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## Clinical and Laboratory Parameters of Patients with Ischemic Heart Disease Complicated by Heart Failure of III-IV Functional Class with The Inclusion of Plasmapheresis in The Treatment Program.

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### ABSTRACT

The article studies the effect of PA in the complex therapy on the clinical and laboratory parameters of patients with heart failure. An experiment was conducted among patients to find out which therapy is better traditional or combined. The conducted studies showed that patients with ischemic heart disease of III-IV functional class with combined therapy experienced positive changes in the basic laboratory and hemodynamic parameters.

**Keywords:** ischemic heart disease, plasmapheresis, heart failure, functional class of angina pectoris,

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## INTRODUCTION

According to various sources, the frequency of occurrence of heart failure (HF) varies between 0.2 and 4% [1, 2, 8, 9], and it is approximately 5.5% in Russia [2].

The use of angiotensin-converting enzyme (ACE) inhibitors, diuretics with a different mechanism of action, cardiac glycosides are the main method of therapy for heart failure in ischemic heart disease (IHD). Drug therapy has several limitations and is not always effective in advanced HF. The steady annual increase in the number of patients with this pathology, the relatively high incidence of side effects and the insufficient effectiveness of traditional medicinal therapy contribute to the improvement of classical methods of HF therapy. Plasmapheresis (PA) has a pronounced clinical efficacy among alternative therapies that have a beneficial effect in IHD [3, 4, 5]. Plasmapheresis exerts detoxification, immunomodulating, hemocirculatory, coagulogenic and diffusion effects [6, 7].

The purpose of this study was to study the effect of PA in the complex therapy on clinical and laboratory indicators of patients with cardiac insufficiency(CH)of III-IV FC.

## MATERIALS AND METHODS

A study of the effect of the PA method as part of complex therapy on clinical and laboratory parameters of patients with post infarction cardio sclerosis complicated by HF of the III-IV functional class (FC) (according to the NYHA-New York Heart Association classification) was performed in 67 patients treated in Federal Research Center Krasnoyarsk Scientific Center of the Siberian Branch of the RAS. There were 49 males and 18 females, the age of the patients was 55 to 75 years.

53 patients had a myocardial infarction (MI). 32 patients had MI once, 17 patients had MI twice and 5 patients had MI thrice. 46 of 67 patients with heart failure were diagnosed with IHD of III FC, 21 people were diagnosed with IHD of IV FC. 33 patients had a type II diabetes, 42 patients had an II-III hypertensive disease according to the WHO classification, 31 patients had excess weight and a body mass index (BMI) equal to or greater than 32.

Patients of first group received 2 to 4 sessions of PA in a day, along with traditional therapy (beta-blockers, nitrates, ACE inhibitors, diuretics, cardiac glycosides - digoxin, antiaggregants, etc.). Some patients with CH of IV FC and some patients with CH of III FC passed PA sessions every 2 -3 days, depending on the severity of the disease. Duration of the disease in patients of this group was from 2 years to 27 years. The duration of treatment in the hospital was approximately 3 weeks (from 2 to 4 weeks). Pevzner's diet No. 10 was prescribed to all patients in this group.

The second group consisted of 29 patients with a diagnosis of IHD of III-IV FC, aged 54 to 75 years, of which 20 men and 9 women with a disease duration from 3 to 26 years. CH of III FC was diagnosed in 20 patients, CH of IV FC in 9 patients. 12 patients in the anamnesis had type 2 diabetes, 17 patients had a history II-III hypertensive disease (WHO). Patients of this group were treated with the traditional method - drug treatment (diuretics, ACE inhibitors, cardiac glycosides - digoxin, beta-blockers, antiaggregants, nitrates, calcium channel blockers). The duration of treatment in the hospital, as well as in the first group, was approximately 3 weeks (from 2 to 4 weeks). All patients of this group are prescribed diet No. 10 for Pevzner.

The patients underwent clinical, laboratory and instrumental examinations before the treatment and at different periods after the start of treatment - in a week, 1 month and 6 months.

Comparable groups did not differ in age, functional class of angina pectoris, duration of treatment, concomitant diseases. The programs for the Microsoft 2000 electronic table for Windows 2000 and the statistical software package "Statistica" were used in the processing of the results.

## EXPERIMENTAL

The effectiveness of combined treatment is observed from the first day after PA (Table 1). There was a significant decrease in cholesterol (TC) and triglyceride (TG) by 12.5 and 8.2%,  $P < 0.001$ . The decrease was

also noted for the indices of central hemodynamics-a decrease in the heart rate (HR), systolic (SBP) and diastolic (DBP) blood pressure and double product (DP) by 7.6%, 10.4%, 4.4% and 9, 7%, P <0.001, relative to the reference values. Clinical improvement is characterized by a decrease in the number of anginal pain (NAP), pain duration (PD), the number of tablets of nitroglycerin(NTI)by 74.2%, 87.6% and 95.7%, respectively, and an increase in the rate of physical activity test (PAT) and a 6-minute walk test (SMWT) by 97, 9% and 54.7%, P <0.001, relative to the reference values. The functional class of angina pectoris was reduced by 27.8%, amounting to  $2.42 \pm 0.33$ , P <0.001. Favorable changes in clinical and laboratory indicators persist at various times after the onset of combination therapy.

**Table 1: Clinical and laboratory indicators with the inclusion of PA in the program of treatment of patients with postinfarction atherosclerosis, complicated by cardiac insufficiency of III - IV CH (M ± Sx, N = 67)**

Parameters	Outcome	After PA	Δ <sub>0</sub>	7 days	Δ <sub>0</sub>	1month	Δ <sub>0</sub>	6 months	Δ <sub>0</sub>
TCmol /l	7,12±1,15 ***	6,23±1,23 ***^	-12,5	5,99±0,98 ***^	-15,9	5,86±0,90 ***^	-17,7	6,28±1,31 ***^	-11,8
TG mol /l	1,82±0,25 ***	1,67±0,25 ***^	-8,2	1,71±0,25 ***^	-6,0	1,72±0,33 ***^	-5,5	1,73±0,33 ***	-4,9
HR bpm	77,8±8,2 ***	71,9±8,2 ^^	-7,6	67,5±7,4 ^^	-13,2	68,7±7,4 ^^	-11,7	72,4±8,2 ^^	-6,9
SBDmmHg	144,7±19,6 ***	129,6±17,2 ***^	-10,4	131,8±18,0 ***^	-8,9	135,2±18,8 ***^	-6,6	136,2±19,6*** ^	-5,9
DBPmmHg	86,7±9,8 ***	82,9±9,8 ***^	-4,4	83,0±10,6 ***^	-4,3	84,5±9,0 ***	-2,5	86,2±9,0 ***	-0,6
DP	114,5±16,4 ***	103,4±17,2 ***^	-9,7	89,5±15,6 *^^	-21,8	92,7±14,7 ***^	-19,0	98,3±15,6 ***^	-14,1
NAPper day	5,19±0,74	1,34±0,25 ^^	-74,2	1,45±0,25 ^^	-72,1	2,12±0,25 ^^	-59,2	2,48±0,33 ***^	-52,2
PDmin	8,36±2,37	1,04±0,16 ^^	-87,6	2,38±0,41 ^^	-71,5	3,16±0,49 ^^	-62,2	3,89±0,74 ***^	-53,5
NTI per day	4,23±0,82	0,18±0,05 ^^	-95,7	0,51±0,16 ^^	-87,9	1,01±0,25 ^^	-76,1	2,11±0,57 ***^	-50,1
PETmeter	87,7±18,8 ***	173,6±19,6 ***^	97,9	171,2±20,5 ***^	95,2	166,9±21,3 ***^	90,3	159,2±20,5 ***^	81,5
SMWTmeter	187,2±63,0 ***	289,6±75,3 ***^	54,7	277,5±86,8 ***^	48,2	272,5±81,0 ***^	45,6	234,5±82,7 ***^	25,3
FC	3,22±0,49	2,42±0,33 ^^	-24,8	2,53±0,33 ^^	-21,4	2,49±0,25 ^^	-22,7	2,67±0,33 ***^	-17,1

Note: statistically significant difference:

1. with normative indicators: \* – p < 0,05; \*\* – p < 0,01; \*\*\* – p < 0,001
2. with baseline indicators: ^ – p<sub>0</sub> < 0,05; ^^ – p<sub>0</sub> < 0,01; ^^ – p<sub>0</sub> < 0,001

Functional class of angina pectoris, which is an indicator of clinical improvement in IHD patients, remains significantly lower than baseline values by 21.4% ( $2.53 \pm 0.33$ ), P <0.001 at 7 days after initiation of combination therapy, by 22.7% ( $2.49 \pm 0.25$ ), P <0.001, in a month and by 17.1% ( $2.67 \pm 0.33$ ), P <0.001 at 6 months. Improvement of laboratory parameters is characterized by a significant decrease in the level of cholesterol and TG by 15.9% ( $5.99 \pm 0.98$ ), P <0.001 and 6.0% ( $1.71 \pm 0.25$ ), P <0.05, respectively, remaining after 1 month, remaining below the initial values, respectively, by 17.7 and 5.5%, P <0.001 - 0.05. With the support of PA, the cholesterol concentration can be kept below the initial values 6 months after the start of therapy (by 11.8%, P <0.001).

The indices of central hemodynamics of HR, systolic blood pressure (SBD), DP remain stable (significantly lower than baseline values) for the entire time of observations. After 6 months, these indicators are set below the initial values. HR decreased by 6.9%, SBP by 5.9% and DP by 14.1%, P <0.05 - 0.001. Improvement of hemodynamic parameters promotes improvement of clinical symptoms of the disease. There was a decrease in NAP, PD, NTI relative to baseline by 72.1%, 71.5% and 87.9%, amounting to  $1.45 \pm 0.25$ ,  $2.38$

± 0.41 and 0.51 ± 0, 16, P <0.001. The above indicators remain lower relative to the baseline values until the end of the study period - NAP decreased by 52.2%, DP by 53.5% and SBD by 50.1% after 6 months, P <0.001.

The physical activity test (PAT) and the six-meter walking test (SMWT) increased after PA, with continuing medical therapy remaining above the baseline data by 95.2% and 48.2% in a week, P <0.001. After 1 month and 6 months, these indicators remain significantly higher than the baseline indicators: PAT is higher by 81.5% and SMWT is higher by 25.3%, correspondingly, 159.2 ± 20.5 meters and 234.5 ± 82.7 meter, P <0.001.

Comparative analysis of traditional and combined (with the use of PA) therapy for cardiac insufficiency of III - IV FC (Table 2) revealed lower rates for NAP, PD and NTI per day with combined therapy a week after the start of treatment. The data for combined therapy were lower after traditional therapy by 45.7%, 58.0% and 71.2%, amounting to 1.45 ± 0.25 per day, 2.38 ± 0.41 min. and 0.514 ± 0.16 per day, respectively. Combined therapy also showed an increase in exercise tolerance, which was manifested by an increase in the rates of PAT and SMWT by 9.7% and 24.2%, P <0.01 - 0.001, compared with patients treated with the traditional method.

**Table 2: Differences in clinical and laboratory parameters in patients with postinfarction cardiosclerosis complicated by cardiac insufficiency of III - IV FC with traditional treatment and inclusion of the PA program of treatment M ± Sx**

Parameters	Traditional treatment N = 29			Treatment with PA N = 67					
	After 7 days	After 1 month	After 6 months	After 7 days	Δs	After 1 month	Δs	After 6 months	Δs
TCmol / l	6,79±1,45	6,81±1,35	6,83±1,40	5,99±0,98 ##	-11,8	5,86±0,90 ###	-14,0	6,28±1,31	-8,1
TG mol / l	1,78±0,38	1,73±0,48	1,82±0,54	1,71±0,25	-3,9	1,72±0,33	-0,6	1,73±0,33	-4,9
HR bpm	67,7±8,6	66,3±10,2	72,2±10,8	67,5±7,4	-0,3	68,7±7,4	3,6	72,4±8,2	0,3
SBDmmHg	132,2±18,8	128,0±21,0	133,2±22,1	131,8±18,0	-0,3	135,2±18,8	5,6	136,2±19,6	2,3
DBPmmHg	85,4±15,6	85,9±15,1	86,2±15,1	83,0±10,6	-2,8	84,5±9,0	-1,6	86,2±9,0	0,0
DP	89,5±18,3	85,9±18,3	96,1±18,8	89,5±15,6	0,0	92,7±14,7	7,9	98,3±15,6	2,3
NAPper day	2,67±0,54	3,56±0,65	3,78±0,70	1,45±0,25 ###	-45,7	2,12±0,25 ###	-40,4	2,48±0,33 ###	-34,4
PDmin	5,67±1,24	4,78±1,02	5,09±1,08	2,38±0,41 ###	-58,0	3,16±0,49 ###	-33,9	3,89±0,74 ###	-23,6
NTI per day	1,77±0,38	1,82±0,32	2,19±0,43	0,51±0,16 ###	-71,2	1,01±0,25 ###	-44,5	2,11±0,57	-3,7
PETmeter	156,1±26,9	157,7±26,4	150,5±26,9	171,2±20,5 ##	9,7	166,9±21,3	5,8	159,2±20,5	5,8
SMWTmeter	223,5±44,2	233,9±49,0	225,4±51,2	277,5±86,8 ##	24,2	272,5±81,0 #	16,5	234,5±82,7	4,0
FC	2,89±0,65	2,86±0,70	2,92±0,75	2,53±0,33 ###	-12,5	2,49±0,25 ###	-12,9	2,67±0,33 #	-8,6

Note: statistically significant difference with the parameters of the comparison group:

# – p<sub>s</sub> < 0,05; ## – p<sub>s</sub> < 0,01; ### – p<sub>s</sub> < 0,001

The above changes in the clinical picture of the disease with PA therapy contributed to a significant decrease (by 12.5%) of the functional class of HF during the first week of observation, Table 2.

One month after initiation of therapy, the level of cholesterol, NAP, PD and NTI were also lower with combined therapy by 14%, 40.4%, 33.9% and 44.5%,  $P < 0.001$  and SMWT was higher by 16.5% ( $272.5 \pm 81.0$ ),  $P < 0.05$  with respect to similar parameters for traditional therapy. Heart failure is  $2.49 \pm 0.25$ , which is 12.9% lower than in patients with medication alone,  $P < 0.001$ . There was a decrease in NAB and PD with combined therapy at 34.4% and 23.6%,  $P < 0.001$ , relative to conventional therapy at 6 months. The use of PA as part of traditional therapy contributed to a decrease in heart failure by 8.6%,  $P < 0.05$ , relative to patients treated with the traditional method.

## RESULTS AND DISCUSSION

Plasmapheresis aggressively and extensively affects modifiable risk factors for coronary artery disease, reduces blood cholesterol and blood viscosity, improves fluidity of blood, lowers the coagulation potential of blood, corrects blood pressure (BP), normalizes the level of glycemia.

The proposed method of including plasmapheresis in the complex treatment of patients with cardiac insufficiency of III - IV FC promotes improvement of clinical and laboratory indicators. The study of laboratory and clinical parameters was performed prior to plasmapheresis and within 6 months after the last procedure of plasmapheresis. The first study was conducted during the first 24 hours after the termination of the plasmapheresis course.

The conducted studies showed that patients with IHD of III-IV FC with combined therapy experienced positive changes in the basic laboratory and hemodynamic parameters. A significant decrease in the level of TC and TG with respect to the initial data was established by 12.5 and 8.2%. The parameters of hemodynamics are characterized by a significant decrease in HR, SBD, DBP and DP, which leads to a decrease in myocardial oxygen demand, improvement in symptoms of the disease and the need for drug therapy (nitrates). Clinically, this is manifested by a decrease in NAP, PD, NTI per day.

The improvement in the clinical picture of the disease is accompanied by a statistically significant decrease in the initial data of the functional class of heart failure by 24.8%. Favorable changes in clinical and laboratory indicators persist at various times after the onset of combination therapy.

Functional class of angina pectoris, which is an indicator of clinical improvement in IHD patients with cardiac insufficiency of III-IV FC, remains significantly lower than baseline values by 21.4% at 7 days after initiation of combination therapy, 22.7% at 1 month and 17.1% at 6 months.

This is confirmed by a significant decrease in the symptoms of the disease (NAP, PD, NTI per day), increased exercise tolerance (PAT, SMWT) and a decrease in the concentration of cholesterol and TG observed over the entire study period (up to 6 months).

Comparison of the results of clinical and laboratory indicators of patients with cardiac insufficiency of III - IV FC after combined and traditional therapy showed significant effectiveness of the first method. This is manifested reliably low values of cholesterol plasma, and the main indicators reflecting the clinical course of the disease - NAP, PD, NTI per day, PAT and SMWT, which are lower than the corresponding values obtained after traditional therapy. The functional class of heart failure undergoes more favorable changes also with combined therapy. It should be noted that the advantage of combined therapy is relatively traditional over the entire study period for 6 months.

## CONCLUSIONS

It should be concluded that the use of therapeutic plasmapheresis in treatment programs for IHD patients with HF of III - IV FC favorably affects the clinical course of the disease, the tolerance of physical exertion and the state of lipid metabolism, which in turn leads to an improvement in the contractility of the heart muscle and the improvement of the functional class heart failure. At the same time, the effectiveness of combining therapy is maintained over a long period of time.

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