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MYOCARDIAL INFARCTION: NEUROHUMORAL DISORDERS AND PROTEOLYTIC PROCESSES AGAINST THE GROUND OF CHRONIC KIDNEY DISEASE

Abstract. *Certain peculiarities of intracardiac hemodynamics and neurohumoral regulation have been found during examination of patients with acute myocardial infarction and renal dysfunction available with the indices of glomerular filtration rate ≤ 90 ml/hour and > 90 ml/hour. In patients with acute myocardial infarction and glomerular filtration rate ≤ 90 ml/hour a reliable decrease of blood minute volume was detected (p<0,05), a reliable increase of aldosterone level (p<0,05) and reliably higher concentration of angiotensin converting enzyme (ACE) (p<0,05), increase of blood serum proteolytic activity by the level of asocaseinolysis (p<0,05).*

Key words: *myocardial infarction, heart failure, aldosterone, angiotensin converting enzyme (ACE), atrial natriuretic peptide, Willebrand factor.*

Introduction. According to certain studies even mild dysfunction of the kidneys irrespective of other risk factors and treatment is accompanied by more frequent cardio-vascular complications up to 40%. Acute myocardial infarction (AMI) associated with acute renal damage is connected with three times increase of early mortality and twice as often long-term mortality [1]. According to the data obtained after analysis of a hospital sampling of 753 782 patients admitted to the hospital with AMI during 2007-2012, in 17,8% of them the diagnosis of chronic kidney disease (CKD) was confirmed. In patients with CKD the rate of hospital mortality appeared to be higher (8,4% against 5,0%; OS 1,55, 95% CI 1,51-1,59) [2].

Objective: to study the dynamics of intracardiac hemodynamics, neurohumoral disorders, proteolytic activity in patients with acute myocardial infarction against the ground of chronic kidney disease.

Materials and methods. 106 patients were examined who stayed in the hospital concerning acute Q-myocardial infarction with heart failure (HF). The diagnosis was verified according to the standards of the European Association of Cardiologists. An average age of patients was 51,5±3,94. CKD was diagnosed in all the patients against the ground of chronic pyelonephritis in remission phase, who depending on glomerular filtration rate (GFR) formed 2 groups: the 1st group included patients with GFR ≤90 ml/hour, the 2nd group – with GFR >90 ml/hour. The parameters of the myocardial functional state were detected by means of echocardiography (echoCG) from the parasternal and apical positions along the short and long axes with the following calculation of cardiohemodynamic indices: left ventricular final diastolic size (LVFDS), left ventricular final systolic size (LVFSS), intraventricular septum thickness in systole and diastole (IVSTs and IVSTd), left ventricular posterior wall thickness in systole and diastole (LVPWTs and LVPWTd). A number of indices was calculated by certain formulae: ejection fraction (EF), final diastolic volume (FDV), final systolic volume (FSV), stroke volume (SV), myocardial mass (MM) of the left ventricle, and myocardial mass index (MMI) of the left ventricle. By means of immunoenzyme method hormone levels were detected in all the patients: aldosterone, angiotensin converting enzyme (ACE), atrial natriuretic peptide (ANUP), and Willebrand factor. GFR was detected by means of Cockcroft-Gault formula. The results of the investigation were statistically processed with the use of electron tables Microsoft® Office Excel (build 11.5612.5703), program for statistical processing Statgraphics Plus5.1 Enterprise edition

(®Statistical Graphics corp. 2001).

Results and discussion. The data obtained (Table 1) are indicative of the fact that patients with AMI with GFR ≤ 90 ml/hour present a reliable decrease of the blood minute volume (BMV) (5290,20±301,09 against 5990,42±296,38 L/min respectively; p<0,05), proving the availability of considerable disorders of pumping ability of the heart and determining more severe course of the disease at the expense of circulating blood volume and an increased preload.

Other indices of EchoCG in both groups did not differ statistically reliably. The examination of levels of neurohumoral messengers in patients with AMI revealed (Table 2) that in patients with GFR ≤90 ml/hour aldosterone level was reliably higher than in patients with GFR >90 ml/hour (251,54±9,34 against 236,24±8,83 pmole/L; p<0,05).

It proves the literature data [3], that aldosterone in case of AMI and acute HF inhibits functional activity of the kidneys. Reduction of GFR promotes retention of water ad electrolytes in the body resulting in progressing of HF. It is important that ANUP concentration in the groups of investigation did not have reliable statistical difference (p>0,05), that can be one of the signs of

Table 1

Indices of intracardiac hemodynamics in patients with AMI with different stages of kidney dysfunction

№	Index	GFR ≤90 ml/hour (n=26)	GFR >90 ml/hour (n=26)	P
1.	FDS (cm)	4,98±0,08	4,81±0,07	p>0,05
2.	FSS (cm)	3,59±0,13	3,49±0,07	p>0,05
3.	IVSTs (cm)	1,06±0,06	1,12±0,03	p>0,05
4.	IVSTd (cm)	1,02±0,05	1,02±0,03	p>0,05
5.	LVPWTs (cm)	1,00±0,03	1,11±0,03	p>0,05
6.	LVPWTd (cm)	0,96±0,06	1,06±0,03	p>0,05
7.	FDV (ml)	119,92±9,65	110,31±4,66	p>0,05
8.	FSV (ml)	55,38±4,42	51,75±2,47	p>0,05
9.	SV (ml)	64,54±7,33	58,56±2,57	p>0,05
10.	EF (%)	52,62±0,86	53,19±0,83	p>0,05
11.	BMV (L/min)	5990,42±296,38	5290,20±301,09	p<0,05
12.	ΔS%	27,57±0,60	27,49±0,44	p>0,01
13.	ΔTзс (%)	0,17±0,05	0,13±0,02	p>0,05
14.	ΔTmH (%)	0,15±0,04	0,15±0,02	p>0,05
15.	Δp (%)	0,41±0,03	0,44±0,01	p>0,05
16.	MM of the LV (g)	180,38±11,21	186,69±7,69	p>0,05
17.	IMM of the LV (g/m²)	91,04±5,55	94,00±3,96	p>0,05
18.	wall thickness of the LV	0,40±0,02	0,44±0,01	p>0,05

Table 2

Indices of neurohumoral regulation of patients with myocardial infarction with different stages of kidney dysfunction

№	Index	GFR ≤90 ml/hour (n=13)	GFR >90 ml/hour (n=93)	P
1.	Aldosterone (pmole/L)	251,54±9,34	236,24±8,83	<0,05
2.	Atrial natriuretic peptide (pg/ml)	54,46±4,81	59,01±3,77	>0,05
3.	Angiotensin converting factor (ACF) (mcmole/min/L)	72,83±2,43	65,28±3,81	<0,05
4.	Willebrand factor (mg/L)	1,06±0,13	1,20±0,07	>0,05

imbalance of the neurohumoral regulatory systems, що може бути одним із проявів дисбалансу нейрогуморальних регуляторних систем. ACF concentration in patients with GFR ≤90 ml/hour was reliably higher that in the groups of comparison (72,83±2,43 against 65,28±3,81 mcmole/min/L; p<0,05). The results obtained prove literature data concerning angiotensin inhibition of II filtration ability of the kidneys through a marked vasoconstriction of glomerular vessels [4]. The level of Willebrand factor in the groups of patients with GFR value did not differ much statistically (Table 3).

Examination of correlation relations between neurohumoral factors and the indices of intracardiac hemodynamics found (Table 3) that aldosterone level correlated positively with the degree of systolic thickening of the intraventricular septum (ΔTmH) (r=0,27; p<0,01), which proves aldosterone effect on this index. ANUP concentration correlated negatively with SV (r=-0,21; p<0,05), EF (r=-0,27; p<0,01) and BMV (r=-0,21; p<0,05). A positive correlation connection was found between the level of ANUP and ΔTmH (r=0,27; p<0,05). Willebrand factor was characterized by negative correlation relations with ΔTmH (r=-0,21; p<0,05) and ΔTзс (r=-0,23; p<0,01).

Table 4 illustrates that in patients with GFR ≤90 ml/hour increased proteolytic activity of the venous blood serum, although reliable differences were found only concerning azocasein (p<0,05).

Considering the fact that the contents of average molecular peptides include biologically active substances participating in the regulation of the vascular tonus and kidney functions, the results obtained can reflect disorders of humoral mechanisms of GFR regulation.

A highly reliable negative correlation relation of aldosterone level with proteolysis activity by azocollagen (r- 0,36;p < 0,01). Nowadays an important participation of the proteolytic blood system in ischemic damage of the myocardium, development of HF and processes of myocardium remodeling is an established factor which regulates the rate of collagen structures formation both in cardiomyocytes and extracellular space [5, 6].

Table 3

Correlation coefficient between the indices of the myocardial functional state and parameters of neurohumoral regulation factors activity

№	Index	Aldosterone	ACF	ANUP	Willebrand factor
1.	FDS (cm)	-0,03	0,01	-0,1	0,02
2.	FSS (cm)	-0,04	0,10	0,05	-0,006
3.	IVSTs (cm)	-0,04	-0,05	0,09	0,14
4.	IVSTd (cm)	0,08	-0,05	-0,09	0,07
5.	LVPWTs (cm)	-0,03	0,04	0,01	0,002
6.	LVPWTd (cm)	0,08	0,09	-0,06	0,29
7.	FDV (ml)	-0,03	0,01	-0,1	0,02
8.	FSV (ml)	0,10	-0,03	0,05	-0,002
9.	SV (ml)	-0,0009	0,02	-0,20*	0,04
10.	EF (%)	0,01	-0,14	-0,27**	-0,09
11.	BMV (L/min)	0,03	0,04	-0,20*	0,01
12.	ΔS%	0,02	-0,11	-0,28**	-0,09
13.	ΔTзс	0,19	0,06	-0,03	-0,23**
14.	ΔTmH	0,27**	0,15	0,26*	-0,20*
15.	Δp	-0,04	0,05	0,009	0,15
16.	MM of the LV (g)	0,11	0,12	-0,13	0,16
17.	IMM of the LV (g/m²)	0,10	0,09	-0,12	0,17
18.	wall thickness of the LV	0,04	-0,05	0,02	0,16

Note: * - probability ratio p < 0,05; ** - < 0,01(only statistically reliable differences are presented)

Table 4

Proteolytic activity of blood serum in patients with myocardial infarction with different stages of kidney dysfunction

№	Index	GFR ≤90 ml/hour (n=13)	GFR >90 ml/hour (n=93)	P
1.	Azoalbumin (E440/ml/hour)	0,179±0,003	0,176±0,003	>0,05
2.	Azocasein (E440/ml/hour)	0,180±0,001	0,175±0,002	<0,05
3.	Azocollagen (E440/ml/hour)	0,011±0,001	0,009±0,001	>0,05

Conclusions. 1. Patients with acute myocardial infarction with II stage of chronic kidney disease present a reliable reduction of the minute blood volume ($p<0,05$), a reliable increase of aldosterone ($p<0,05$) and reliably higher concentration of angiotensin converting enzyme ($p<0,05$). 2. With reduced glomerular filtration rate ≤ 90 ml/hour in patients with acute myocardial infarction against the ground of chronic kidney disease an increased proteolytic activity of the blood serum was found by the level of azocaseinolysis ($p<0,05$).

Prospects of further studies. Investigations of fibrinolytic system in patients with acute myocardial infarction with progressing heart failure against chronic kidney disease are rather reasonable.

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