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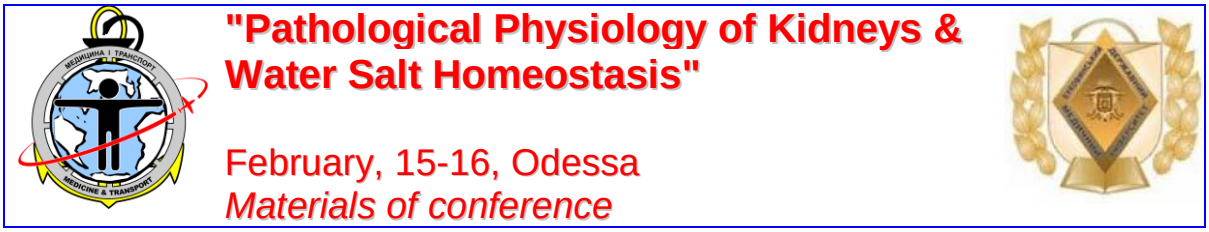

CARDIO-RENAL MECHANISMS OF ADAPTATION IN NORMAL AND WITH HEART FAILURE

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Abstract

The pathogenesis of chronic heart failure (CHF) is a complex multifactorial process, which is a close combination of manifestations of the effects on the cardiovascular system of the etiological factor (s) and the mobilization of a whole complex of compensatory mechanisms [30].

According to the first conceptual models (cardiac (1950s) and cardiorenal (1960s)) pathogenesis, the main role in the formation of CHF belonged to a decrease in cardiac contractility (systolic dysfunction), as well as electrolyte retention and body water. [4, 14, 39].

The aim of the study was to study the role of the renin-angiotensin-aldosterone system and the natriuretic hormone in adaptive changes in water-salt homeostasis with an increase in venous blood return to the heart in healthy and in patients with stable ischemic heart disease with chronic heart failure stage I (stage I).

The results of the study concluded: - in healthy individuals, an increase in venous return of blood to the heart (preload) in anti-orthostasis on the background of 0.5% water load is accompanied by adaptive changes in cardiohemodynamics, volemic homeostasis and neurohumoral regulation of water-salt metabolism, manifested by an increased influence of the parasympathetic department ANS, a decrease in heart rate, an increase in ASI while maintaining the IOC at the same level, an increase in diuresis, a decrease in the activity of the RAAS, an increase in the content of α-PNOG; - in patients with coronary artery disease with HNK I st. with an increase in preload at the 30th minute of anti-orthostasis, changes in cardio hemodynamics (decrease in IOC) and cardiac rhythmograms were revealed, indicating a depletion of myocardial reserve capacity and vegetative regulation of heart rhythm. The lack of heart rate dynamics and cardiac rhythmograms in anti-orthostasis reflects an increase in the activity of the sympathetic section of the autonomic nervous system in patients with coronary artery disease with the initial stage of HNK; - kidney reaction to anti-orthostasis and 0.5% water load in patients with coronary artery disease with HNK, I st. expressed in increased diuresis in the absence of changes in the activity of the RAAS, which indicates the predominance of antinatriuretic systems over natriuretic; - the earliest indicator of the development of heart failure in patients with coronary artery disease is sodium retention, aimed at increasing the BCC, venous return of blood to the heart and stimulation of the heterometric mechanism of Frank-Starling.

Keywords: chronic heart failure, renin-angiotensin-aldosterone system, natriuretic hormone, water-salt homeostasis

The pathogenesis of chronic heart failure (CHF) is a complex multifactorial process, which is a close combination of manifestations of the effects on the cardiovascular system of the etiological factor (s) and the mobilization of a whole complex of compensatory mechanisms [30].

According to the first conceptual models (cardiac (1950s) and cardiorenal (1960s)) pathogenesis, the main role in the formation of CHF belonged to a decrease in cardiac contractility (systolic dysfunction), as well as electrolyte retention and body water. [4, 14, 39].

It should be noted that within the framework of this paradigm, the mechanisms of violation of the filling of the ventricles with blood during the development of circulatory failure were not considered. The widespread use of this concept led to the active use of cardiac glycosides in clinical practice, and then diuretics for the treatment of congestive syndrome. [24, 31].

In the mid-70s. In the past century, the cardiocirculatory model was the most popular [14, 25, 39]. It is known that in the event of myocardial dysfunction, compensatory hemodynamic shifts develop, which can be divided into heterometric (increased preload, myocardial hypertrophy) and homeometric (increased heart rate, increased total peripheral resistance). These changes in hemocirculation, initially aimed at increasing the stroke volume and (or) maintaining blood pressure while reducing cardiac output due to Frank-Starling mechanisms (increase in strength and speed of contraction with increasing fiber length), Bowdich (increase in strength and speed of contractions with increasing rhythm Hearts), Anrep (increase in the force of contraction of the heart with an increase in afterload), over time, play a negative role (increase in myocardial oxygen demand, dilatation of the heart cavities itieni relative valve insufficiency, etc.), causing the progression of cardiac decompensation. From the hemodynamic point of view, the combination of a decrease in the pumping function of the myocardium and impaired peripheral circulation associated with changes in pre- and post-loading characteristics is the direct cause of CHF manifestation [14]. According to this theory, drugs that affect both central and peripheral hemodynamics were introduced into the practice of treating CHF [25, 36]. However, numerous clinical studies have led to disappointment in inotropic stimulants (sympathomimetics, phosphodiesterase inhibitors) and a far from unequivocal assessment of the efficacy and safety of vasodilators in left ventricular dysfunction (LV) [14, 25].

1980s - early 1990s characterized by the creation of the neurohumoral theory of the pathogenesis of CHF, according to which heart failure is the result of the negative impact on target organs of prolonged neurohumoral hyperactivation at the circulatory and, more importantly, tissue level [14, 20, 25, 39]. Currently, the neurohumoral model is widely recognized and confirmed by the results of numerous studies that demonstrate an increase in the survival rate of patients with CHF as a result of neurohumoral heart discharge using angiotensin-converting enzyme inhibitors (ACE inhibitors) [25, 37, 38, 40, 41].

According to the neurohumoral model of heart failure, a decrease in cardiac output causes a pronounced activation of neurohumoral systems (sympathetic-adrenal, renin-angiotensin, endothelium, etc.), which occurs according to the vicious circle principle (compensatory stimulation of neurohumoral factors, which in turn aggravates heart overload, further reduces cardiac output and again stimulates the neurohumoral system). As a result of a decrease in cardiac output, the blood supply of organs and tissues, including the kidneys, is deteriorating, which is accompanied by the inclusion of the renal link in the pathogenesis of CHF. To maintain a normal level of blood pressure with a reduced cardiac output increases

the activity of the sympathetic-adrenal system. Increased secretion of catecholamines, mainly norepinephrine, leads to a narrowing of the arterioles and venules. Insufficient blood supply to the kidneys leads to activation of the renin-angiotensin-aldosterone system (RAAS). Excess angiotensin II (AT II), a powerful vasoconstrictor, further increases peripheral vasospasm. At the same time, AT II stimulates the formation of aldosterone, which increases sodium reabsorption, increases plasma osmolarity, and contributes to the activation of the production of antidiuretic hormone (ADH) in the posterior pituitary gland. Increasing the level of ADH leads to a delay in the body fluid, an increase in circulating blood volume (BCC), the formation of edema, an increase in venous return. Vasopressin (ADH), as well as norepinephrine, and AT II, enhances vasoconstriction of peripheral vessels. As the venous return of blood to the heart increases, there is an overflow of vessels in the pulmonary circulation, an increase in the diastolic filling of the affected left ventricle with blood. There is a further expansion of the ventricle and an increasing decrease in cardiac output.

The aim of our study was to study the role of the RAAS and natriuretic hormone in adaptive changes in water-salt homeostasis with an increase in venous return (IV) of blood to the heart in healthy and in patients with stable ischemic heart disease (CHD) with heart failure stage I (stage I). A total of 73 people were examined, of them 46 patients with coronary artery disease, manifested by stable stenocardia of the II-III functional classes, and 27 healthy individuals. Among the patients examined, men (31 people) prevailed. The age of patients ranged from 34 to 62 years. The diagnosis of coronary artery disease was established on the basis of the clinic and instrumental study, which included an ECG, Holter ECG monitoring, EchoKS, and measured physical activity on a bicycle ergometer. 33 patients were diagnosed with chronic circulatory failure (HNC) stage I (stage I) according to the classification of N.D. Strazhesko, V.H. Vasilenko, and at the 13 - 0 stage. Of the total number of patients, 12 people previously had not Q and Q myocardial infarction for 1 year or more. The study did not include persons with concomitant hypertension, rhythm disturbances, diabetes, lung, liver and kidney diseases.

Among healthy individuals, men also prevailed (14 out of 20). The age of the subjects ranged from 22 to 52 years.

The survey was conducted in a hospital and clinic in the conditions of the main exchange. 5-7 days prior to the study, patients and persons in the control group were transferred to diet No. 10 with a daily intake of table salt up to 8-10 g and 1.5 liters of liquid. Cardiac glycosides were canceled 5 days prior to the study, calcium antagonists and beta-blockers for 2 days. Nitrates were used only when indicated. The method of EchoKS received

valuable information for the differential diagnosis of coronary artery disease with cardiomyopathies and heart defects. Considering that the assessment of left ventricular volumes and ejection fractions obtained using this method may be distorted due to myocardial asynergy [17], when studying central hemodynamics (CHD) we preferred tetrapolar thoracic rheography (TPRG).

When diagnosing HNC, the dependence of dyspnea on the degree of physical exertion, the presence of tachycardia at rest, and changes in the small and large circles of blood circulation were taken into account. When HNK I Art. signs of heart failure - shortness of breath, palpitations - occurred only with the usual loads.

For objectification HNK I Art. Bicycle ergometry was performed in conjunction with TPRG. A sign of latent decompensation was considered to be a decrease in stroke blood volume (ACE) at the level of submaximal exercise [22, 23]. In cases where the coronary reserve was depleted earlier myocardial in the HEM test, the diagnosis of HNK was based on the clinic and EchoX data at rest (an increase in the final diastolic size of the left ventricle, a decrease in the ejection fraction, the rate of circular shortening of the muscle fibers).

To stabilize diuresis, to study the degree of conjugation of the functions of the heart and kidneys in healthy and IHD patients in order to diagnose incipient heart failure, we have developed an original research method, protected by copyright evidence [1]

Studies were performed in the morning on an empty stomach after emptying the bladder and resting in the functional diagnostics room for 15-20 minutes, air temperature - 200. To ensure stable diuresis, a water load was performed by ingesting water at the rate of 0.5% of body weight (boiled water at room temperature). After the water load, the subject was placed on a couch in a horizontal position (Klinostasis - CS) for 1 hour. At the 55th minute, blood pressure (BP) was measured, ECG, TPRG were recorded. At the 60th minute, blood was taken from the cubital vein, then urine was collected. After that, the water load was repeated in the same volume, but in combination with the volume load using passive lifting of the lower limbs and fixing them at an angle of 450 (anti-apostostasis - AOC). At the 55th minute after lifting the legs, blood pressure was measured, ECG, TPRG were recorded, blood was taken from a vein, and urine was collected. Compared the obtained results of the study of the functions of the heart and kidneys in the provisions of the COP and AOC.

As shown by the results of studies [3], passive lifting of the legs by 30-450 provides an increase in the diastolic pressure of the pulmonary artery by 2-3 mm Hg. Art., which is enough to change the shock index in accordance with Frank-Starling law.

In patients and healthy individuals, the heart rate (HR), systolic (DM) and diastolic (DD) blood pressure, mean dynamic pressure (DMD) were determined by well-known methods. The CHD indicators were investigated by the TPRG method on an RPG2-02 device using the Kubitschek method modified by Yu.T. Pushkar et al. [28]. The stroke volume of blood (ASM), minute volume of blood (IOC), total peripheral vascular resistance (CPS), ejection power (P), left ventricular function (A beats.) Were calculated using the generally accepted formulas.

The vegetative regulation of cardiac rhythm was investigated using rhythmography [2]. At the same time, 200 ECG complexes in the second standard lead were recorded sequentially at a belt speed of 25 mm / s. Rhythmograms were recorded at the 15th minute of the CS and the 30th minute of the AOC. The average duration of R-R intervals (-R-R), the standard deviation of R-R (σR-R), reflecting the dispersion of the rhythmogram, and the variation range (BP) were determined. Conducted a graphical construction variational intervalogram.

In urine samples, creatinine content was determined by Folin [5], and in blood plasma - by Popper modified by A.K. Merzon et al. [26]. According to the standard formulas, glomerular filtration and tubular reabsorption of water were calculated [35]. The concentration of sodium and potassium in the blood plasma, erythrocytes and urine was studied by photometry using the FPL-1 apparatus in appropriate dilutions [21]. Excretion of sodium (ENa), potassium was studied. The sodium clearance, the filtered fraction of sodium and potassium were calculated, the MOK coefficient was sodium excretion (MOK / ENa). The main indicators of kidney activity were calculated per 1 m2 of the body surface.

Investigated the state of the RAAS and the content of atrial natriuretic hormone (α-PUGH) blood plasma according to radioimmunological studies using the International CIS (France), Sorin Biomedica (Italy), Buhlmann Laboratories (Switzerland), International Inc. kits. "(GDR) on the domestic gamma counter" Gamma-12 ".

Indicators of cardiohemodynamics and rhythmograms of the heart in 20 healthy people with an increase in IV of blood to the heart in the AOC position are presented in Table 1.

As can be seen from the data presented in Table 1, an increase in the blood BB to the heart in the AOC position led to a significant decrease in the heart rate (-7.3%), an increase in ASI (+ 11.3%), WWS (+ 10.5%), P (+ 9.6%), And beats. (+ 11.5%).

Table 1

Indicators of CHD and rhythmograms of the heart in healthy individuals (n = 20) in the provisions of the KS (1 h) and AOC (1 h) on the background of 0.5% water load

Indicators	KS ***(M±m)***	***AOC (M±m)***
HR, 1 min	68,4±2,07	63,45±1,99*
DM, mmHg st.	126,15±2,72	122,65±3,34
DD, mm Hg st.	80,85±2,2	83,75±2,64
SDD, mm Hg st.	96,18±2,39	96,72±2,74
Stroke volume, ml	87,06±4,3	96,92±4,48*
Minute volume of blood, l/min	5,9±0,29	6,12±0,29
Total peripheral vascular resistance, dns.cm^{-5}	1364,4±75,46	1327,6±79,85
WWS, ml / s	342,89±15,43	379,04±15,25*
R, W	4,37±0,22	4,79±0,2*
A beats., J	1,13±0,06	1,26±0,05*
IR-R, c	0,846±0,045	0,889±0,041*
σ_{R-R}	0,039±0,007	0,0504±0,008*
Variation scale, c	0,218±0,044	0,262±0,038*

Note: KS - klinostasis; AOC –antiotostasis; * - $p < 0,05$.

Due to the fact that the SDD almost did not change, and the IOC increased only by 3.7%, the dynamics of the results of the PPSS turned out to be insignificant.

The study of the vegetative regulation of heart rhythm according to the cardiac rhythmography (Table 1) revealed in AOC a significant lengthening of the IR-R, an increase in σR-R and BP, a shift to the right and a flattening of the variation intervalogram. The reorganization of the periodic structure of the cardiac rhythm observed in the studied healthy individuals indicates a significant increase in the influence of the parasympathetic division of the autonomic nervous system (ANS) on the cardiovascular system in anti-orthostasis.

To study the degree of conjugation of the functions of the heart and kidneys in healthy studies of the parameters of cardio hemodynamics (see Table 1) were carried out under conditions of twice used 0.5% water load with urine collection after 1 h of CS and 1 h of AOC. Along with the renal functions, the activity of the RAAS, the content of α-PUG blood plasma were determined (Table 2).

As can be seen from the data of table 2, after 1 h AOC significantly increased diuresis by reducing tubular reabsorption of water. A significant decrease in the specific gravity of urine, a decrease in the concentration of creatinine, sodium, urine potassium, and creatinine excretion were also established. The excretion of sodium and potassium changed slightly due to a significant increase in diuresis after an increase in IV of blood to the heart in the AOC position.

Table 2

Indicators of renal function, the activity of the RAAS and the content of α-PUG blood plasma in healthy individuals (n = 20) in the provisions of the KS (1 h) and AOC (1 h) against 0.5% water load

Indicators	KS ***(M±m)***	***AOC (M±m)***
Diuresis, ml / h / m^2	187,12±22,85	277,01±17,6*
Urine specific gravity	1005,6±1,34	1001,1±0,43*
Creatinine plasma, μmol / l	92,61±3,13	89,12±3,79
Creatinine urine, mmol / l	5,95±1,08	2,99±0,39*
Creatinine excretion, mmol / h.m^2	0,86±0,09	0,72±0,06*
Glomerular filtration, ml / min.m^2	160,3±19,11	141,81±15,49
Tubular water reabsorption, %	97,36±0,47	95,64±0,65*
Sodium urine, mmol / l	75,58±10,73	46,55±5,72*
Urine potassium, mmol / l	38,49±6,69	23,13±4,02*
Renin activity, ng / ml.h	2,55±0,29	1,94±0,36*
Aldosterone, pg / ml	242,33±42,05	166,17±38,15*
Antidiuretic hormone, PG / ml	3,64±0,89	2,1±0,6*
α-PUG, pg / ml	32,53±3,06	41,0±3,22*

Note: KS - klinostasis; AOC –antiotostasis; * - $p < 0,05$

In order to clarify the role of the RAAS in adaptive changes of cardiohemodynamics and volumetric regulation of the kidney when the value of the explosives of blood to the heart changes in healthy people, plasma renin activity, aldosterone, ADH and α-PNUG plasma levels were studied after 1 h of CS and 1 h of AOS against 0.5 % water load (table. 2). At the same time, a significant reduction in the content of all components of the RAAS was found in the AOC, an increase in the content of α-PNUG in blood plasma.

Consequently, when transferring healthy persons from a klinostasis to an anti-orthostasis, a humoral reorganization of the regulation of water-salt metabolism is observed in the form of suppressing the activity of the RAAS against the background of an increase in α-POCP of blood plasma, aimed at preventing overflow of small circulation vessels and reducing BCC by removing fluid from the body.

Thus, the most constant reflex response with an increase in the blood level of the blood to the heart in healthy people in our model of preload increase is bradycardia due to the increased activity of the parasympathetic division of the ANS (according to the rhythmogram of the heart). An increase in the CRM at the AOS position should be interpreted as a manifestation of the heterometric mechanism of the Frank-Starling due to the increased stretching of the heart chambers in diastole.

Increased diuresis in the AOC position is primarily due to the reflex humoral reorganization of water-salt metabolism (suppression of the RAAS activity, increase in α-POCH) and, possibly, changes in the intrarenal circulation, since the glomerular filtration has not significantly changed.

To develop diagnostic criteria for the initial stage of heart failure in 30 patients with stable coronary artery disease with stage 0–1 HNK, according to ND Strazhesko, V.H. Vasilenko studied the cardio-renal mechanisms of adaptation when changing the value of hepatic blood supply to the heart (Table 3).

Table 3

Indicators of CHD in patients with IHD with HNK I Art. (n = 17)
in the provisions of the KS (1 h) and AOC (1 h) on the background of 0.5% water load

Indicators	***KS (M±m)***	***AOC (M±m)***
HR, 1 min	66,23±1,91	65,0±2,13
DM, mmHg st.	129,7±3,1	128,82±4,8
DD, mm Hg st.	82,06±2,54	84,4±1,86
SDD, mm Hg st.	99,11±3,33	99,2±2,57
Stroke volume, ml	85,01±5,69	74,52±3,77
Minute volume of blood, l/min	5,65±0,44	4,81±0,29*
Total peripheral vascular resistance, dns.cm^{-5}	1532,0±124,0	1738,5±112,49
WWS, ml / s	346,15±19,99	315,28±15,78
R, W	4,69±0,29	4,18±0,28
A beats., J	1,08±0,08	0,99±0,07

Note: KS - klinostasis; AOC –antiotostasis; * - $p < 0,05$.

As can be seen from the data presented in Table 3, an increase in the blood levels of the blood to the heart in the AOC position against the background of 0.5% water load in patients with coronary artery disease with HNK, I st. did not affect heart rate. The IOC, in contrast to the corresponding indicator in healthy, significantly decreased. They showed a tendency to a decrease in ASI, OSV, P, OPSS slightly increased, but did not change. In the group of healthy (see Table 1), the dynamics of the indicated parameters of cardio hemodynamics was the opposite.

Along with the indices of cardiohemodynamics, the functions of the kidneys, the state of the RAAS of blood plasma after 1 h of KS and 1 h of AOC against the background of 0.5% water load were determined in patients (Table 4).

In contrast to CHD, baseline indicators of renal function in patients with coronary artery disease with HNK I Art. after 1 h, the KS and 0.5% of the water load differed from those in healthy under similar conditions (see Table 2). EN in patients with coronary artery

disease with HNK I Art. after 1 h, the KS was 7.46 ± 1.09 mmol / h.m2, in healthy people - 12.22 ± 1.56 mmol / h.m2 (p <0.02). Sodium retention by the kidneys in patients by increasing its reabsorption (99.37 ± 0.09% in patients and 99.05 ± 0.102% in healthy people, p <0.02), combined with a slight decrease in diuresis and glomerular filtration, affected the clearance and excreted electrolyte fraction (significant decrease).

Table 4

Indicators of renal function, the activity of the RAAS and the content of α-PUG blood plasma in patients with coronary artery disease with HNK I Art. (n = 17) in the provisions of the KS (1 h) and AOC (1 h) on the background of 0.5% water load

Indicators	***KS (M±m)***	***AOC (M±m)***
Diuresis, ml / h / m^2	147,43±21,02	273,94±22,48*
Urine specific gravity	1003,6±0,75	100,7±0,43*
Creatinine plasma, μmol / l	91,4±4,07	97,03±3,78*
Creatinine urine, mmol / l	8,2±1,56	2,86±0,41*
Creatinine excretion, mmol / h.m^2	0,76±0,1	0,62±0,06
Glomerular filtration, ml / min.m^2	120,9±9,37	110,81±8,85
Tubular water reabsorption, %	98,15±0,36	95,87±0,49*
Sodium blood plasma, mmol / l	148,96±3,16	150,1±3,37
Sodium urine, mmol / l	76,98±11,37	43,09±7,29*
Sodium excretion, mmol / h.m^2	7,46±1,09	9,02±1,19
Filtration of sodium, mmol / min	33,17±2,53	31,73±2,73
Excreted sodium fraction, %	0,62±0,09	0,95±0,15*
Reabsorbable fraction of sodium, %	99,37±0,09	99,04±0,15*
Potassium blood plasma, mmol / l	4,27±0,11	4,29±0,11
Urine potassium, mmol / l	36,42±5,56	19,99±4,35*
Excretion of potassium, mmol / h.m^2	3,74±0,52	4,58±0,83
Renin activity, ng / ml.h	3,25±0,34	2,84±0,25
Aldosterone, pg / ml	289,14±39,55	284,43±47,14
ADH, pg / ml	4,56±0,89	3,6±0,71

Note: KS - klinostasis; AOC –antiotostasis; * - p < 0,05

An increase in blood IV to the heart under AOS conditions and water load was accompanied, as in healthy people (see Table 2), by a significant increase in diuresis due to a decrease in tubular water reabsorption, a decrease in specific gravity and urine concentration of creatinine, sodium, potassium. A slight but significant increase in plasma creatinine concentration in the AOC did not significantly affect the level of glomerular filtration.

Unlike healthy in patients with coronary artery disease with HNK I Art. The reaction of the kidneys to AOC and water load resulted in a greater increase in hourly diuresis (+36.6 ml). A certain tendency to an increase in the excretion and clearance of sodium was also revealed with a significant increase in the excreted and a decrease in the reabsorbable fraction

(p <0.02). The ratio of IOC / ENA in patients with coronary artery disease with HNK I Art. due to the retention of sodium significantly more (34.68 ± 6.51 units) than in healthy ones (20.7 ± 2.83 units, p <0.02). With an increase in the blood BB to the heart in AOC, the IOC / ENa ratio due to a significant decrease in IOC and a slight increase in sodium excretion significantly decreased (23.55 ± 4.14 units, P <0.02).

The study of the role of blood RAAS in adaptive changes in water-salt homeostasis with an increase in blood IV to the heart in IHD patients with HNK, I st. (Table 4) did not reveal significant changes in the content of renin, aldosterone and ADH in blood plasma with an increase in the preload in the AOC.

To clarify the nature of the hemodynamic response to the COP and AOC in time in 7 healthy and 7 patients with HNK I Art. TPRG was recorded every 15 min of CS (4 times), and then every 15 min of AOS (4 times) against a background of 0.5% water load. Determined heart rate, wak, IOC. It was established that in klinostasis, the fluctuations of the listed parameters in healthy and sick patients are minimal. In healthy people, a decrease in heart rate, an increase in CRM is noted already at the 15th min of AOS and remains almost at the same level until the end of the study. In patients with coronary artery disease with HNK I Art. The heart rate in AOS is reduced slightly, and the maximum reduction in ASM and IOC is registered at the 30th and 60th minute of the increase in preload.

In connection with the above, further studies of cardiohemodynamics were conducted only at the 15th minute of the KS and the 30th minute of the AOC without water load. This model of the increase in BB to the heart is used to study the characteristics of the hemodynamic response to AOS in patients with coronary artery disease with chronic ocular carcinoma 0-1 and the development of diagnostic criteria for the initial stage (HNK I st.) of heart failure.

The indices of CHD and rhythmograms of the heart were studied in 22 CHD patients with HNK 0-I st. on the 15th minute of the KS and the 30th minute of the AOC without water load (Table 5).

It has been established that in patients with IHD with HNK 0 tbsp. on the 30th minute, the AOC heart rate decreased insignificantly, the CRI, IOC, OSV, R, A beats increased significantly, the CRSD decreased, and there were no significant changes in the SDD (Table 5). In terms of their direction, these shifts resemble those of healthy people, with an increase in the blood supply of the blood to the heart at the 60th minute of the AOC and 0.5% of the water load (see Table 1). The exception is HR and IOC. In healthy AOC, there is a significant

increase in CRM, however, due to a significant decrease in heart rate, the IOC practically remained at the level of baseline values.

Table 5

Indicators of CHD and heart rhythmograms in patients with coronary heart disease with HNK 0 tbsp. (n = 13) and HNK I Art. (n = 9) at the 15th minute of the KS and the 30th minute of the AOC

Indicators	***KS (M±m)***	***AOC (M±m)***
HR, 1 min	1. 65,5±2,21 2. 60,5±3,35	1. 64,85±2,71 2. 60,89±3,18
SDD, mm Hg st.	1. 99,75±2,79 2. 102,95±4,12	1. 103,09±3,88 2. 105,73±3,95*
Stroke volume, ml	1. 80,41±5,38 2. 81,07±4,6	1. 90,04±4,97* 2. 74,8±5,18*
Minute volume of blood, l/min	1. 5,24±0,37 2. 4,92±0,37	1. 5,78±0,35* 2. 4,54±0,36*
Total peripheral vascular resistance, dns.cm^{-5}	1. 1606,6±114,8 2. 1772,1±180,6	1. 1466,6±74,64* 2. 1995,2±227,5*
WWS, ml / s	1. 315,84±25,49 2. 304,89±19,97	1. 348,54±25,08* 2. 290,11±23,86
R, W	1. 4,22±0,39 2. 4,22±0,38	1. 4,78±0,41* 2. 4,14±0,45
A beats., J	1. 1,09±0,08 2. 1,15±0,1	1. 1,26±0,08* 2. 1,09±0,11
IR-R, c	1. 0,934±0,042 2. 1,022±0,053	1. 0,983±0,042* 2. 1,038±0,054
σ_{R-R}	1. 0,035±0,003 2. 0,042±0,013	1. 0,042±0,003* 2. 0,048±0,012
Variation scale, c	1. 0,196±0,016 2. 0,257±0,052	1. 0,223±0,027 2. 0,277±0,048

Note: KS - klinostasis; AOC –antiotostasis; * - p <0.05.

1 - HNK 0 st, 2 - HNK I st.

Despite an insignificant decrease in heart rate in AOC in patients with ischemic heart disease with HNK 0 stage, according to the cardiac rhythmogram, after an increase in preload, signs of an increase in parasympathetic activity are seen in the form of a significant increase in IR-R, σR-R (Table 5). In patients with coronary artery disease with HNK I Art. no significant changes in the IR-R, σR-R indices in anti-orthostasis were noted.

Conclusions

1. In healthy individuals, an increase in venous return of blood to the heart (preload) in anti-orthostasis on the background of 0.5% water load is accompanied by adaptive changes in cardiohemodynamics, volemic homeostasis and neurohumoral regulation

of water-salt metabolism, manifested by an increased effect of the parasympathetic division of the ANS, a decrease in heart rate, an increase CRM while maintaining the same level of IOC, increased diuresis, a decrease in the activity of the RAAS, an increase in the content of α-PUG.

2. 2. In patients with coronary artery disease with HNK I Art. with an increase in preload at the 30th minute of anti-orthostasis, changes in cardio hemodynamics (decrease in IOC) and cardiac rhythmograms were revealed, indicating a depletion of myocardial reserve capacity and vegetative regulation of heart rhythm. The lack of dynamics of heart rate and heart rhythmogram indices in anti-orthostasis reflects an increase in the activity of the sympathetic section of the autonomic nervous system in IHD patients with the initial stage of HNK.

3. The reaction of the kidneys to antiortostasis and 0.5% water load in patients with coronary artery disease with HNK I Art. expressed in increased diuresis in the absence of changes in the activity of the RAAS, which indicates the predominance of anti-natriuretic systems over natriuretic.

4. The earliest indicator of the development of heart failure in patients with coronary artery disease is sodium retention, aimed at increasing the BCC, venous return of blood to the heart and stimulation of the heterometric mechanism of Frank-Starling.

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