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The Effect of the Combined Use of Mechanical and Drug Revascularization in Acute Coronary Syndrome in Patients Working in Environmentally Polluted Conditions

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Abstract: The aim of the study was to evaluate the effect of the complex use of cardiotex (meldonium), obzidan (propranolol), cyto-mac, cardiket, preductal OD, ARBII, in combination with percutaneous intervention (PCI) and separately performed PCI on ecoendotoxicosis (AMP), on hemodynamics, cardiodynamics and clinical course of non-ST elevation acute coronary syndrome (NSTE ACS). The results of complex medical and mechanical revascularization and separately performed PCI were compared. The study included 63 patients with NSTE ACS aged 35 to 65 years (56.7 ± 1.20) (50 (79.4%) men, 13 (20.6%) women) and randomized into 3 groups (21 people each). 1st group got cardiotex, cyto-mac, obzidan (propranolol) were given anti-ischemic, isosorbidedinitrate (cardiket), antihypoxant - a biologically active food supplement vascard and PCI was performed. In group 2, cytomac and obzidan (propranolol), cardiotex were administered, anti-ischemic, antihypoxant – vascard, preductal OD, ARBII - losartan were given and PCI was performed a day later; in the 3rd group, only PCI was performed. All patients got heparin according to the schemes. During hospitalization and within a year after discharge drug therapy was carried out, including aspirin-cardio+clopidogril. At the same time, 2 times a year for 3 months, one capsule of vascard was taken once a day, one tablet of preductal OD once a day+losartan 12.5 (25) mg once a day, cardiotex was administered intravenously at 500 mg once per day for 15 days. In all groups, the degree of ecoendotoxicosis was determined in the blood, using echocardiography and Doppler echocardiography, the values of end systolic (ESV) and end diastolic (EDV) volumes, ejection fraction (EF), stroke index (SI), cardiac index (CI), local contractility disorder index (LCDI) of the left ventricle, restenosis-with the help of repeated coronary angiography, ECG for ST-segment elevation and repeated anginal pain. The dynamics of BPs and BPd and the clinical course of NSTE ACS were established. In patients of all groups the dynamics of BPs and BPd was recorded, indicators stabilized central hemodynamics. By reducing the degree of ecoendotoxicosis, EDV and ESV, LCDI, LV systolic function improves, EF increases (group 1-2). However, in the first and third groups, single ventricular extrasystoles were recorded in one patient. AHF was recorded in one patient In patients of 1st group. In the PCI-only group, 2 patients developed recurrent NT ACS, 3 had restenosis, 3 had AHF, and 2 patients died. The results of this study show that the complex use of drug therapy with PCI allows to get a prognostically positive result, in contrast to a separate PCI therapy.

Keywords: NSTE ACS, Ecoendotoxicosis (AMP), Drug Therapy+PCI, Central Hemodynamics, Cardiohemodynamics, Clinical Course

1. Introduction

The main task in the treatment of patients with acute coronary syndrome (ACS) - without ST segment elevation myocardial infarction (NSTEMI) is the rapid medical or mechanical revascularization of the infarct-related coronary artery [1-4, 18]. The complex use of percutaneous coronary intervention (PCI) and medical revascularization opens up a new direction in the prevention of complications in patients with ACS, primarily heart failure and mortality [2-4, 12, 18, 20].

The progress of the industry increases the dispersion of various substances in the atmosphere, soil, water, heating of the environment, electromagnetic radiation, the power of explosions, etc., which cause progressive environmental degradation of the environment, deterioration in human health, and contributes to the development of disease and mortality. According to the WHO data [5], at present, a significant part of diseases is a derivative of the impact of anthropo-emergency factors (H_2SO_4, SO_2, CO_2, CO, NO, electromagnetic radiation, etc.) on the human body, causing chronic poisoning, which contributes to an increase in average peptide molecules (AMP) [1, 5, 10]. The level of average peptide molecules is a test that characterizes the severity of endotoxicosis, which enhances the impact of risk factors for coronary artery disease, increases myocardial hypoxia, reduces tissue resistance, worsens blood rheology and disrupts microcirculation [5-7, 10]. All this together causes extensive myocardial damage, which leads to a complication of MI and contributes to the development of heart failure (HF) and sudden coronary death in ACS [1-3, 6, 10]. The failure of ACS treatment often depends on the insufficiency of assessing the severity of environmental exo- and endotoxicosis associated with the massive intake of catabolism products from the focus of necrosis and xenobiotics into the bloodstream [2, 6, 8]. In this regard, a search is currently underway for new methods of exposure that help reduce AMP, prevent or reduce the development of various complications in the early stages of ACS [1-4, 9]. In recent years, thrombolytic therapy and PCI have been used to reduce the complications of ACS [3, 8, 12, 20]. However, there is evidence that after thrombolytic therapy, every third patient develops reperfusion syndrome on the first day, relapses of MI, which are observed in the following days [4, 18, 19]. After medical revascularization (MR), stenosis remodeling continues in the infarct-associated artery for 1-2 months. In 30% of patients, already on the first day of thrombolytic treatment (TLL), relapses of ACS: NSTEMI are noted and continue to be detected in the future. However, relapses of NSTEMI are not always manifested by clinical symptoms, which makes it difficult to detect it in time and leads to the death of patients. It has been established that mechanical reperfusion in the early stages of ACS increases the incidence of adverse outcomes [3, 18, 21]. In connection with this and another reason, M. Y. Ruda [12, 21] believes that anticoagulant and thrombolytic therapy should not be abandoned as the most accessible and very effective way to treat ACS. In recent years, the combined use of medical (enhanced anticoagulant and/or thrombolytic) and mechanical reperfusion in the early stages of NSTEMI is considered effective. According to Kang S. et alt. [18] Sharma S. K. et alt. [20] Mechanical reperfusion combined with thrombolytic and anticoagulant therapy significantly reduces mortality in ACS. Nevertheless, the effectiveness and safety of the combined use of medical and mechanical revascularization remains the subject of discussion, and there is no consensus on their use. In addition, according to some sources, despite the early recovery of blood flow in the infarct-related coronary artery, the area of myocardial necrosis is formed of a rather large size [18, 19].

Another study [3, 4, 17, 21] noted that during PCI-induced reperfusion, CRP and IL-6 increased in the blood after 24 hours, which is associated with an increased risk of death and the development of cardiogenic shock. Considering all this, intracoronary stands were used, which made it possible to reduce the frequency of restenosis in the coronary arteries compared to PCI. However, stenting does not inhibit thrombosis, inflammation, and intimal hyperplasia and does not completely solve the problem [19, 21]. Therefore, the idea arose that, a few days after successful medical revascularization, PCI could increase the effectiveness of ACS therapy in the early stages.

Losartan blocking angiotensin II receptors (ARBII) reduces blood pressure fluctuations, stabilizes systolic and diastolic blood pressure, promotes favorable hemodynamic conditions for the functioning of the left ventricle [1-3, 13, 20]. An optimal level of coronary perfusion, a functional state of the endothelium of the coronary arteries is created. At the same time, losartan has a unique ability to reduce the vasoconstrictor neuropeptide endothelin and slow down the breakdown of bradykinin, which blocks angiotensin II. All these qualities of losartan contribute to the anti-ischemic effect, lead to a decrease in the violation of systolic and diastolic dysfunction of the left ventricle, and restore myocardial function [1, 2, 13].

Peri-invasive use of β-blockers in ACS: NSTEMI is considered as an important component of myocardial protection, providing a decrease in mortality in patients of this category [9, 20]. At the same time, therapy with β-blockers is associated with a lower frequency, development of atrial fibrillation in the early mechanical reperfusion period [3, 9, 12, 17].

There are no data in the literature on the combined use of thrombolytics, anticoagulants, β-blockers and ARBII, Cytomac in combination with PCI in environmental endotoxicosis in patients working in environmentally unfavorable conditions contaminated with xenobiotics [2, 3, 14-16]. Meanwhile, the issues of the combined use of ARBII (losartan), β-blockers (propranolol), antihypoxant, antiischemiccardiotext (meldonium), antitoxic, antihypoxant, antiischemic drug Cyto-Mac, propranolol, then (ARBII-losartan), antiischemic biologically active food supplement drug vascard, cardiket (isosorbidedinitrate), trimetazidine (preductal OD), which has a cytocardioprotective effect, directly affecting metabolic disorders that develop under conditions of myocardial ischemia or reperfusion. It preserves the energy potential in the cardiomyocyte, establishes a high level of ATF in the ischemic heart muscle, etc., high doses of anticoagulants (heparin) in combination with PCI have not yet been fully disclosed [1-3, 14, 17, 21, 22].

Taking into account all the latest literature data, we conducted this study to study the effectiveness of the combined use of medical and non-mechanical revascularization and separately performed PCI in the acute period and during the observation period of NSTE ACS in

patients working in xenobiotic-contaminated environmentally unfavorable conditions.

2. Material and Research Methods

We studied 63 patients with ACS - myocardial infarction without ST segment elevation (NSTEMI) aged 30 to 70 (56.7±1.20) years. The study included 56± (93.3%) men and 7 (11.3%) women. By the method of individual randomization, patients were divided into 3 groups of 21 people each. In the 1st group, an antitoxic, antihypoxant, anti-ischemic drug Cyto-Mak, β-blocker (propranolol), an anti-ischemic drug - a biologically active food supplement Vascard, isosorbidedinitrate (cardiket) were administered, and PCI was performed a day later. In the 2nd - Cyto-Mac, β-adrenergic blocker (propranolol), cardiotex (moldenium), then Vascard was prescribed 1 capsule per day for 3 months, preductal OD 1 times a day for 3-4 months, ARBII. A day later, PCI was performed. In group 3, only PCI was performed. All patients were administered high doses of anticoagulants (heparin). In the 2nd - Cyto-Mac, β-adrenergic blocker (propranolol), cardiotex (meldonium), then Vascard was prescribed 1 capsule per day for 3 months, preductal OD 1 times a day for 3-4 months, ARBII). A day later, PCI was performed. In group 3, only PCI was performed. All patients were administered high doses of anticoagulants (heparin).

Patients were hospitalized within 1-3 hours from the moment of illness. The diagnosis was made on the basis of criteria recommended by WHO experts (1991). All patients worked in environmentally unfavorable conditions contaminated withxenobiotics under the influence of anthropo-emergency factors (CO, CO_2, H_2SO_4, SO, S_2H, NO, electromagnetic radiation, etc.) (Table 1).

Table 1. *Characteristics of patients working in environmentally stressful conditions.*

Environmentally stressful conditions (n =63)	Cito-Mac, propranolol, then anti-ischemic vascar, cardiket, after a day of PCI (n=21)		Cito-Mac, propranolol, cardiotext, Daily vascard, preduktal Mr35mg, brA II (losartan) after a day of PCI (n=21)		PCI (n=21)	
	Number of patients (n=21)	Work experience (years)	Number of patients (n=21)	Work experience (years)	Number of patients (n=21)	Work experience (years)
Oil and gas producing plants	2	12,2±1,30	2	10,90± 3,00	3 12,30 ±310	10,31±3,10
Oil and gas processing plants	3	11,90±3,60	3	10,60 ±3,22	2 11,05 ±3,00	10,20±2,20
Chemical plants	3	12,15 ± 1,0	4	11,81±3,00	3 11,60 ±2,60	10,49±3,00
Electrotherm Plant	1	10,95± 2,75	1	10,50 ± 2,60	2 10,00 ±2,10	12,11±1.40
Synthetic Rubber Plant	2	10,95± 3,0	3	10,31 ±3, 10	4 10, 93±3,10	10,23±2,10
Motor vehicle fleets	4	1 3, 21±1,0	3	12,05±1,40	3 12,0±0,96	10,95±2,91
Car repair parks	3	12,05±1,40	2	12,00 ±2,10	2 12,31±1,56	13,61 ±1,45
Rubber products factory (tire factory), etc.	1	11,49±1,60	1	11,56 ±2,10	1 12,00 ±1,40	11,90±3,32
Greenhouse economy	2	12,35±2,30	2	11,93±1,40	111,08 ±1,35	12,50±1,40
Time of hospitalization	1 -3 hours		1 -3 hours		1 -3 hours	

In all groups, the clinical course of the disease was assessed: BPs, BPd, SI, CI, HR, ecoendotoxicosis (average molecules peptide - AMP), the occurrence of early restenosis, recurrence of NSTE ACS, the development of AHF during the observation period. At the same time, AHF was determined according to the Killip classification within 7 days. Cardiohemodynamics was studied using echocardiography with ananSonoScape – S40. End systolic (ESV), end diastolic (EDV) volumes, local contractility disorder index (LCDI), LV ejection fractions (EF) were determined. The degree of ecoendotoxicosis (AMP) was determined according to the method of V. I. Lipatov et al. in the modification of O. A. Yakovleva by the spectrophotometric method. With the help of repeated coronorography for 1.5 months, restenosis was established. In addition, the ST segment elevation was recorded on the ECG. There were repeated anginal pains.

The antitoxic, antiischemic, antihypoxantCyto-Mac was administered to patients of the 1st group in the following way: first, 15 mg as a bolus, then 15 mg of Cyto-Mac was diluted in 150 ml of 0.9% sodium chloride solution and administered at 20-25 drops per minute 3 times a day for 3 days. Propranolol at a dose of 0.1%-5 mg was administered intravenously over 5 minutes. Then, 0.02 mg/kg/min was administered intravenously 4 times within 24 hours, then oral administration of the drug was used at a dose of 80-120 mg per day. Vascard 1 capsule per day for 3 months, cardioket (isosorbidedinitrate) 40 mg 2 times a day, preductal OD 1 times a day for 3-4 months. Patients of the 2nd group Cyto-Mac, Propranolol were administered as in the 1st group. Cardiotex 500 mg (5 ml) was administered intravenously for 5 minutes once a day for 10-15 days. Vascard was given 1 capsule per day for 3 months, preductal OD 3 months 1 times a day, ARBII (losartan) the first 3 days, 12.5 mg once at night, then 25 mg per day for 7 days, then 50 mg /day on the following days and PCI was performed. Group 3 patients underwent only PCI. Patients of the 1st and 2nd groups used heparin: 40,000 IU was first administered intravenously and simultaneously, 10,000 IU subcutaneously, followed by administration every 6 hours on the 1st day., on days 2-3 - 10,000 IU every 8 h, for 4-5 days - 10000 IU every 12 hours, for the 6th day - 10000 IU once a day. subsequent appointment of aspirin-cardio and clopidogrel.

During hospitalization and within a year after discharge, drug therapy was carried out, including aspirin-cardio in

conjunction with clopidogril. At the same time, Vascard was taken 1 capsule per day 2 times a year for 3 months. Preductal OD once a day for 3 months. Losartan 12.5 (25) mg once a day for a year, intravenously administered cardiotext 500 mg once a day for 15 days 2 times a year.

The material was statistically processed using the "Statistics 6.0" software package, the M values, standard errors (m) and 95% reliable interval were calculated. In this case, the nonparametric Mann-Whitney test, R. Fisher's exact test were used. Differences were considered significant at $p<0.05$.

3. Research Results

Indicators of BPs, BPd, AMP, SI, CI, HR, ESV, EDV, EF, INLS in all groups upon admission of patients to the hospital were approximately ($p>0.05$; see table 2). At the same time, hyper- and eukinetic variants of hemodynamics were mainly observed in all patients.

Against the background of the introduction of Cyto-Mac, propranolol, heparin and the ingestion of vascard, cardiket (isosorbidedinitrate) and PCI (group 1), there was a decrease in blood pressure after 12 hours and until the end of the study from 138.4 ± 2.2 - to 118.8±1.8 mmHg. However, there was no significant decrease compared to baseline blood pressure values ($p>0.05$; table 2). In this group, in 3 patients with initially low blood pressure, there was a tendency to increase it (before treatment 110/60, after - 115/65 mm Hg). In 5 patients, the level of blood pressure did not change significantly. A decrease in AMP was registered from 6.05± 0.35 up to 0.30+0.10 units.

With the introduction of cyto-mac and propranolol, cardiotex, heparin and ingestion of vascard, preductal OD, losartan and PCI (group 2), after a day, blood pressure almost stabilized: after 24 hours it was already 118.0 ± 2.2 mmHg and by the end of the observation - 120.2 ± 2.3 mm Hg. At the same time, blood pressure gradually decreased and on the 7th day of treatment was 80.20±1.4 mm Hg. AMP decreased from 6.15 ±0.06 up to 024±0.10 units. However, these indicators did not significantly differ from the 1-st group ($p>0.05$; table 2).

The dynamics of changes in central hemodynamic parameters on the days of treatment is presented in Table 2 ($p>0.05$).

In patients of the 1st group, a significant decrease in SI and CI was not observed. A day later, they increased and at the end of the study amounted to 58.9±1.6 ml/m^2 ($p<0.01$) and 4.8±1.3 l/min/m^2, respectively ($p=0.05$; see Table 2). In patients of the 2nd group, after 12 hours, SI and CI did not decrease, on the contrary, SI increased from 39.9±0.3 ml/m^2 to 61.3±1.8 ml/m^2 and CI from 3.92±0,03 l/min/m^2 to 4.95±0.08 l/min/m^2) and significantly differed from baseline ($p<0.01$; see Table 2).

Subsequently, the values of SI and CI in the 1st and 2nd groups did not differ ($p>0.05$; see Table 2). Separate analysis of CI indicators revealed that in the 1st group, who received Cyto-Mac, propranolol, heparin and ingestion of vascard, cardiket (isosorbidedinitrate) and PCI in 8 patients, CI increased from 3.00±0,08 to 4,91±0,03 l/min/m^2, in 7 - from 3.25±0,07 to 4.90±0,02 l/min/m^2, in 5 - from 3.64±0,06 - to 4.78±0,03 l/min/m^2, in one patient, significant changes in CI were not recorded and were not reliably differed from the data of the 2nd group ($p>0.05$; see table 2).

In patients of the 2nd group treated with Cytomac, propranolol, cardiotex, heparin ingestion of vascard, preductal OD 80 mg, lozartan in combination with PCI, in 7 patients CI increased from 3.00±0,06 l/min/m^2 to 4.95±0,04 l/min/m^2, in 5 - from 3.25±0,06 l/min/m^2 - to 4.95±0,04 l/min/m^2, in 7 - from 3.91±0,08 l/min/m^2 - to 5.10±0,02 l/min/m^2, in 5 - from 3.72-±0,03 l/min/m^2 to 4.87±0,06 l/min/m^2, two patients showed no significant changes (from 3.6±0,05 to 3.77±0,06 l/min/m^2).

A significant decrease in HR in patients of the 1st group was observed after 24 hours - from 100.0±3.10 to 75.0±2.1 beats/min and persisted until the end of the study. In patients of the 2nd group, the heart rate decreased from 98.6±3.10 to 75.5±1.6 beats/min (see table 2).

Changes in indicators characterizing LV function during the study are presented in Table 2. In our study, the initial indicators of LV function did not differ significantly ($p>0.05$; see table).

EDV during infusion of Cyto-Mac, propranolol, heparin administration, ingestion of vascard, cardiket, PCI during observation and treatment decreased. After 12 hours of the disease, it progressively decreased and statistically significantly differed from that before treatment with NSTE ACS. With the infusion of Cyto-Mac, propranolol, the introduction of cardiotex, heparin and the ingestion of vascard, preductal OD 80 mg together with PCI, a decrease in EDV was also recorded. However, the value of this indicator did not significantly differ from that obtained in the 1st group ($p>0.05$). In patients of the 3rd group, who underwent only PCI, there was a tendency to decrease in EDV (see Table 2): the values of these data significantly differed from the results obtained in the 1st and 2nd groups.

In an individual analysis, in 92% of patients of the 1st group, in 96% of the 2nd group, a decrease in LV EDV was noted ($p> 0.05$; see table), LV ESV in groups 1 and 2 decreased by 43.3 and 44.4%, respectively ($p>0.05$; see table).

The initial values of EF as the main indicator of LV systolic function did not differ between the groups ($p>0.05$; see Table 2). The change in LV EF was considered significant above 45% or below 40%. In the 1st group, by the end of the 1st day and on the 7th day, the EF increased (51.34±2.61% and 59.31±2.14%), and these figures did not differ from the values in the 2nd group (55.12±1.9% and 61.4±2.17%). An individual analysis of the indicators revealed an increase in LV EF in 96% of patients of the 1st group, in 99% of the 2nd group. A decrease in LV contractile function was noted in 2 (9.5%) patients of the 1st group, in 1 (4.8%) - of the 2nd group.

Table 2. *Indicators of central hemodynamics, LV systolic function and clinical course in patients working in environmentally stressful conditions (M ± m).*

Indicators	Cito-Mac, propranolol, then anti-ischemic vascar, cardiket, after a day of PCI (n=21)				
	Time since the start of treatment				
	Before treatment	12 h	24 h	72 h	7 day
Systolic blood pressure, mm Hg	143,0±2,3; P>0,05	123,0±2,3	126,0±1,6	125,2±1,6	118,8±1,8
Blood pressure diastolic, mm Hg	86,7±1,3; P>0,05	78,7±1,7	73,7±1,6	65,1±3,3	75,9±3,2
Average Molecule of Peptides, c.u.	6,05 ± 0,35	4,62± 0,26	3,43 ± 0,11	0,30± 0,14	0,30 ± 0,10
Impact index, ml/m^2	38,00±1,4	40,5±1,9	39,6±2,0	44,5±1,6	58,9±16
Cardiac Index, l/min/m^2	3,92±0, 03	2,90±0,08	3,0±0,07	4,80±0,13	4,93±1,3
Heart rate, beats / min	100±3,10; P>0, 05	88,6±2,8	75,00±2,1	75,72±2,1	75,0±2,0
End-systolic volume, ml	90,20±2,90; P>0,05	70,23±2,31	65,90±2,42	53,2±2,61	51,34±2,61.
End-diastolic volume, ml	165,10±2,90; P>0,05	150,11±2,29	143,71±2,15	135,82±2,17	135,82±2,17
Ejection fraction,%	45,69±2,5; P>0,05	50,21±2,2	51,34±2,61	58,24± 2,17	59,31±2,14
Local contractility disorder index	1,81± 0,10 P>0,05	1,48± 0,23	1,35± 0,30	0,81±0,17	0,82±0,14
Restenosis	0				
Relapse	0				
Acute heart failure	1				
Mortality	0				

Indicators	Cito-Mac, propranolol, cardiotext, Daily vascard, preduktal Mr35mg, brA II (losartan) after a day of PCI (n=21)				
	Time since the start of treatment				
	Before treatment	12 h	24 h	72 h	7 day
Blood pressure systolic, mm Hg	138,4±2,2; P>0,05	125,5±2,1	118,0±2,2	121,0±3,7	120,2±2,3
Blood pressure diastolic, mm Hg	87,9±1,2; P>0,05	87,6±1, 4	82,6±1,4	80,0±1,3	, 80,2±1,4
Average Molecule of Peptides, c.u.	6,15 ± 0,06	3,80 ± 0,20	3,75 ± 0,15	0,3 0 ± 0,12	0,24 ± 0,10
Stroke index, ml/m^2	39,9±0,3	39,9±0,2	40,7±1,1	42,5±1,2	61,3±1,8
Cardiac Index, l/min/m^2	3,92±0,03	4,40±0,04	4,90±0,12	4,95±0,17	4,95±0,18
Heart rate, beats / min	98,6±3,10; P>0,05	95,5±2,2	96,3±1,9	84,32±2,1	75,50±1,6
End-systolic volume, ml	90,32±2,6; P 0,05	68,25±2,31	60,90±2,42	51,34±2,61	50,23±2,5
End-diastolic volume, ml	164,18±2,00; P>0,05	146,27±2,11	142,32±2,19	134,31±2,22	131,7±2,13
Ejection fraction,%	46,80±2,30; P>0,05	52,30±2,11	55,12±1,90	59,32±2,13	61,4± 2,17
Local contractility disorder index	1,78± 0,19; P>0,05	1,45 ±0,17	1,31±0,15	0,82±0,14	0,80 ±0,12
Restenosis	0				
Relapse	0				
Acute heart failure	0				
Mortality	0				

Indicators	PCI (n=21)					P_1
	Time since the start of treatment					
	Before treatment	12 h	24 h	72 h	7 day	
Blood pressure systolic, mm Hg	142,4±2,2; P>0,05	135,2±1,6	127,8±3,4	125,5±2,2	125,5±1,8	<0,05
Blood pressure diastolic, mm Hg	85,9±1,2; P>0,05	75,0±1,0	74,00±2,40	72,4±1,3	65,1±1,6	<0,05
Average Molecule of Peptides, c.u.	6,10± 0,20	6,13 ± 0,25	5,6 2 ± 0,25	4,9 ± 0,16	5,1 5± 0, 30	<0,05
Stroke index, ml/m^2	39,9±0,3	40,8±1,4	41,86±1,14	40,8±1,4,	48,5±1,6	<0,01
Cardiac Index, l/min/m^2	3,82±0,03	3,98±0,12	3,98±0,17	3,98±0,12	3,98±0,17	=0,05
Heart rate, beats / min	100,0±2,4; P>0,05	98,50±±1,6	96,20±1,9	86,32±2,1	78,14±1,9	<0,01
End-systolic volume, ml	89,33±3,4; P 0,05	87,50±1, 6	88,23±2,3	78,20±2,1	67,10±2, 4	<0,01
End-diastolic volume, ml	164,18±2,00; P>0,05	159,82±2,16	155,92±2,12	151,82±2,16.	148,92±2,12.	>0,05
Ejection fraction,%	45,90±2,10; P>0,05	45,73±1,61	48,82±1,53	50,71±1,47	55,31±2,14	<0,01
Local contractility disorder index	1,78± 0,16; P>0,05	1,651±0,21	1,58±0,15	1,29±0,14	0,99±0,12	<0,001
Restenosis	2					
Relapse	3					
Acute heart failure	2					
Mortality	1					

Note: P is a significant difference in baseline indicators, P1 is a significant difference in the final results between groups.

LV LCDI values were different (see Table 2). As a quantitative indicator, impaired local LV contractility has predictive value in the acute period of NSTE-ACS. Due to a significant decrease in the volume of the lesion, the degree of myocardial asynergy in patients of the 1st group of LV LCDI decreased (before treatment 1.81±0.10, at the end of treatment 0.82±0.14). Infusions of Cyto-Mac, propranolol and administration of cardiotex, ingestion of vascard, preductal OD 80 mg, losartan in combination with PCI contributed to a decrease in LV LCDI from 1.78±0.13 to 0.80±0.12. The data did not significantly differ from the 1st group. In the 1st group, 93% of patients, in the 2nd - in 98% of patients, there was a significant decrease in LV LCDI.

There were no significant differences in the clinical

condition of patients on the 1st day. The complex use of Cyto-Mac, propranolol, the introduction of heparin, the ingestion of vascard, cardiket, plus PCI, as well as the infusion of Cyto-Mac, propranolol, the introduction of cardiotex, heparin, the ingestion of vascard, preductal OD 80 mg, losartan orally in combination with PCI prevented the development of functional LV inferiority and led to a reduction in the incidence of other complications of NSTE-ACS.

So, if before the study, anginal pains were noted in the 1st group in 19 (90.5%), in the 2nd - in 20 (95.2%), in the 3rd group 19 (90.5%) patients, then, against the background of ongoing therapy, pain disappeared in 17 (89.5%), 18 (90%) and 17 (89.5%) patients, respectively. The frequency of postinfarction angina in the 1st group was 3%, in the 2nd - 5%.

Recurrent course of NSTE ACS in the 1st and 2nd groups was not observed. In the 1st group, one patient developed AHF on the 7th day. No AHF was observed in the 2nd group. In both groups, restenosis and mortality were not recorded. In the 3rd group, 2 patients had AHF, 2-restenosis, 3-relapses, one patient died.

Thus, recanalization of the coronary arteries using the combined use of Cyto-Mac heparin, propranolol, administration of cardiotex, ingestion of vascard, preductal OD 80 mg, losartan in combination with PCI, as well as the administration of heparin, cyto-mac, infusion of propranolol, administration of vascard, cardiket plus PCI contributed to a decrease in ESV, EDV, LCDI and an increase in LV EF in the acute period of NSTE ACS. Stabilized hemodynamic parameters without leading to a critical decrease in blood pressure, prevented the development of restenosis of the coronary arteries, relapse of ACS and mortality.

Separate PCI as an alternative to coronary artery bypass grafting in the treatment of NSTEACS is widely used as an effective and safe method of therapy. However, restenosis of the coronary arteries is the main limitation of the effectiveness of this method [3, 7, 10-12, 17, 21].

In this regard, the search for new drugs and methods to prevent these complications and improve the prognosis of ACS remains an urgent task [3, 7, 11, 12]. In recent years, much attention has been paid to the use of medical and mechanical reperfusion in ACS [3, 6, 7]. However, there is no consensus on their combined use. There is evidence that standard PCI performed immediately after successful thrombolysis increases the incidence of complications such as AHF, restenosis, and recurrent MI [9, 13]. After medical reperfusion, remodeling of residual infarct-associated artery stenosis continues from the next week [3, 5, 7, 11, 18, 21]. Restoration of coronary blood flow with the help of drugs (anticoagulants, ARBII, β-blockers, thrombolytics) and mechanical revascularization contribute not only to the revival of the local kinetics of segments with a dormant myocardium in the peri-infarction zone, but also to a decrease in ESV, EDV, LCDI and an increase in the total EF of the left ventricle [3, 9, 13, 20, 21].

Separate PCI as an alternative to coronary artery bypass grafting in the treatment of NSTEACS in the acute period is widely used as an effective and safe method of therapy. However, restenosis of the coronary arteries is the main limitation of the effectiveness of this method [3, 4, 7, 9, 11, 12, 17, 19, 21]. Available clinical data [4, 9, 20], as well as the results of our studies [2, 3] show that the use of β-blockers, in particular propranolol, metoprolol succinate, cyto-mac, cardiotex before PCI and coronary bypass grafting can be considered in as an important component of myocardial protection and mortality reduction in this category of patients [2, 5, 9, 20].

However, due to hypotension and negative inotropic and other effects, they were used in only 20-35% of ACS patients. At the same time, therapy with β-blockers is associated with a lower incidence of atrial fibrillation in the early period of PCI. But the use of β-blockers (propranolol, metoprolol succinate) before PCI and coronary artery bypass grafting, in addition to significantly reducing non-fatal myocardial infarction or non-fatal cardiac arrest, increases the risk of death from other causes and the development of strokes in this group of patients [7, 9, 11, 13, 14, 19].

Meanwhile, according to literature data and our experience, taking into account reasonable contraindications, the use of propranolol or metoprolol succinate does not give negative consequences [2, 3, 7, 13]. In addition, in recent years, much attention has been paid to the use of ACE inhibitors and ARBII [1, 2, 4, 8, 13] in order to prevent the development of postinfarction LV remodeling, HF during the observation period of ACS. One of the last representatives of ARBII is losartan, which is widely used in hypertension and Congestive Heart Failure (CHF). As our studies show, heparin, improving the rheological properties of blood, in large doses has a thrombolytic effect [1, 6], increases blood supply in the peri-infarction zone.

Taking into account the above and the lack of data on the combined use of Cytomac, β-adrenergic blocker propranolol, cardiotex together with ARBII, heparin and PCI, as well as Cytomac therapy with propranolol infusion, heparin, Cytomac and taking ARBII with PCI and a separate mechanical revascularization of infarct-related arteries in NSTE ACS with environmental endotoxicosis, we conducted a number of studies and obtained positive results.

The complex use of Cyto-Mac, propranolol, cardiotex together with vascard, preductal OD, heparin and PCI in NSTEMI gives a good therapeutic effect and allows us to consider their use pathogenetically justified to prevent left ventricular dysfunction, relapses and restenosis of the infarct-related coronary artery in PCI. The positive effect of ACE inhibitors on the processes of LV remodeling in necrosis and studies on the use of ACE inhibitors in the acute period of MI (ISIS-4-kaptopril; GISSI-lizinopril; AIRE-ramipril, etc.) confirm the feasibility of using ACE inhibitors or ARBII in the critical period of MI.

In the early stages of MI, the use of a β-adrenergic blocker (propranolol) and high doses of heparin can achieve revascularization of the infarct-related coronary artery and preserve the viability of the peri-infarction necrosis zone,

thereby preventing the "expansion of the necrosis zone" and the development of various complications. Currently, systemic thrombolysis and mechanical revascularization of the infarct-related coronary artery are used. This method of treatment in combination with anticoagulant and antiplatelet therapy resulted in a significant reduction in relapses, restenosis and mortality in ACS patients [1, 3, 7, 9, 10, 12, 14].

The combined use of heparin, propranolol, cytomac, cardiotex, taking losartan, vascard, preductal OD and performing PCI in the acute period of myocardial infarction prevents LV remodeling, relapse and restenosis [2]. According to F. T. Ageev, B. A. Sidorenko, M. Ya. Ruda [1, 8, 12, 13], in the acute period of NSTEMI anterior localization of ACE inhibitors, also ARBII gives a good effect.

The results of our studies show that the combined use of a β-adrenergic blocker (propranolol) together with Cyto-Mac, cardiotex, ARBII (losartan), heparin and PCI, as well as heparin, propranolol, Cytomac, Vascard, cardiket and PCI reduces AMP, gives a positive hemodynamic effect, improves LV systolic function. Similar data were obtained by other researchers [3, 4, 10, 15, 16]. The best therapeutic effect was registered in patients with arterial hypertension.

Our studies, as well as other authors, have established that Cyto-Mac reduces ecoendotoxicosis [2, 3, 14, 15], high doses of heparin promote revascularization of the infarct-related coronary artery. Losartan reduces fluctuations in blood pressure, blood pressure and, in general, together with propranolol, stabilizes blood pressure without leading to critical hypotension, slowly reduces and stabilizes systolic and diastolic blood pressure, and contributes to favorable hemodynamic conditions for the functioning of the left ventricle [2, 8]. An optimal level of systolic afterload is created, which determines the myocardial oxygen demand, the level of coronary perfusion, and the functional state of the coronary artery endothelium. At the same time, losartan has the unique ability to reduce the vasoconstrictor neuropeptide endothelin and slow down the breakdown of bradykinin, which blocks angiotensin II. Perhaps all these qualities contribute to the anti-ischemic effect, and the combined use of propranolol, which reduces the need for oxygen, leads to neurogenic unloading, stabilizes cardiomyocyte membranes, reduces disturbances in systolic and diastolic LV dysfunction, and restores myocardial function.

When administered intravenously, Cyto-Mac significantly reduces ecoendotoxicosis (AMP), the serum lactic acid level that is commonly elevated in ACS [2, 3, 14-16, 22].

As is known, a decrease in global LV contractility depends on the size of the lesion and is associated with the degree of ecoendotoxicosis and myocardial ischemia. Survival of patients after ACS depends on the values of ESV, EDV, LV EF, as well as on the level of AMP and the degree of impairment of local LV contractility. The results of our studies indicate a positive effect of the combined use of high doses of heparin, propranolol, cyto-mac, cardiotex, losartan, vascard, preductal OD and PCI; heparin, propranolol, Cyto-Maka, losartan, vascard, cardiket and PCI on the processes of early LV remodeling. In both groups, after 12 hours, there was a significant decrease in AMP, ESV, EDV, LCDI, an increase in LV EF, SI, CI. At the same time, only during PCI due to the development of relapse from the 3rd day there was an unreliable decrease in ESV, EDV. An insignificant increase in LV EF was observed after 72 hours, however, at the end of the study, the increase was significant and amounted to 55.31±2.14%. Combined use of Cyto-Mac, high doses of heparin, propranolol, cardiotex, losartan, preductal OD and PCI; heparin, propranolol, Cyto-Mac, vascard, cardiket and PCI in NSTE ACS prevents restenosis of infarct-related arteries, reduces ecoendotoxicosis (AMP) and the volume of myocardial damage, stabilizes hemodynamic parameters, and prevents early left ventricular remodeling of the heart. As a result of recurrence of myocardial infarction and mortality were not observed, AHF was also not registered.

It is acceptable to use high doses of heparin, which to some extent has thrombolytic and anticoagulant effects, lyses a thrombus in the coronary artery, and promotes myocardial revascularization. The positive effect of losartan is associated with its ability to reduce pre- and afterload on the left ventricle. The impact of the kallikrein-kinin system on the vascular wall with the formation of prostacyclin and nitric oxide leads to the expansion of the coronary vessels in the peri-infarction area and intact areas of the myocardium. The mechanisms of action of losartan, negative ion- and chronotropic effects, reduction of neurogenic load on the myocardium under the influence of propranolol in the complex use of these drugs with mechanical revascularization of the infarct-associated artery in NSTEMI prevent the expansion of myocardial damage and LV dysfunction.

Thus, the combined use of Cyto-Mac, high doses of heparin, propranolol, cardiotex, losartan, vascard, preductal OD and PCI, as well as heparin, propranolol, Cyto-Mac, losartan, vascard, cardioket and PCI in NSTE ACS, prevents restenosis infarction-associated arteries, relapse of ACS, stabilizes hemodynamic parameters, reduces disturbances in systolic and diastolic functions of the left ventricle, prevents the progression of LV dilatation, improves the clinical course of the disease.

4. Conclusion

1) Combined use of Cyto-Mac, high doses of heparin, propranolol, cardiotex, losartan, vascard, preductal OD and PCI, as well as heparin, propranolol, Cyto-Mac, losartan, vascard, cardiket and PCI in NSTE ACS stabilizes hemodynamic parameters, promotes reduction of ecoendotoxicosis (AMP) and disorders of systolic and diastolic functions of the left ventricle, prevents early remodeling of the LV.
2) In the group of patients treated with Cyto-Mac, high doses of heparin, propranolol, cardiotex, losartan, vascard, preductal OD with PCI, there was a more favorable clinical course of the disease, AHF, relapse, restenosis in the infarct-related coronary artery, and no

mortality was observed. However, there were no significant differences from the group treated with heparin, propranolol, Cyto-Mac, losartan, vascard, cardiket with PCI.

3) In the group of patients where only PCI was used, relapse was often observed, restenosis of the infarct-related coronary artery and AHF was recorded. One patient died.

Conflict of Interest

The authors declare no conflict of interest.

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