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THE EFFECTIVENESS OF SARTANS AND ACE INHIBITORS IN ACUTE MYOCARDIAL INFARCTION ON THE BACKGROUND OF HYPERTENSION DISEASE

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ABSTRACT

Mortality and disability of the population from coronary heart disease (CHD), in particular from acute myocardial infarction, remains the most urgent public health problem worldwide. The wide prevalence, severity of the course, high disability of patients indicate the importance of timely diagnosis and effective treatment of this disease [1,2,3]. However, despite the progress in diagnosis and treatment, acute myocardial infarction (AMI) retains the first place in the structure of mortality and disability in the population of economically developed countries, including our country. The level of lethality and disability in this disease is largely determined by the size of the lesion [4,5].

Myocardial infakt (MI) is one of the main causes of heart failure (HF). Patients who survive the acute stage of MI remain at high risk of developing HF. In 25% of patients, HF develops during the first 10 years after MI.

The problem of rational pharmacotherapy of AMI attracts attention due to a number of reasons. There are a huge number of drugs and non-drug treatments used in the treatment of AMI patients. But often there is no objective information about the comparative effectiveness of various drugs and treatment regimens. Endothelial dysfunction is the first link in the pathophysiology of the cardiovascular-renal continuum, which is based on progressive vascular damage [6], aggravated by the action of risk factors, in particular, arterial hypertension (AH) and leading to renal and heart failure and death [7] . Blockade of the renin-angiotensin-aldosterone system (RAAS) with ACE inhibitors and sartans and elimination of the negative effects of angiotensin II is a rational approach to achieving regression of endothelial dysfunction [7,8].

Despite the fact that all ACE inhibitors have the same mechanism of action, they differ in data on improved prognosis (STUDIES ELITE, RESOLVD, ValHeFT, CHARM), which to date should be considered the most compelling reason for their use in clinical practice[8]. Differences in pharmacokinetic and pharmacodynamic characteristics of ACE inhibitors may cause differences in the effectiveness of drugs within the class. The results of the HOPE study and EUROPA, PEACE testified to the effectiveness of the use of perindopril in reducing the risk of complications of cardiovascular diseases (CVD).. The SMILE study proved the effect on the prognosis of zophenopril in patients with MI. However, despite the advantages of ACE inhibitors in the long-term therapy of CHF, when using these drugs, the level of angiotensin II remains high. I in angiotensin II [9]. These facts served as a starting point for clinical studiesof angiotensin receptor inhibitors.

Recently, data on additional metabolic and organoprotective properties of the two most important competing groups of cardiovascular drugs have begun to appear.

PURPOSE OF THE STUDY

On the effectiveness of sartans and ACE inhibitors in acute myocardial infarction against the background of hypertension

MATERIALS AND METHODS OF RESEARCH

The work is based on clinical observations and studies performed on the basis of the cardiology department of the City Clinical Hospital No. 7 in Tashkent. The work was a retrospective study of patients admitted to the City Clinical Hospital No. 7 in Tashkent with IM. Patients of both sexes were included. As a result of screening patients in accordance with the criteria, 631 of them were included in 546 patients with MI against the background of hypertension. The open randomized prospective comparative study included 141 patients with an established diagnosis of AMI and HYPERTENSION. The study did not include patients older than 80 years, with the phenomena of decompensated hepatic and renal failure, decompensation of diabetes mellitus, chronic heart failure (CHF) of more than stage III and III FC at the time of admission to the hospital. Randomization of patients was carried out random choice. Group 1 - 66 patients receiving losartan in an average daily dosage of 61.9±32.5 mg (losavin, "British fharm", India), group 2 - 75 patients - enalapril in an average daily dosage of 6.5± 2.0 mg (berlipril, "Berlin-Chemie", Germany).

The selected groups were comparable in initial characteristics (sex, age, premorbid background, myocardial lesion volume, degree of hypertension, concomitant pathology), in the level of reduction in the number of heartbeats (heart rate).

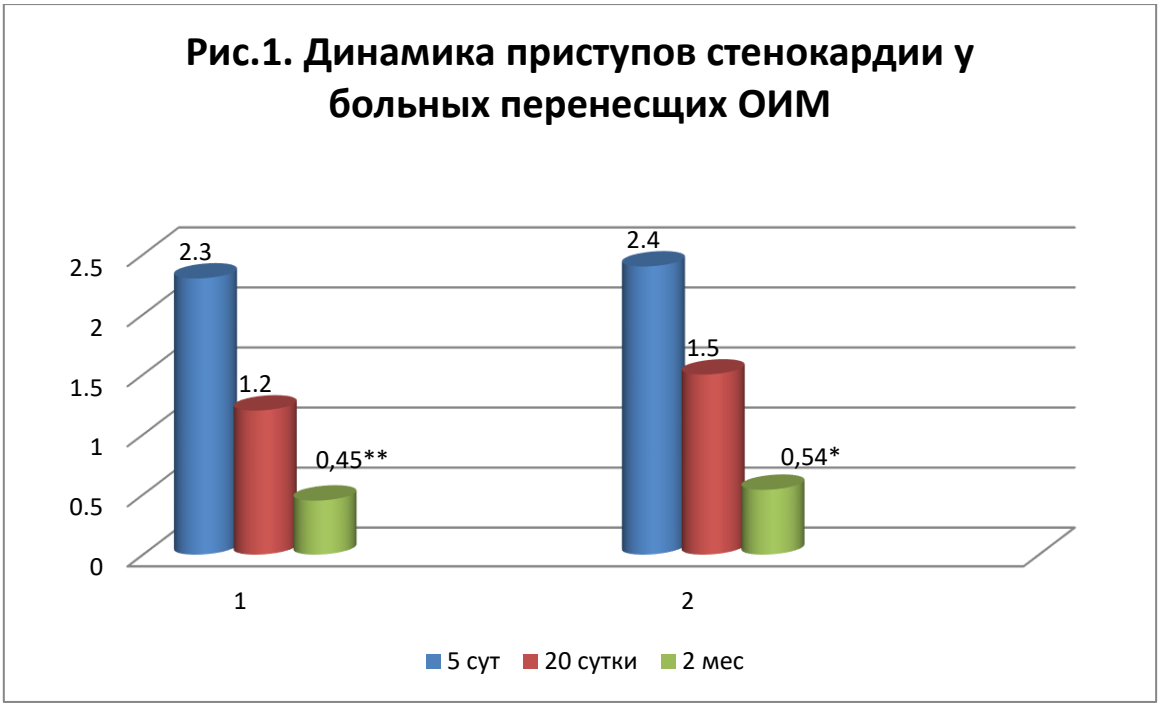
All patients received standard therapy for 2 months (including ß-blockers in 21.1% of cases, statins - 29.6%, disaggregants - 82%, diuretics - 31%, calcium antagonists - 15%, retard forms of nitrates - 64.74%). Patients of group 1 received losavin in an average daily dosage of 61.9 $\pm$ 32.5 mg, group 2 received berlipril - 6.5± 2.0 mg. For all patients, a survey, questionnaire, comprehensive examination and prospective analysis of medical histories were conducted. A comprehensive examination included stratification of risk factors: measurement in the dynamics of blood pressure, heart rate, urinalysis, complete blood count, biochemical blood test (including: lipid spectrum, coagulogram, troponin I, indicators of the antioxidant system of the blood, electrocardiogram (ECG), echocardiogram (Echocardiography). All patientswere evaluated within 5 days from the moment of admission and after 2 months. For 2 months, dynamic telephone monitoring of the patients' condition, taking medications, visiting the clinic 3 times, keeping patients' diaries of self-control was constantly carried out.

Methods of statisticalanalysis of the results of the study were performed using the package of applied statistical programs MEDIOSTAT. Standard methods of variational statistics were used: calculation of the average, standard deviation (M±m), Student's criteria ($p<0.05$).

THE RESULTS OF THE STUDY AND THEIR DISCUSSION

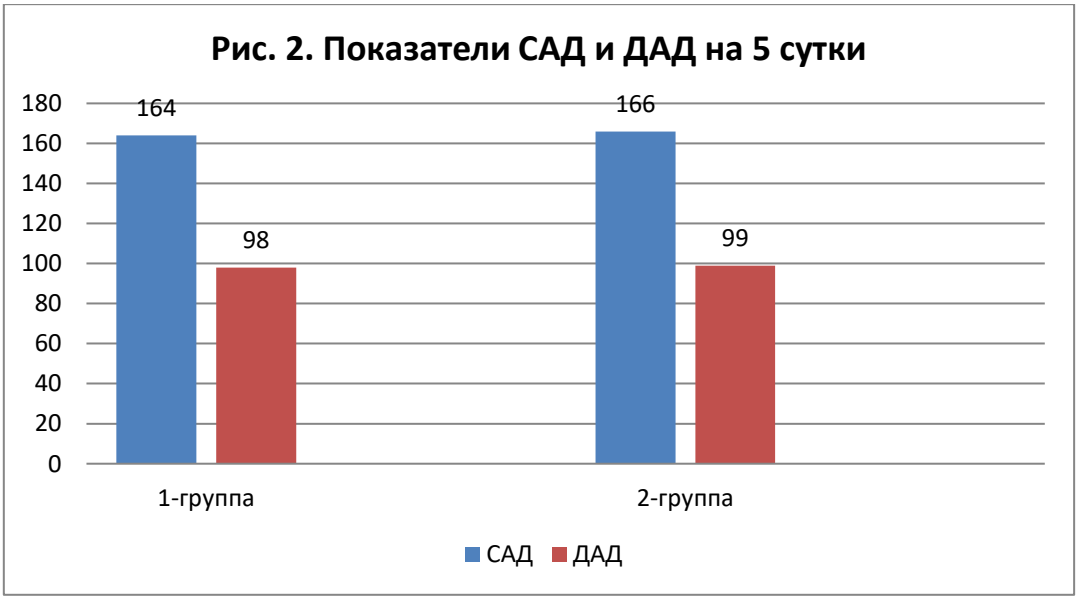
For the quality of life, it has a subjective assessment of anginal manifestations by patients. During inpatient treatment, on the 5th day from the moment I was includedin the study, 20-25 days, 2 months of eggs after the development of AMI, patients analyzed the number of pain attacks during the day or sensations of discomfort behind the sternum, in the region of the heart, which caused anxiety or required nitroglycerin. In both groups, patients noted a decrease

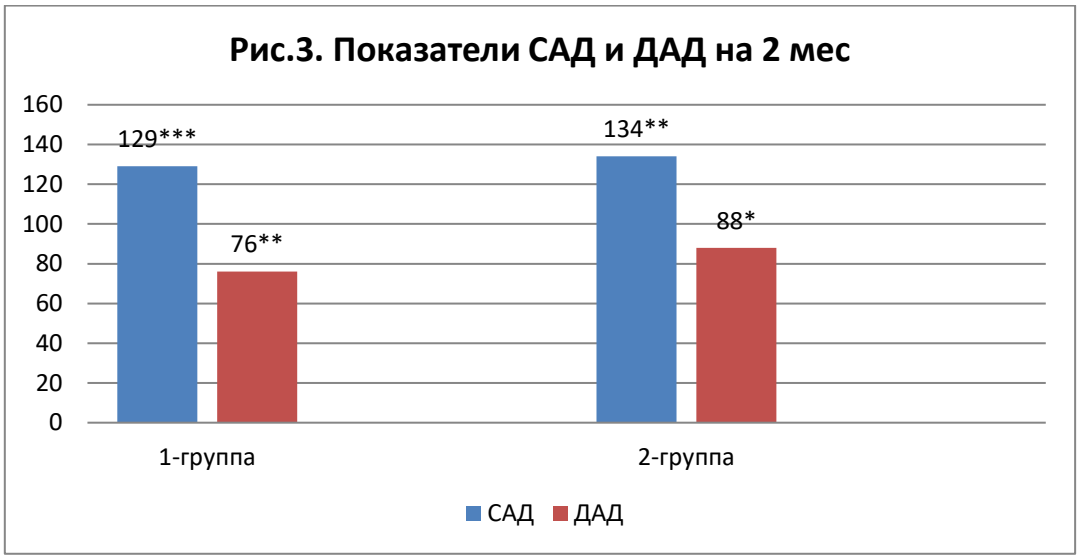
in anginal manifestations, a slightly lesser antianginal effect of therapy was noted in group 2 (rice. 1).



Note: Reliability of differences with respect to reference values p*>0.05; p** >0.01.

One of the most important factors damaging the endothelium is hypertension. In patients who underwent MI, upon admission, systolic blood pressure (SBP) and diastolic blood pressure (DBP) were high (Fig. 2). For 2 months. observation, all patients kept diaries of self-control with a reflection of blood pressure, heart rate and well-being. Comparison of average SBP indicators to 20-25 days and 2 months. , revealed a significant advantage in the hypotensive effect of losavina, to a significantly lesser extent compared to it - berlipril (Fig. 3).





*Note: p***<0.001; r**<0,01 *; p <0.05 compared to baseline values*

In the 1st group, the decrease inthe SDA was 27% (p<0.001), and in the 2nd group 23% (p<0.01). The DDA indicator in the 1st group of sniis squeezed by 29% (p<0.01), by 12% (p<0.01) in the 2nd group of the study.

The average day and night heart rate at the beginning and end of the studydoes not differ between the groups studied.

Table 1. Indicators of activity of the POL-AOS system, the ratio of POL / AOS in the blood serum of patients with AMI (M±m)

Group	MDA, nmol/L	SOD , UE/ml	CT, mkkat/min/l	PAUL/AOC
1-группаN=66	8,5±0,20*	1,44±0,03*	14,0±0,17*	6,70±0,30**
2-группаN=75	9,3±0,8*	1,4±0,21*	14,5±1,6*	7,1±0,7**
Control group, n = 20	3,3±0,08	2,4±0,03	16,9±0,16	2,2±0,1

*Note. *p< 0.05;**p < 0.01 confidence differences compared to the control group. MDA-malondialdihyde, SOD-superoxide dismutase, CT-catalase.*

In both studiedgroups, the MDA indicator increases by 37% and 37% (p<0.05) in relation to control. The ratio of POL / AOS, also in both groups, is almost the sameas the increase in comparison with the control group (33% and 31%) (p<0.05).Along with the increase in the above indicators, there is a decrease in ODS (60% and 50%) (p<0.05), as well as CT (33% and 31%) (p<0.05).

Thus, in patients with AMI in the blood serum, the intensification of POL is due to a significant inhibition of the activity of AOS enzymes - SOD and CT.

Table 2 Resource requirements by subprogramme

Indicators of activity of the POL-AOS system, the ratio of POL / AOS in the serum of patients with AMI for 2 months of the study (M±m)

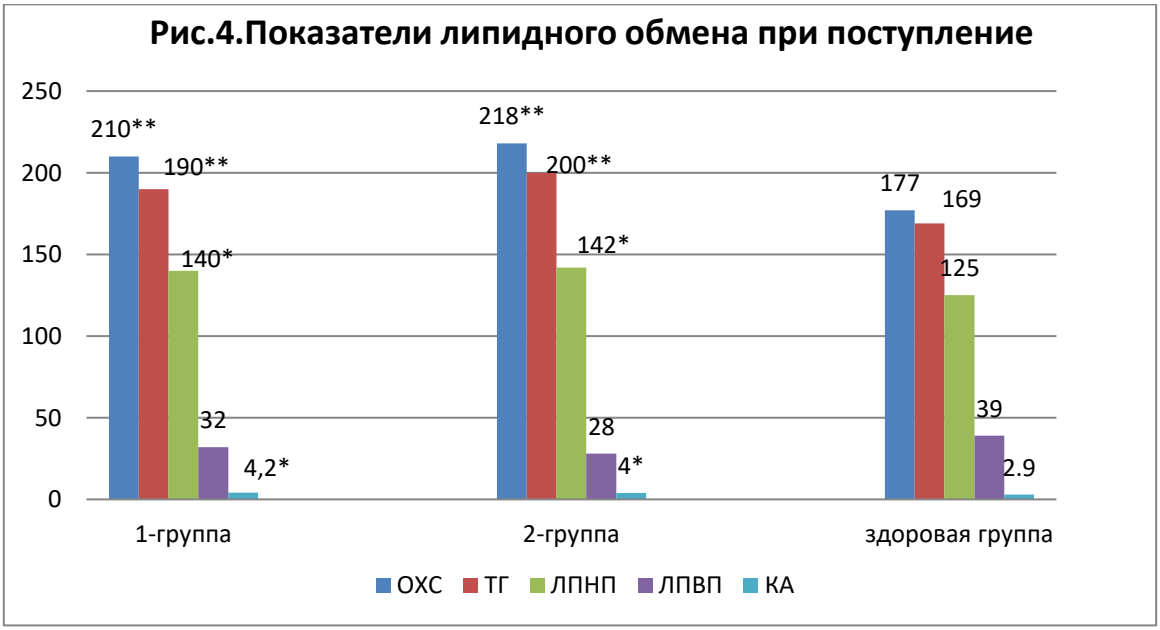
Group	MDA, nmol/L	SOD , UE/ml	CT, mkkat/min/l	PAUL/AOC
1-группаN=66	5,0±0,07**	1,66±0,03	15,99±0,57	3,32±0,07**
2-группаN=75	6,36±0,12*	1,67±0,02	15,82±0,55	4,21±0,26*
Control group, n = 20	3,3±0,08	2,4±0,03	16,9±0,16	2,2±0,1

*Note. *p< 0,05; **p < 0.01 confidence compared to the control group.*

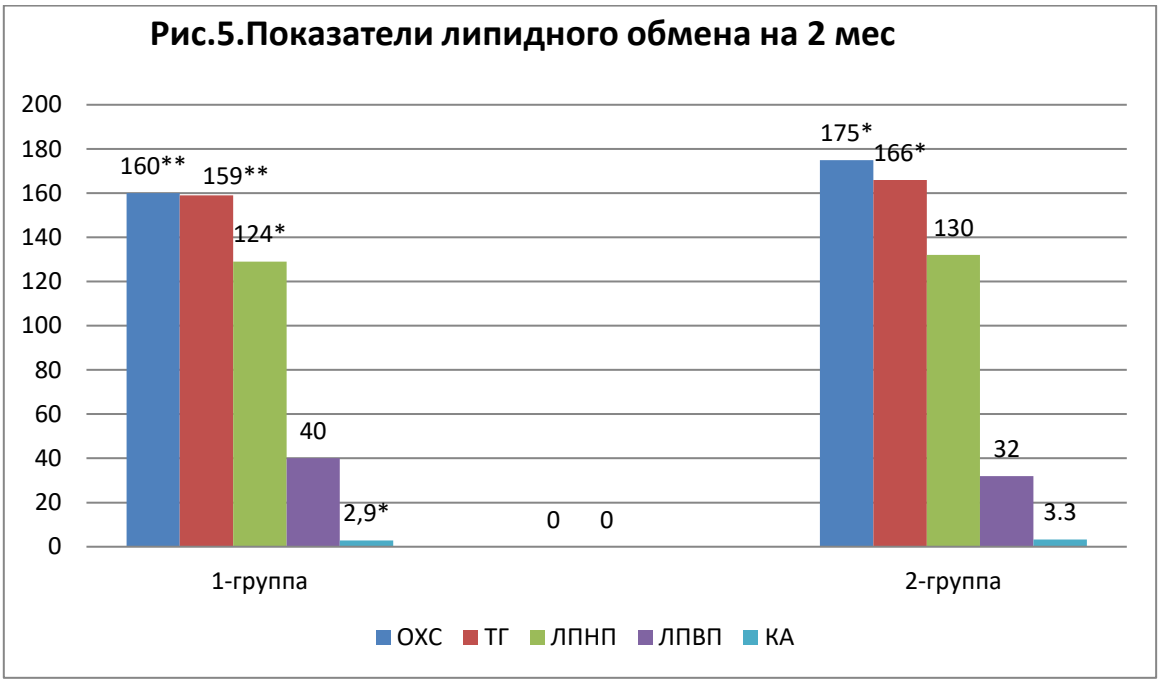
In our research for 2 months. therapy in group 1, the level of MDA in the blood serum decreased by 59% (p<0.01), and in group 2 - by 35.5% (p>0.05).Consequently, berlipril and losavin reduce the processes of free radical oxidation in the blood of patients with AMI, which is undoubtedly of fundamental importance for improving the functional activity of the NO system. It was found that losavin to a greater extent than berlipril inhibited the activity of the POL process, and consequently, free radical oxidation in the body of patients. One of the reasons for the decrease in the activity of the POL process in the body of patients with AMI was the activation of anti-radical protection enzymes - SOD and CT.

Studies have shown thatthe activity of SOD in the blood of patients with AMI who took berlipril and losavin is relatively increased and the results do not differ in statistical reliability. A similar picture can be traced from ct.

Studies of the integral index of POL / AOS reveal a more reliable positive dynamics in the group of patients who received losavin (Table No. 2).

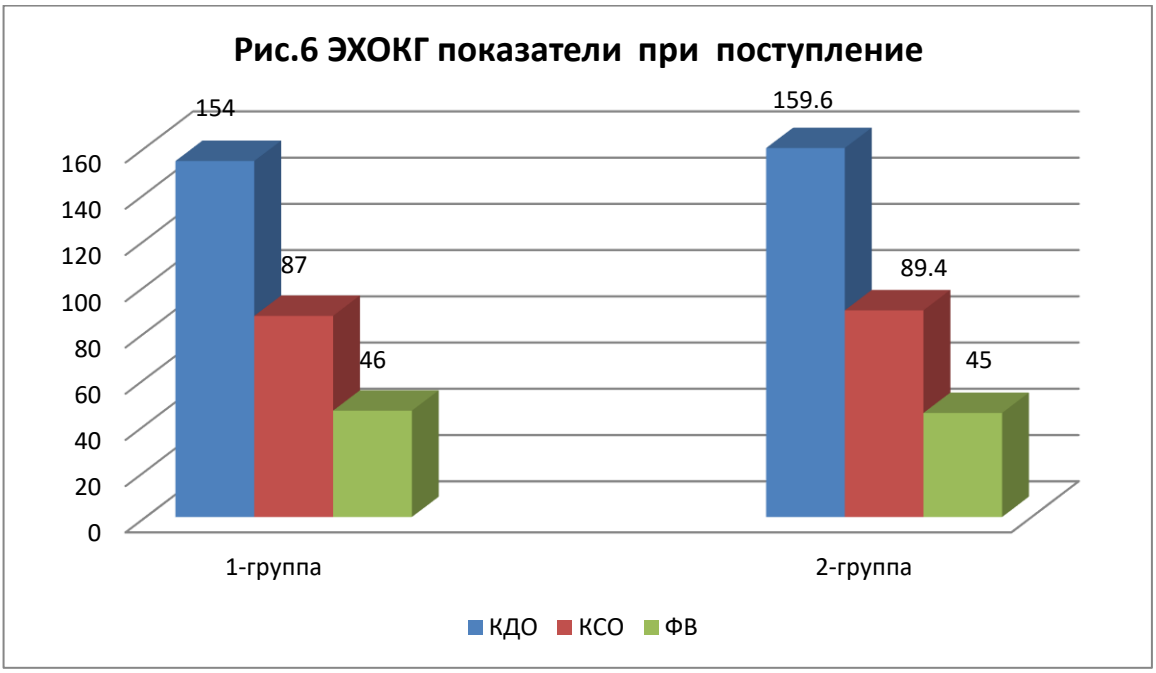


Note: p**<0.01; p* <0.05 compared to baseline values. *OH-total cholesterol, T-triglycerides, HDL-high-density lipoproteins, very low-density VLDL lipoproteins, low-density LDL lipoproteins, CA-atrogenicity coefficient*



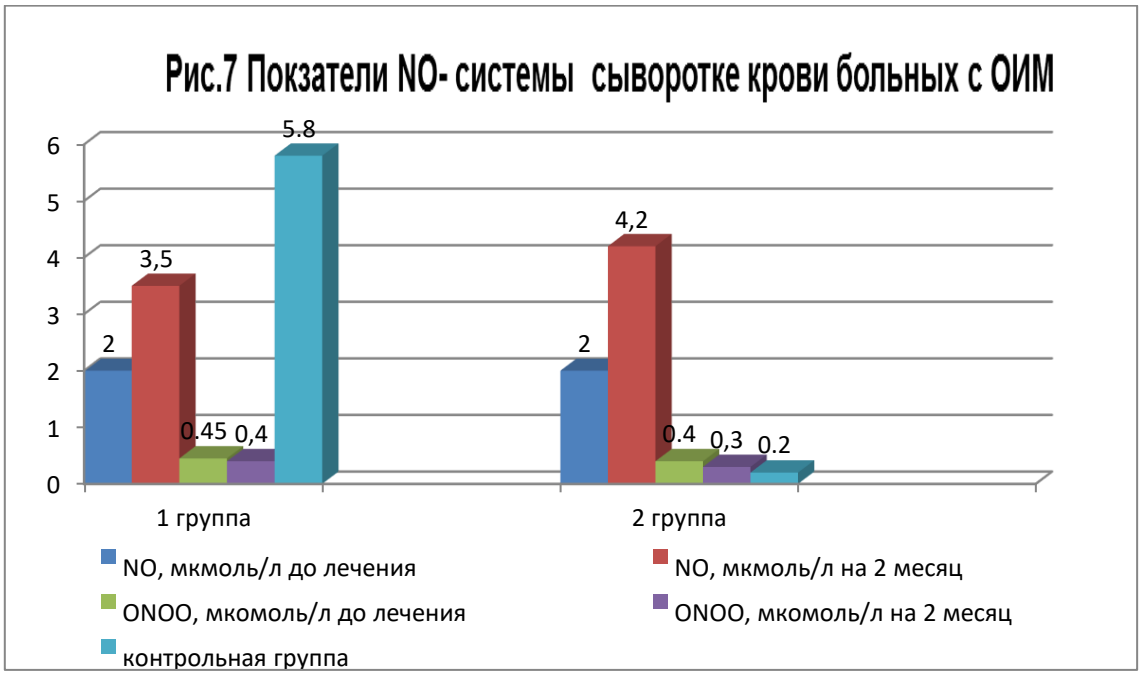
Note: p**<0.01; p* <0.05 confidence of differences between groups. *OH-total cholesterol, T-triglycerides, HDL-high-density lipoproteins, very low-density VLDL lipoproteins, low-density LDL lipoproteins, CA-atrogenicity coefficient*

There is a positive trend in both groups for 2 months, in relation to blood lipids in patients with MI, which are characterized by a decrease inm with the possession of OCHS (31% p<0.01; 24.5% p<0.01), TG (19.5%p<0.01; 20,0% p<0.05) LDL (13.% p<0.05; 9% unreliable (ND)).
All patients on the 5th day from the moment of admission and after 2 months performed Echocardiography. Echocardiography, which is given a paramount role in the diagnosis of MI and CHF, due to its ease of implementation, safety and ubiquity. This imaging technique allows you to solve the main diagnostic task - to clarify the very fact of dysfunction and its nature, as well as to conduct a dynamic assessment of the state of the heart and hemodynamics. In numerous studies, it has been proven that in patients with AMI there is a pronounced dilatation of the left ventricletoa (LV).
In our study, the initial volume parameters of the LV did not significantly differ between the comparative groups. The final systolic volume (CSR) in group 1 of studies was 89.41±1.4 ml and in the 2nd group 87.07±1.7 ml;, and the indicator of final diastolic volumea (CDO) in group 1 1 59.6±2.101 ml and in group 2 154.45±2.161 ml . The data are presented in Fig. 6. The most important hemodynamic parameter is the left ventricular ejection fraction (LV FV), which reflects the contractility of the LV myocardium. As an indicator with a high probability indicating the preservation of systolic function, we can recommend the level of LV FV ≥ 50%, calculated by the method of 2-dimensional Echocardiography according to Simpson. The degree of decrease in LV FV is associated with the severity of systolic dysfunction, is used to determine the risk of surgical treatment; the dynamics of LV FV is an indicator of the progression of the disease and the effectiveness of therapy, low LV FV isa marker of a negative prognosis.
In our studies in patients with AMI, the FB index was 45.21±0.54 (group 1), 46.14±0.61% (group 2), no differences between groups were detected (Fig. 6).



At the 2nd month of therapy in groups 1 and 2, there is a significantly less significant decrease in CDO, CSR and an increase in FV.

Analysis of the results showed that both berlipril and losavin in patients with AMI lead to an increase in serum of the main METABOLITES of NO. Thus, after 2 months of serum berlipril therapy, the activity of the NO complex increased by 49% ($p>0.05$). When taking losavin50.0% ($p>0.05$) in relation to To the original value. (fig.7).



However, in patients in both groups, the level of NO still remained significantly below control. There was a decrease to ONOO oncentration by 29% ($p<0.05$) in the first group and by 11% ($p<0.05$) in the second group.

Thus, 2 months of therapy with berlipril and losavin, against the background of basic therapy, showed effectiveness in relation to the development of regression of the pathological process, an increase in AOS, a decrease in the activity of the POL process, a decrease in the fraction of atherogenic lipids, an improvement in endothelial dysfunction and the restoration of secretions. attic capacity of the myocardium. According to our research, the dynamics of MI who took lo savin are more pronounced and reliable dynamics were revealed in PATIENTS taking losavin.

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