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CORRECTION OF COMPLICATIONS IN CHRONIC HEART FAILURE DEPENDING ON THE FUNCTIONAL STATE OF THE KIDNEYS

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Abstract:
The work is devoted to the study of the effectiveness of the treatment of CHF in patients of the older age group taking into account the functional state of the kidneys.
We examined 52 patients aged 62 to 86 years after a myocardial infarction complicated by the development of CHF. All patients received basic therapy of CHF.
All patients included in the study at baseline, after 3 and 12 months, were clinically examined, the functional class of CHF was determined, echocardiography was performed, and the functional state of the kidneys and heart rate variability (HRV) were examined. Depending on the effect of treatment on the state of the kidney two groups of patients: group 1 (n=33) had no adverse effects on the kidneys (nephroprotective effect) according to the study glomerular filtration rate (GFR) and microalbuminuria (MA); group 2 (n=19) consisted of patients in whom the therapy of CHF led to the decline of GFR and initiated the emergence of or a buildup of MA (nephronegative effect).

Keywords: *chronic heart failure, the effectiveness of treatment, the functionalstate of the kidneys, microalbuminuria, old age.*

INTRODUCTION

In recent years, much attention has been paid to the violation of kidney function in cardiovascular diseases. The kidneys have a leading role in the formation and development of chronic heart failure (CHF), through the kidneys, the action of most pathogenetic agents for the treatment of CHF is realized. In addition, the risk of nephrotoxic effects of a number of drugs in patients with CHF is significantly higher than in the general population [4]. The functional state of the kidneys, their response to treatment in many respects define the adequacy and effectiveness of the therapy, as well as the destiny of the patient [9,10,11]. The results of four large studies (SOLVD, TRACE, SAVE, VALIANT) showed that a decrease in glomerular filtration rate (GFR) to less than 60 ml/min was associated with high mortality due to cardiovascular complications [8]. In recent years, the attention of doctors has been drawn to the identification of microalbuminuria (MA) as a very reliable, achievable and previous marker of the pathological process in the kidney [12]. Microalbuminuria is also considered as a criterion of cardiovascular distress [1]. Early diagnosis of microalbuminuria allows you to quickly intervene in the fate of the patient, prevent or significantly slow down the progression of renal failure and the development of cardiovascular complications. In clinical practice, various objective methods are used to assess the effectiveness of treatment of CHF – such as the dynamics of the ejection fraction, the total diastolic volume of the left ventricle(LV), oxygen consumption at the maximum of physical activity, etc. The aim

of the work is to establish the possibility of predicting the effectiveness of long-term therapy of CHF in elderly and senile patients, taking into account the functional state of the kidneys.

MATERIALS AND METHODS

Were examined 52patients (33 men and 19 women) aged from 62 to 86 years (average age 68.7+0.87 years) after a myocardial infarction (MI), complicated by the development of CHF. 23 patients had MI with a Q wave; 29-without a Q wave; 42 patients had a history of hypertension. To verify the functional class (FC) of CHF, the New York Classification of CHF and the 6-minute walk test (TSH) were used. 27 patients (33.8%) were assigned to FC II, 51 (63.7%) were diagnosed with FC III, and 2 (2.5%) had FC IV. All included in the study patients had no contraindications to the appointment of beta-blockers and in 100% of cases received aceis (ramipril, captopril, perindopril, enalapril) and antiplatelet agents (aspirin, clopidogrel, kurantil, warfarin), 43 (82,7%) took statins, 44 patients (84,6%) – diuretics, 48 (92,3%) – long-acting nitrates or molsidomine, 6 (11,5%) – cardiac glycosides.

Systolic left ventricular function was assessed by ejection fraction (LVEF), diastolic ratio of the maximum speed early peak E and systole the Atria, as well As time isovolumic relaxation and deceleration time of mitral flow. Changes in the following parameters were considered a violation of diastolic function: IVRT>105 m s, E/A<0.5, and DT>280 m s [6]. To study the state of the kidneys was investigated in sodium and blood creatinine, GFR was determined by clearance of endogenous creatinine, calculated daily excretion of sodium tubular reabsorption of water, was determined relative density morning urine. The excretion of 30 to 300 mg / day was considered microalbuminuria (MA). The ECG was recorded for 5 minutes in the morning at rest in one of the standard leads in the "lying down" position and during an active orthostatic test. The results of the study were processed using parametric and nonparametric statistics. We used the statistical data processing program "BNDP" and the built-in statistical analysis package Microsoft Excel. $P<0.05$ was taken as the statistical significance of the differences.

RESULTS

Depending on the effect of treatment on the state of the kidney two groups of patients: group 1 (n=33) had no adverse effects on the kidneys (nephroprotection effect) according to the study of GFR and MA. This group included patients with CHF, which GFR normalizability, and MA was not detected either before or at the end of treatment, either decreased or disappeared during therapy; group 2 (n=19) consisted of patients in whom the therapy of CHF led to the decline of GFR and initiated the emergence or the increase in MA (nephronegativity effect). Both groups were comparable in age, gender, severity of the disease, the main clinical and hemodynamic parameters, and the doses of standard therapy used. The characteristics of both groups are presented in Table 1.

During 12 months of follow-up, 1 patient (3.4%) died in group 2, and there were no deaths in group 1. At the end of the study, there was a statistically significant increase in exercise tolerance in the two groups according to the TSH data (by 29.4% and 20.4% in the 1st and 2nd groups, respectively). The difference in the final result is significant. In the 1st group, FC decreased statistically significantly CHF – by 30.6%, in the 2nd - by 18.8%. The difference between the groups according to the final result did not reach the reliability criteria. The quality of life of patients with a favorable effect on the therapy of CHF the buds on the results of the MLHFQ questionnaire by the end of the observation period increased by 17.4% to 31.7 points, and adverse effects – 5% to 37.9 points. In patients with a nephroprotective effect, after 12 weeks.

Tab 1.

Clinical characteristics of patients taking into account the nephrotropic effect of basic CHF therapy

Parameter	1-gr nephroprotective effect	2-gr nephronegativity effect
Number of patients	33	19
Age, years	68,25+2,34	69,2+2,29
Man / women	21/12	12/7
QIM / Non-QIM	18(54,5%) / 15(45,5%)	5(26,3%) / 14(73,7%)
Post-infarction cardiosclerosis (%)	8(26,4%)	7(36,8%)
Patients with AH / without AH, (%)	27(81,8%) / 6(18,2%)	15(78,9%) / 4(21,1%)
The duration of AH, age	13,6+2,89	15,9+3,18
% of patients with FC II	37,3%	27,6%

% of patients with FC III	62,7%	65,5%
% of patients with FC IV	-	6,9%
Distance of a 6-minute walk, meters	287,6+9,05	272,6+8,36
SBP, mmHg	126,5+3,74	132,3+3,96
DBP, mmHg	76,7+2,86	78,3+2,81
Heart rate, min	67,7+2,88	64,8+2,76
Ejection fraction %	38,8+2,64	38,4+2,09
Blood creatinine, mmol/l	123,9+5,12	119,8+4,49
Average dose of berlipril, mg / day	10,3+2,78	12,6+3,36
Average dose of concor, mg / day	5,83+1,54	5,86+1,80
Average dose of carvedilol, mg / day	32,9+3,74	29,9+2,16
Average dose of berlipril, mg/day	10,3+2,78	12,6+3,36
Average concor dose, mg/day	5,83+1,54	5,86+1,80
The average dose of carvedilol (acridilole), mg/day	32,9+3,74	29,9+2,16
Patients on bisoprolol (%)	76,5%	79,3%
Patients in the carvedilol (%)	23,5%	20,7%

Note:* the difference is p<0.05 compared to the initial indicators.

of follow-up, an increase was noted FV from 38.7% to 41.0% (+5.94%; p<0.05). This trend was observed in the future, and by the end of the study, the EF was 44.3% (p<0.05). In the group with a nephronegative effect, systolic function deteriorated slightly during the first 12 weeks (a decrease in EF from 39.3% to 37.9%). Subsequently, there was an unreliable increase in this indicator, and at the end of the study, the FV increased by 4.3%. The difference in the final result between the 1st and 2nd groups after 1 year of observation did not reach the confidence criterion. Similar dynamics were observed in relation to the diastolic function of the heart. Thus, in group 1, the IVRT value during the first 12 weeks decreased from
129.3 ms to 121.9 m s (J5. 72%; p<0.05) and continued to decrease to 117.0 ms by the end of the follow-up period (p<0.05 compared to the result before treatment). In group 2, the IVRT score increased significantly from 121.2 ms to 126.3 ms after 12 weeks and to 129.3ms at the end of the study. The difference in the final result between the groups is at the trend level (p<0.1). Improvement of the functional state of the kidneys in group 1 was accompanied by a significant decrease in the total number of patients with concentric hypertrophy (KG) and eccentric hypertrophy (EG) of the left ventricle (LV) from 96.1% to 80.4% (J16.3%; p=0.008) after 12 weeks. By the end of the study, the number of patients with concentric hypertrophy and eccentric hypertrophy decreased to 72.5% (p<0.001 compared to the baseline value). The number of patients with normal LV geometry significantly increased from 3.9% to 17.7% at the end of the study. In the group with the nephronegative effect of therapy, the frequency of detection of LV CG and EG decreased slightly from 93.2% to 86.2% by the end of follow-up. Also, in group 2, after 48 weeks of treatment, the percentage of patients with concentric remodeling and normal LV geometry increased significantly from 6.8% to 13.8%. The difference between the groups in the frequency of detection of concentric LV hypertrophy after 1 year of follow-up is statistically significant.
The study of the autonomic regulation of the heart rate depending on the state of the kidneys indicates multidirectional shifts in the main indicators in patients of the 1st and 2nd groups. Thus, in the group with the nephroprotective effect, there was an increase in the mean square deviation (SDNN) both in the "lying" position - by 50% (from 25.8 ms to 38.7 ms; p<0.05), and during the orthostatic test – by 36.3% (from 30.6 ms to 41.7 ms; p<0.05), which is a prognostically favorable sign; and a decrease in the stress index (SI) of regulatory systems by

59.6% ($p<0.01$) in the "lying" position and by 59.3% ($p<0.01$) – when performing an active orthostatic test compared to the initial values. In patients with the nephronegative effect of basic CHF therapy, SDN decreased by 19.2% and 18.1%, while SI significantly increased by 49.7% and 16.7% in the "lying" position and during the ortho-test, respectively, compared to the initial values, which indicates an increase in the activity of the sympathetic link of the autonomic nervous system. An active orthostatic test was used to assess the functional reserves of the body.

The total power of the spectrum significantly decreased in the two groups during the first three months of observation and continued to decrease in the second group. At the same time, patients with the nephroprotective effect of basic CHF therapy showed a significant increase in this indicator due to an increase in the HF and LF components of the spectrum and a decrease in the specific weight of slow waves of the 2nd order (VLF). In the group with a negative effect of basic CHF therapy on the

functional state of the kidneys, the opposite dynamics was revealed: a decrease in HF, LF-and an increase in the VLF component. In patients of group 1, when performing the ortho-roba, there was an increase in the total power of the spectrum (by 17.6% compared to the initial values by the end of the study) and the power of the low-frequency wave range (LF), reflecting the baroreflective activity of the sympathetic division. At the same time, in patients of group 2, instead of LF increased VLF power. The dynamics of the functional state of the kidneys in patients with CHF with nephronegative and nephroprotective effects of therapy is shown in Table 2.

In both groups, by the end of the study, there was an unreliable increase in the average values of blood creatinine. At the same time, the percentage of patients with a clinically significant increase in serum creatinine (more than 124 mmol/l for women and more than 133mmol / l for men) in the group with the nephronegative effect of therapy significantly increased compared to the initial data from 27.5% to 51.7%, and in the 1st group slightly from 21.5% to 31.4%. The difference in the final result between the 1st and 2nd groups is statistically significant. In patients with a positive effect of basic therapy of CHF on the state of the kidneys, GFR significantly increased from 64.9 ml / min/1.73 m^2 up to 81.3 ml / min/1.73 m^2 after 12 weeks and continued to increase in dynamics, amounting to 93.0 ml / min/1.73 m^2 after 48 weeks ($p<0.05$). At the same time, after 3 months, the percentage of patients with GFR<60 ml/min/1.73 m^2 significantly decreased from 52.9% to 29.4% ($p=0.007$) and continued to decrease further to 5.88% by the end of the year ($p<0.001$ compared to the baseline). Urinary albumin excretion significantly decreased from 154.7 mg/day to 85.7 mg/day, and the number of patients with detectable MA decreased from 82.4% to 37.3% by the end of the study. In patients with CHF of the 2nd group, an unreliable decrease in GFR was found-from 68.7 ml/min/1, 73m^2 to 65.4 ml/min/1.73 m^2 and 56.5 ml/min /1.73 m^2 after 12 and 48 weeks, respectively. At the same time, the percentage of patients with GFR<60 ml/min/1.73 m2 increased from 27.6% to 31.0% after 3 months of follow-up, reaching 55.2% by the end of the year ($p=0.016$ compared to baseline). Urinary albumin excretion increased from 140.5 mg/day to 148.5mg/day, and the number of patients with detectable MA increased from 89.7% to 96.6% by the end of the study. The difference in the final result in the two groups between the GFR values, the average values of MA and the frequency of detection of albuminuria is highly reliable. A statistically significant difference in the detection rate of patients with GFR<60 ml/min/1.73m^2 between the two groups at the beginning of the study is noteworthy. In group 1, after 1 year of follow-up, the daily sodium excretion increased significantly – from 224.1+9.12 to 262.3+10.6 mmol/day, while in group 2, this indicator decreased from 186.9+8.83 to 180.9+8.34 mmol/day. The difference in the final result between the groups is highly significant. Similar dynamics were observed in relation to the relative density of the morning portion of urine. In patients with a positive effect of basic therapy CHF on renal function after 1 year of follow – up, there was a statistically significant increase in CR-from 97.6±1.23% to 98.8±0.82%.At the same time, in patients with a nephroactive effect of treatment, this indicator tended to decrease from 98.3=1.07% to 97.6=1.36%.

Table 2.

Dynamics of the functional state of the kidneys in patients with CHF with nephronegative and nephroprotective effects of therapy

Group	Indicator	Source code	12 weeks	Δ%	48 weeks	Δ% compared to the original indicator
1-gr nephroprotective effect	MA, mg/day	154,7±10,2	110,3±8,55	-27,7*	85,7±5,75#	-44,6*
	MA, % of patients	82,4	72,5	-12,0*	37,3#	-54,7*
	GFR, ml / min/1.73 m2	64,9±6,38	81,3±4,88	25,3*	93,0±4,93#	43,3*
	GFR less than 60 ml / min/1.73 m2, % of patients	52,9	29,4	-44,4*	5.88	-88,9*

	The excretion of Na, mmol/day	224,1±9,12	232,4±8,90	3,70	262,3±10,6#	17,1*
	Relative density of urine	1009,6±2,18	1010,8±2,20	0,12	1012,8±2,21	0,32*
	Tubular reabsorption,%	97,6±1,23	97,9±1,19	0,31	98,8±0,82	1,23*
	Blood creatinine, mmol/l	120,6+5,05	126,8±4,62	5,14	124,3±4,84	3,07
	% of patients with elevated blood creatinine	20,5	-	-	31,7#	47,0
2-gr nephronegativite effect	MA, mg/day	141,5±7,86	137,7±8,49	-0,57	147,5±9,57#	5,79
	MA, % of patients	89,1	92,1	3,79	96,6#	7,39
	GFR, ml / min/1.73 m2	68,7±4,76	65,4±4,65	-4,90	57,5±6,86#	-16,8
	GFR less than 60 ml / min/1.73 m2, % of patients	27,9	32,0	12,9	54,2	98*
	The excretion of Na,mmol/day	185,9±8,38	193,4±7,79	4,09	181,9±8,40#	-3,27
	Relative density of urine	1010,5±2,29	1011,7±1,99	0,097	1010,1±2,19	-0,03
	Tubular reabsorption,%	97,9±1,01	97,9±0,91	-0,12	97,2±1,29	-0,69
	Blood create-nine, mmol/l	118,3±4,91	130,9±4,81	10,9	130,1±4,51	9,97
	% of patients with elevated blood creatinine	27,5	-	-	51,3#	88,0*

DISCUSSION

The data obtained by us indicate that there is a close relationship between the state of the kidneys and the cardiovascular system. The results of the study of the effect of long-term therapy of CHF on the kidneys showed that the improvement of the functional state of the latter is accompanied by a more pronounced positive dynamics of the clinical status, quality of life, as well as structural and functional parameters of the heart in elderly and senile patients. LV hypertrophy (LVH) is an important risk factor for cardiovascular disease and mortality that is independent of blood pressure. According to the Framingham study, 35% of men and 20% of women aged 35-64 years die when signs of LVH appear on an ECG within 5 years. Over 64 years of age – 50% of men and 35% of women, respectively [2]. Therefore, reducing the severity of LVH is an important task, especially in the group of elderly patients, where the presence of myocardial hypertrophy is the main factor in the development of decompensation of CHF. The analysis of changes in the geometric model of the HLV, taking into account the nephrotropic effect of the basic therapy of CHF, suggests that the processes of heart remodeling are less pronounced in the group with a nephroprotective effect. The results of our study show that the positive effect of the basic therapy of CHF on the functional state of the kidneys is accompanied by an improvement in systolic (increased EF) and diastolic (decreased IVRT) heart function.

In the development of CHF, a leading place is occupied by a violation of the balance of neurohumoral systems. A non-invasive method for assessing these changes is to take into account the dynamics of heart rate variability indicators. In patients with CHF, the indicators of heart rate variability are reduced compared to the norm, which, according to large studies, correlates with the risk of sudden death and arrhythmic complications [3]. At the same time, in the

group with a negative effect of basic CHF therapy on kidney function, there is an increase in the activity of the sympathetic link of the autonomic nervous system, which indicates a pronounced strain on the regulatory systems of the body and predicts a significantly higher percentage of cardiovascular complications. The increased activity of the slow waves of the 2nd order (VLF) instead of the slow waves of the 1st order (LF) in patients of the 2nd group when performing the active orthostatic test indicates the transition to the regulation of heart rate reflex level of leadership more low – humoral-metabolic, which is also a poor prognostic sign [3]. In healthy individuals, a decrease in TP is observed during the ortho-test. The increase in the total spectral power, as well as SDNN in patients of group 1 during the ortho-test can be regarded as a hypercompensatory reaction of the body to physical activity. The increase in the total spectral power, as well as SDNN in patients of group 1 during the ortho-test can be regarded as a hyper-compensatory reaction of the body to physical activity. A comprehensive study of the dynamics of the functional state of the kidneys (glomeruli and tubules) in patients with CHF with nephroprotective and nephronegative effects of therapy indicates differently directed shifts. So, in the 1st group, the increase in cardiac output, a decrease in the activity of the sympathetic division of the autonomic nervous system accompanied by improved renal filtration function (an increase in GFR, a reduction in the percentage of patients with reduced GFR), the normalization condition tubular system (increase in daily sodium excretion and the relative density of morning urine). In group 2, on the contrary, there was a decrease in GFR and an increase in the percentage of patients with GFR<60 ml / min/1.73 m^2, which indicates the depletion of compensatory mechanisms aimed at maintaining glomerular filtration at the proper level. In the dynamics of observation, the deterioration of the concentration function of the kidneys progresses, which is reflected in a decrease in the relative density of the morning portion of urine. The ability of the kidneys to remove sodium in patients of group 2 steadily decreases with the progression of CHF, which indicates a deterioration in the volumetric function of the kidneys. In the group with the nephroprotective effect of treatment, there is a decrease or disappearance of MA, which is a criterion for improving the prognosis of patients with CHF. At the same time, among patients with a negative effect of basic CHF therapy on the kidneys, the opposite dynamics of MA is noted, which indicates a violation of glomerular microcirculation. With an increase in the duration of CHF, the nitrogen-releasing function of the kidneys progressively worsens, most clearly expressed in patients with the nephronegative effect of basic CHF therapy. This is accompanied by a statistically significant increase in the number of patients with elevated serum creatinine levels in group 2 and is associated with an unfavorable prognosis.

CONCLUSIONS

1. In patients with MI, complicated by CHF, impaired renal function should be considered as a predictor of cardiovascular problems.
2. The effectiveness of treatment of CHF in the elderly and senile depends on the nephrotropic effect of basic therapy. A decrease or disappearance of MA, normalization of GFR at the end of the 12th week of treatment predicts a subsequent (12 months) good or satisfactory clinical effect: an increase in exercise tolerance, an increase in LVEF, a favorable effect on the processes of heart remodeling and autonomic homeostasis, and an improvement in the quality of life of patients with CHF.

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