telmisartan on hemodynamic parameters, diastolic function (DF) of the left ventricle (LV) in patients with coronary heart disease (CHD) with concomitant arterial hypertension. Material: 51 patients (men) with a stable course of coronary heart disease, the average age is 57.3±3.4 years. Methods: general clinical and laboratory studies, daily blood pressure monitoring, Holter ECG monitoring, echocardiography. Results and conclusions: course therapy with additional inclusion telmisartan (micardis) in patients with coronary heart disease with LV diastolic dysfunction by type of abnormal relaxation allowed to improve the parameters of transmittal diastolic flow: IVRT values decreased to 25%, DT – up to 13.4%, the E/A ratio increased to 23%. Improvement in diastolic function was accompanied by a decrease in LV myocardial mass index to 5.6%, a decrease in daily myocardial ischemia; improvement in LV systolic function was noted: an increase in LV ejection fraction to 9.6%, a fraction of systolic shortening anterior-posterior LV size by 17.2%. Significant differences between the groups of patients with diastolic dysfunction of the left ventricle are associated with the optimization of relaxation and conditions of filling of the left ventricle during early and late diastole.

**Key words:** coronary heart disease, diastolic dysfunction of the left ventricle, angiotensin receptor antagonists.

## INTRODUCTION

In heart disease, the main indicator determining its outcome is the degree of dysfunction of the heart muscle, which underlies the heart failure syndrome. However, if we take into account patients with asymptomatic left ventricular dysfunction, then we can talk about 11.7% of the population. CHF increases the risk of mortality by 4 times, the mortality rate of patients ranges from 15 to 50% during the year, it is patients with coronary heart disease with left ventricular dysfunction who have the worst survival prognosis. The continued increase in the prevalence of CHF it indicates an insufficient assessment of the functional state of cardiac patients with drug correction. In this regard, the blockade of RAAS is pathogenetically justified and promising, and the ability of the drug to have additional organoprotective effects can be regarded as one of the decisive conditions for choosing a treatment method. There is no clear answer to this question today. Indications for the use of angiotensin converting enzyme inhibitors (ACE inhibitors) and angiotensin II receptor antagonists (ARA) are identical. Both classes of drugs provide a reduction in blood pressure (BP), slowing the progression of chronic heart failure (CHF) and protection of target organs. However, in practice, ACE inhibitors are used much more often than ARA, since drugs of this class have been studied in more detail, are more familiar to doctors and are more accessible to patients. The purpose of the study: to study the effect of enalapril and telmisartan on hemodynamic parameters, diastolic function of the left ventricle (LV DF) in patients with coronary heart disease (CHD) with concomitant arterial hypertension (AH).

## MATERIALS AND METHODS OF RESEARCH

The study included men aged no older than 65 years with a stable course of coronary heart disease during the previous month, with echocardiographic signs of impaired diastolic function of the left ventricle by the type of abnormal relaxation, while the left ventricular ejection fraction should have been at least 45%. Exclusion criteria: grade 3 hypertension (blood pressure above 180/110 mmHg); presence of valvular heart defects; presence of chronic hepatic, renal insufficiency, presence of myocardial infarction or cerebral stroke less than 1 year old. To the study 51 patients were included, the average age was 57.3±3.4 years. Against the background of standard therapy (disaggregants, statins, nitrates), in the main group (n= 26), the drug of the ARA group – telmisartan was additionally prescribed, in the comparison group (n = 25) – the drug of the ACE group -enalapril. In choosing a comparison drug, we were guided by the recommendations, according to which enalapril is classified as an ACE inhibitor with the highest degree of evidence in the treatment of CHF. Blood pressure measurement for all patients (SAD and DAD) was performed in a sitting position after 10 minutes of rest on both hands, the average values of 3 measurements were taken into account. The TM-2425/TM-2025 (AND) kit was used for daily blood pressure monitoring (SMAD). According to the results of blood pressure monitoring, the average values were determined blood pressure per day, day and night; pressure load indicators (hypertension time index) per day, day and night; daily index (degree of nocturnal decrease BP), the daily variability of SAD and DAD. The state of myocardial contractility was assessed by the size of the ejection fraction (PV, %) and the degree of shortening of the anterior-posterior LV size in the systole (FS, %). Traditional methods of studying transmittal

flow and blood flow in the pulmonary veins were used to analyze LV DF. The control volume was placed at the level of the fetal tract of the left ventricle (LV) immediately above the place of closure of the mitral valve flaps and at the level of the confluence of the pulmonary veins into the left atrium. At the same time, the following speed and time indicators were recorded: maximum blood flow rate of early diastolic filling (E), maximum blood flow rate during atrial systole (A), blood flow deceleration time of early diastolic LV filling (DT), isovolumetric relaxation time (IVRT), E/A ratio, maximum blood flow rate in pulmonary veins, ratio of blood flow rates in pulmonary veins during systole and diastoles. By Echocardiography calculated the relative thickness of the walls LV (OTC), LV myocardial mass index (LVMI).

## THE RESULTS AND THEIR DISCUSSION

When analyzing the initial SMAD data, an increase in the average daily SAD was noted in both groups and DAD with a pronounced hypertension time index: accordingly, in the comparison group – 78.5 + 5.2 and 69.4 + 4.5%, in the main group – 80.4 + 5.3% and 66.7 + 3.4%. When assessing the circadian rhythm, a pathological profile (“non-dipper”, “night picker”) was detected in 71% of patients in the comparison group and in 72.7% of patients in the main group. The analysis of echocardiography data indicates the numerical values of the parameters of central hemodynamics and parameters of transmittal diastolic flow (TMDP) comparable by groups initially. After 24 weeks, SAD/DAD decreased to 14.4 + 3.5/3.6 + 1.1 mmHg in the enalapril application group, up to 21.3 + 5.1/5.0 + 1.3 mmHg in the main group (+telmisartan). In patients in the telmisartan group, a slightly more pronounced decrease in blood pressure was noted during the entire

study period than in patients in the enalapril group (the difference in the decrease in SAD/DAD is, on average, by 6.8+1.7 / 1.5+ 0.26 mmHg). By the end of the follow-up period in the main group, 84.6% (22) patients noted an improvement in exercise tolerance, a decrease in seizures angina pectoris and the amount of nitroglycerin intake, 15.6% (4) of patients indicated the absence of there are no obvious changes in the subjective state. In the comparison group, 72% of patients gave a positive subjective assessment of the change in physical status, 28% of patients characterized the condition as stable. Repeated studies of Holter ECG monitoring showed that after 24 weeks, the daily myocardial ischemia (SIM) in the telmisartan group decreased from 36.2 + 3.3 min to 15.3 + 2.1min with a significant decrease in the number of both painful, and pain-free episodes of ischemia. In the comparison group (+enalapril) we noted a decrease in SIM from 33.4 + 2.2 min to 24.5 + 3.1 min,  $p < 0.05$ , however, a decrease in the number of BEMS and BIM periods it was unreliable. After 24 weeks, against the background of therapy regimens with ace inhibitors and ARA, the obtained positive dynamics of the clinical condition of patients led to a change FC CHF. In the main group, the number of patients with CHF manifestations decreased from 50% initially to 19.2% at the end of the observed period,  $p < 0.01$ , while at the end of course therapy with telmisartan, there were no manifestations of CHF III FC in the observed patients. In the comparison group, the additional inclusion of enalapril improved the functional status of patients: the number of people with I and II decreased CHF FC, from 44% initially to 28% during therapy. In the main group, the positive effect of telmisartan on the left ventricular remodeling process was noted: a decrease in the final diastolic volume (BDO) and final systolic volume (CSR) by 10% and 13.9%, respectively, an increase in the ejection fraction by 10.6% at  $p < 0.05$ . The fraction of systolic shortening of the anterior-

posterior size of the left ventricle increased by 17.2%. Through 24 weeks of course therapy with telmisartan showed a decrease in the anterior-posterior size of the left atrium from  $40.33 \pm 0.34$  mm to  $37.2 \pm 0.21$  mm, which indicated a decrease in hemodynamic load on the left atrium. The results obtained, in our opinion, are due to an improvement in relaxation conditions, which we associate with a decrease in LV stiffness, an improvement in its filling conditions not only during early but also late diastole. The LV diastolic function is the LV's ability to relax and fully replenish its chamber during diastole. In coronary heart disease, such pathological processes as hypertrophy, fibrosis, and myocardial necrosis in patients Coronary heart disease reduces LV extensibility during diastolic filling. The results of experimental studies conducted in recent years, It has been shown that angiotensin II plays an important role in the development of interstitial myocardial fibrosis, which can directly stimulate collagen synthesis and inhibit the activity of collagenase, a key enzyme in the process of collagen breakdown. The result of increased angiotensin II formation may be myocardial fibrosis, which, in turn, worsens myocardial relaxation and left ventricular extensibility and leads to an increase in diastolic pressure at any fixed filling volume. Undoubtedly, the renin-angiotensin system plays a key role the role in the pathophysiology of diastolic dysfunction. Based on this, the use of ace inhibitors and ARA is justified – both classes of drugs provide not only a decrease in blood pressure, but also protection of target organs, slowing the progression of chronic heart failure. However, against the background of telmisartan, we obtained a significant improvement in indicators characterizing LV diastolic function: a decrease in IVRT up to 25% and DT up to 13.4%, increasing the E/A ratio to 23%. An indirect sign indicating a decrease in myocardial stiffness may be an increase in the fraction of systolic shortening of the anterior-posterior size of the left ventricle by 17.2%, while LVEF increased to 9.6%. In the comparison group (enalapril), the change in LV diastolic function was statistically insignificant, but we also did not notice a deterioration in myocardial contractility: the ejection fraction increased from  $52.0 \pm 2.9\%$  to  $54.9 \pm 1.7\%$ , a slight increase in the fraction of systolic shortening of the anterior-posterior size of the left ventricle from  $27.8 \pm 0.8\%$  to  $29.2 \pm 0.7\%$ .

## CONCLUSIONS

Thus, course therapy with the additional inclusion of telmisartan (micardis) in patients Coronary heart disease with diastolic dysfunction of the left ventricle allowed to improve the parameters of the transmittal diastolic flow: the values decreased IVRT to 25%, DT to 13.4%, the ratio increased E/A up to 23%. The improvement in LV diastolic function was accompanied by a decrease in LVH to 5.6%, a decrease in daily myocardial ischemia, while an improvement in LV systolic function was noted: an increase in LV ejection fraction to 9.6%, a fraction of systolic shortening of the anterior-posterior LV size by 17.2%. Significant differences in the background between groups of patients with LV diastolic dysfunction by the type of abnormal relaxation are associated with the optimization of relaxation and LV filling conditions during early and late diastole. The revealed positive changes in the parameters of central hemodynamics were accompanied by an improvement in the clinical condition of patients with coronary heart disease with signs of CHF, a decrease in the manifestations of CHF by 30.7%. Modern management of patients with coronary heart disease involves the use of a multicomponent therapy scheme, but in his practice, the doctor is guided by the provision that the treatment of the disease is aimed not only at reducing the severity of symptoms, but also at preventing complications, improving quality and increasing life expectancy. The data obtained make it possible to justify the use

of telmisartan in the treatment regimen of patients with coronary heart disease with diastolic dysfunction with preserved systolic function of the left ventricle, which is associated with the protection of target organs, primarily the heart, from progressive pathological changes.

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