



## LEFT VENTRICULAR DIASTOLIC DYSFUNCTION IN ISCHEMIC HEART DISEASE, EVALUATION OF THE EFFECTIVENESS OF MODERN THERAPY

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### Summary

To study the effect of azelsartan on hemodynamic parameters and left ventricular (LV) diastolic function in patients with coronary heart disease (CHD). Курсовая Course therapy with additional azel azelsartan administration in patients with CHD with LV diastolic dysfunction by the type of abnormal relaxation allowed to improve the parameters of transmitral diastolic flow: IVRT values decreased to 25%, DT-to 13.4%, and the E / A ratio increased to 23%. Improvement of diastolic function parameters was accompanied by a decrease in LV myocardial mass index and a decrease in daily myocardial ischemia. Significant differences between groups of patients with left ventricular diastolic dysfunction are associated with optimization of relaxation and left ventricular filling conditions during early and late diastole.

**Keywords:** coronary heart disease, left ventricular diastolic dysfunction, angiotensin receptor antagonists.

### Introduction

Recent studies дования по have shown that the presence of left ventricular diastolic dysfunction (LVDD) as one and/or several doppler echocardiographic патолоpathologic indicators has a significant prognostic value in patients with сердечно cardiovascular pathology, which increases with increasing LVDD. The main indicator that determines its outcome is the degree of heart muscle dysfunction, which underlies the syndrome of heart failure. However, if we take into account patients with asymptomatic left ventricular dysfunction, we can talk about 11.7% of the population [1]. The continuing increase in the prevalence of CHF indicates an insufficient assessment of the functional state of cardiological patients during drug correction. Indications for the use of angiotensin converting enzyme (ACE) inhibitors and angiotensin-II receptor antagonists (ARA) are identical [2,6,7]. However, in practice, ACE inhibitors are used significantly more often than ARA, since





drugs of this class are can be more thoroughly studied, more familiar to doctors and more accessible to patients.

### **Objective**

To study the effect of ramipril and azilsartan on hemodynamic parameters and left ventricular diastolic function in patients with coronary heart disease.

### **Material and Methods**

The study included patients aged no older than 65 years with a stable course of coronary artery disease during the previous month, with echocardiograph signs of left ventricular diastolic function impairment by the type of abnormal-relaxation, while the left ventricular ejection fraction should have been at least 45%. The study included 45 patients, average age  $55,3 \pm 2,4,4$  years. Against the background of standard therapy (disaggregants, statins, nitrates) in the main group (n=16) additionally

only the drug of the ARA – azilsartan group (Edarbi) was prescribed, in the comparison group (n = 11-5)-the drug of the ACE inhibitor group – ramipril (Amprilan). When choosing the drug, the patients were guided by the recommendations of the IOC, according to which ramipril is classified as an ACE inhibitor with the maximum degree of effectiveness in the treatment of CHF. A kit was used for daily blood pressure monitoring Holter ECG monitoring (XM ECG) was recorded using the Astrocord complex Astrocord.

Echocardiography was performed before the start of treatment and after 24 weeks on a LOGIQ-3 device using a 2.5-3.5 MHz sensor in M-modal and two-dimensional mode in standard echographic positions from parasternal access along the long axis of the heart in the patient's lying position on the left side according to the generally accepted procedure. The method. For the analysis of LV DF, traditional methods of studying transmitral flow and blood flow in the pulmonary veins were used. During echocardiography, the relative thickness of the LV walls (OTs) and the LV myocardial mass index (LVMI) were calculated. Statistical processing of the material was performed using the Microsoft Office Excel 7.0 program, as well as using the Statistica 6.0 application software packages using parametric and nonparametric methods of statistics, correlation analysis, Student confidence criteria, followed by determining the level of confidence of differences with a given 95% reliability level.





## Results and Discussion

As can be seen from Table 1, the maximum level of total cholesterol, triglycerides, LDL is observed in III group III, compared with the control and II groups. The triglyceride content in III group III exceeded the control value by 71%, in II group II by 44.4%. The LDL level in II group II exceeded the control group by 53.8%, the LDL content in III group III increased by 99.7% compared to the healthy group. HDL in groups II and III was reduced compared to the control group.

Table 1 Content of lipids and glucose in blood serum in practically healthy patients

Groups	Total CHOLESTEROL, mmol/l	Triglycerides, mmol/l	LDL, mmol/L	HDL, mmol/L	VLDL, mmol/l	Atherogen index, units
I Group I	4,6±0,1	1,5±0,1	2,6±0,2	1,4±0,1	0,4±0,1	2,8±0,3
II Group II	6.0±0.2	1.8±0,2	4,0±0,2	1,2±0,3	0,5±0,2	4,0±0,2
III Group III	6,8±0,3	2,6±0,1	5,2±0,3	0,9±0,4	0,7±0,3	5,2±0,2
P 1-2	P<0.001	P<0.05	P<0.001	P<0.05	P<0.05	P<0.01
P 1-3	P<0.001	P<0.001	P<0.001	P<0.05	P<0.05	P<0.001
P 2-3	P<0.05	P<0.001	P<0.01	P<0.05	P<0.05	P<0.001

When analyzing the initial ABPM data, an increase in average daily SBP and DBP was noted in both groups with a pronounced hypertension time index: 78.5 + 5.2 and 69.4 + 4.5% in the comparison group, respectively, and 80.4 + 5.3% and 66.7

+ 3.4% in the main group. When assessing the daily rhythm, the pathological profile was detected in 71% of patients in the comparison group and in 72.7% of patients in the main group. Analysis of EchoCG data indicates that the numerical values of central hemodynamic parameters and transmitral diastolic flow parameters are comparable in groups at baseline. After 24 weeks, SBP / DBP decreased to 14,4 + 3,5 / 3,6 + 1,1 mmHg in the ramipril application group, up to 1,3 + 5,1 / 5,0 + 1,3 mmHg in the main group. Patients in the azel sartan group showed a slightly more pronounced decrease in blood pressure during the entire study period than in patients in the ramipril group (the difference in SBP/DBP reduction in

average, by 6,8 + 1,7 / 1,5 + 0,26 mmHg). In the comparison group, 72% of patients gave



A positive subjective assessment of changes in physical status, 28% of patients described the condition as stable. Both groups included CHD patients with clinical signs of CHF. Against the background of the treatment, there was an improvement in the condition of patients, which was confirmed by a reliable decrease in the average score according to the Minneapolis questionnaire (MLHFQ): in the main group from  $24.5 \pm 3.0$  to  $14.0 \pm 1.5$  points,  $p < 0.05$ ; in the comparison group – from  $25.0 \pm 3.5$  to  $18.5 \pm 1.5$  points. After 24 weeks on the background of therapy regimens with ACE inhibitors and ARA, the positive dynamics of the clinical condition of patients led to a change in the FC of CHF. In the main group, the number of patients with manifestations of CHF decreased from 50% at baseline to 19.2% at the end of the observed period,  $p < 0.01$ , while no manifestations of FC III CHF were registered in the observed patients at the end of the course of azelabir-tan therapy. In the comparison group, the additional inclusion of ramipril improved the functional status of patients: the number of patients with FC I and II CHF decreased, from 44% at baseline to 28% during therapy. In the main group, a positive effect of azelsartan on the left ventricular remodeling process was noted: a decrease in the final diastolic volume and final systolic volume by 0% and 13.9%, respectively, and an increase in the ejection fraction by 10.6% at  $p < 0.05$ . The left ventricular rate increased by 17.2%. After 24 weeks of azilsartan therapy, the average posterior size of the left atrium decreased from  $40.33 \pm 0.34$  mm to  $37.2 \pm 0.21$  mm, which indicated a decrease in the hemodynamic load on the left atrium. A study of LV DF parameters after 24 weeks of treatment with azilsartan revealed a decrease in time delay of early left ventricular diastolic filling DT from  $271.0 \pm 12.4$  ms to  $238.7 \pm 8.3$  ms,  $p < 0.05$ . There was also an increase in the maximum blood flow rate during early LV diastolic filling ( $p < 0.03$ ), the value of the E/A TMDP ratio increased from  $0.69 \pm 0.03$  to  $0.93 \pm 0.04$  ( $p < 0.02$ ), and the time of left ventricular isovolumic relaxation (IVRT) decreased by 25%. The results obtained, in our opinion, are caused by an improvement in relaxation conditions, which is associated with a decrease in LV stiffness, an improvement in the conditions of its filling not only in the period of early but also late diastole. The result of increased angiotensin II production 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. 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, with azelsartan, we obtained a significant improvement in LV diastolic function parameters: a decrease in IVRT to 25% and DT to 13.4%, and an increase in the E/A



ratio to 23%. In the comparison group, the change in left ventricular diastolic function was statistically insignificant, but we did not notice any deterioration in myocardial contractility: the ejection fraction increased from  $52.0 \pm 2.9\%$  to  $54.9 \pm 1.7\%$ , and a slight increase in the fraction of systolic shortening of the anterior-posterior left ventricular size from  $27.8 \pm 0.8\%$  to  $29.2 \pm 0.7\%$ . In the azel sartan group, after 24 weeks of therapy, we noted a significant decrease in LVMI from  $131.02 \pm 4.2$  to  $124.4 \pm 4.3$  g / m<sup>2</sup>,  $p < 0.05$ , and OTC from  $0.46 \pm 0.02$  to  $0.42 \pm 0.03$ . The increase in LVMM is based not only on cardiomyocyte hypertrophy, but primarily on remodeling of the myocardial collagen network in the early stages, which increases the rigidity of the heart wall and contributes to the formation of diastolic dysfunction [2, 11]. The obtained data suggest that selective blockade of the activity of tissue RAS plays an important role in the restoration of LV DF. Thus, the favorable pharmacological effects of ARA consist of a direct blocking effect on AT<sub>1</sub> receptors and an indirect stimulating effect on AT<sub>2</sub> receptors.

In practice, the doctor's interaction with the patient is complex and is determined by several groups of factors, including the patient's desire to follow medication prescriptions. High treatment compliance is ensured by safety and good tolerability, as well as the absence of adverse reactions. In the comparison group (ramipril) side effects in the form of a cough reflex were noted in 2 patients (8%), minor headache was indicated in 1 (4%) patient-headache that occurred 1 hour after taking the drug and passed in 2-3 hours without taking additional painkillers.

## Conclusion

Thus, a course of therapy with additional V treatment with azel sartan in patients with CHD with left ventricular diastolic dysfunction- improved the parameters of transmitral diastolic flow: IVRT values decreased to 25%, DT to 13.4%, and the E/A ratio increased to 23%. Improvement in LV diastolic function was accompanied by a decrease in LVMI to 5.6%, a decrease in daily myocardial ischemia, and an improvement in LV systolic function was noted: an increase in the LV ejection fraction to 9.6%, and the 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 relaxation optimization and LV filling conditions during early and late diastole. The obtained data allow us to justify the use of azel sartan in the treatment regimen of patients with CHD with diastolic dysfunction with preserved left ventricular systolic function, which is associated with the protection of target organs, primarily the heart, from progressive pathological changes.





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