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## **CHARACTERISTICS OF LABORATORY INDICATORS WHEN PRESCRIBING NITRATES AND AMLODIPINE TO PATIENTS WITH CHRONIC HEART FAILURE OF ISCHEMIC AND HYPERTENSIVE GENESIS**

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### **Abstract**

On the background of hemodynamic overload of the heart, coronary insufficiency and arterial hypertension, the hypoxic phenomena are formed, which modify metabolic processes in the direction of activation of endogenous intoxication, which are reflected in hematological and biochemical indices. Therefore, the laboratory data reflecting these violations are essential and useful for assessing the patient's condition.

However, in many literary sources there are mostly the peculiarities of clinical and functional parameters that are characteristic of CHF, and, at all, there are no definite comparative characteristic of complex clinical and laboratory studies based on the stages (HF 2A and HF 2B) and their dependence on the prescribed treatment, at that time as the analysis of survival in CHF patients in subgroups, conducted in the framework of multicenter studies SAVE, SOLVD, TRACE, etc., clearly indicates the adverse effects of nitrates on the course and prognosis of CHF

**Objective.** To conduct a comparative analysis of laboratory parameters in course of treatment of patients with ischemic heart disease and hypertension complicated by HF 2A and

2B with the use various vasodilators (nitrates and amlodipine) which are prescribed on the background of standard therapy of CHF.

**Results of the research.** The research was conducted in the cardiology department of the Military Medical Clinical Center of the Southern Region. We examined 84 patients with ischemic heart disease in combination with hypertension, complicated HF 2A: 18 patients were prescribed nitrates and 18 - amlodipine; and 2B: 22 patients were prescribed nitrates and 24 - amlodipine on a background of standard complex therapy of CHF of a corresponding degree. The average age was  $72.29 \pm 1.66$  years, by gender, men dominated (86.7%).

According to hematological and biochemical studies before treatment, more definite changes of inflammatory and intoxication character in patients with ischemic heart disease and hypertension are in groups with HF 2B than HF 2A, which is associated with a more significant endogenous intoxication of the body caused by hemodynamic overload of small and large blood circulation circles.

The prescription of amlodipine, according to most of the studied parameters, was more physiologically than with nitrates, despite their high vasodilating ability.

The obtained dynamics of biochemical indicators showed a moderately expressed negative effect of nitrates on the functional state of the liver and kidneys, which makes it advisable to narrow the indications for their appointment to patients with CHF.

**Key words: ischemic heart disease in combination with arterial hypertension, chronic heart failure, laboratory diagnostics, vasodilators.**

## **ХАРАКТЕРИСТИКА ЛАБОРАТОРНИХ ПОКАЗНИКІВ ПРИ ПРИЗНАЧЕННІ НІТРАТІВ ТА АМЛОДИПІНУ ХВОРИМ НА ХРОНІЧНУ СЕРЦЕВУ НЕДОСТАТНІСТЬ КОРНАРОГЕННОГО ТА ГІПЕРТЕНЗИВНОГО ГЕНЕЗУ**

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### **Реферат**

На тлі гемодинамічного перевантаження серця, коронарної недостатності та артеріальної гіпертензії формуються гіпоксичні явища, що змінюють метаболічні процеси у бік активації ендогенної інтоксикації, які віддзеркалюються гематологічними

та біохімічними показниками. Тому дані лабораторних досліджень, що відображають ці порушення, є суттєвими та доцільними для оцінки стану хворого.

Слід підкреслити, що для постановки діагнозу ХСН необхідними є параметри функціональної діагностики: електрокардіографія, рентгенографія органів грудної клітини та ехокардіографія. Метою інструментальної діагностики є отримання об'єктивних доказів наявності дисфункції серця у хворого з підозрою на ХСН.

Проте, в багатьох літературних джерелах зустрічаються переважно саме особливості клініко-функціональних параметрів, що властиві ХСН, причому, зовсім не визначена порівняльна характеристика комплексних клініко-лабораторних досліджень відповідно стадій (СН 2А і СН 2Б) та залежності їх від призначеного лікування, у той час як аналіз виживаності хворих ХСН в підгрупах, проведений в рамках багатоцентрових досліджень SAVE, SOLVD, TRACE та ін., однозначно свідчить про негативний вплив нітратів, які часто призначаються, на перебіг і прогноз ХСН

**Мета роботи.** Провести порівняльний аналіз лабораторних показників в динаміці курсового лікування хворих на ІХС та АГ із ускладненнями СН 2А та 2Б при застосуванні різних вазодилаторів (нітратів та амлодипіну), призначених на тлі стандартної терапії ХСН.

**Результати досліджень.** Дослідження проводились у кардіологічному відділенні Військово-медичного клінічного центру Південного регіону. Під наглядом перебувало 84 хворих на ІХС у сполученні з АГ, ускладнених СН 2А: 18 осіб вживали нітрати та 18 – амлодипін; та 2Б: 22 хворим призначалися нітрати та 24 – амлодипін на тлі стандартної комплексної терапії ХСН відповідного ступеню. Середній вік склав  $72,29 \pm 1,66$  років, за гендерною ознакою переважали чоловіки (86,7%).

За даними гематологічних та біохімічних досліджень до лікування визначені більш виразні зміни запального та інтоксикаційного характеру у хворих на ІХС та АГ при наявності СН 2Б, ніж СН 2А, що пов'язано з більш значною ендogenous інтоксикацією організму, викликаною гемодинамічним перевантаженням малого та великого кіл кровообігу.

Призначення амлодипіну за більшістю вивчених показників було більше фізіологічно, ніж при вживанні нітратів, не зважаючи на їх високу вазодилатуючу здатність.

Отримана динаміка біохімічних показників свідчила про помірно виразний негативний вплив нітратів на функціональний стан печінки та нирок, що обумовлює доцільність звуження показань щодо їх призначення при ХСН.

**Ключові слова:** ішемічна хвороба серця у сполученні з артеріальною гіпертензією, хронічна серцева недостатність, лабораторна діагностика, вазодилататори.

**ХАРАКТЕРИСТИКА ЛАБОРАТОРНИХ ПОКАЗАТЕЛЕЙ ПРИ НАЗНАЧЕННИИ  
НИТРАТОВ И АМЛОДИПИНА БОЛЬНЫМ ХРОНИЧЕСКОЙ СЕРДЕЧНОЙ  
НЕДОСТАТОЧНОСТЬЮ КОРНАРОГЕННОГО  
И ГИПЕРТЕНЗИВНОГО ГЕНЕЗА**

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**Реферат**

На фоне гемодинамической перегрузки сердца, коронарной недостаточности и артериальной гипертензии формируются гипоксические явления, изменяющие метаболические процессы в сторону активации эндогенной интоксикации, которые отражают гематологические и биохимические показатели. Поэтому данные лабораторных исследований являются существенными и целесообразными для оценки состояния больного.

Однако, во многих литературных источниках встречаются преимущественно именно особенности клинико-функциональных параметров, присущих ХСН. Причем, не проводилась сравнительная характеристика комплексных клинико-лабораторных исследований в зависимости от степени тяжести (СН 2А и СН 2Б) и назначенного лечения. В то же время, анализ выживаемости больных ХСН в подгруппах, проведенный в рамках многоцентровых исследований SAVE, SOLVD, TRACE и др., однозначно свидетельствует о негативном влиянии часто назначаемых нитратов на течение и прогноз этого осложнения.

**Цель работы.** Провести сравнительный анализ лабораторных показателей в динамике курсового лечения больных ИБС и АГ с осложнениями СН 2А и 2Б при применении различных вазодилататоров (нитратов и амлодипина), назначенных на фоне стандартной терапии ХСН.

**Результаты исследований.** Исследования проводились в кардиологическом отделении Военно-медицинского клинического центра Южного региона. Под

наблюдением находилось 84 больных ИБС в сочетании с АГ, осложненных СН 2А: 18 человек употребляли нитраты и 18 - амлодипин; и 2Б: 22 больным назначались нитраты и 24 - амлодипин на фоне стандартной комплексной терапии ХСН соответствующей степени. Средний возраст составил  $72,29 \pm 1,66$  лет, по гендерному признаку преобладали мужчины (86,7%).

По данным гематологических и биохимических исследований до лечения выявлены более отчетливые изменения воспалительного и интоксикационного характера у больных ИБС и АГ при наличии СН 2Б, чем при СН 2А, что связано со значительной эндогенной интоксикацией организма, вызванной гемодинамической перегрузкой малого и большого кругов кровообращения.

Назначение амлодипина по большинству изученных показателей было более физиологично, чем при употреблении нитратов, несмотря на их высокую вазодилатирующую способность.

Полученная динамика биохимических показателей свидетельствовала об умеренно выраженном негативном влиянии нитратов на функциональное состояние печени и почек, что обуславливает целесообразность сужения показаний при их назначении у больных с ХСН.

**Ключевые слова:** ишемическая болезнь сердца в сочетании с артериальной гипертензией, хроническая сердечная недостаточность, лабораторная диагностика, вазодилататоры.

**Actuality.** Clinical laboratory is an integral part of the diagnostic process, capable of reflecting and substantiating the presence of possible pathology, predicting the patient's condition, dynamically monitoring during the therapeutic course, timely choosing the necessary corrective measures aimed at achieving positive results in treatment and objectivizing the last.

It is considered that in our time, clinical laboratory studies provide up to 70-95% of the information required by the clinician [2]. Indicators of laboratory tests are determined for inflammatory diseases caused by infectious agents, autoimmune, cancer, traumatic pathology, metabolic and other disorders of organs and systems.

A special place among the numerous diseases has chronic heart failure (CHF), as it is the result of many somatic pathology, among which the majority are cardiovascular diseases, namely, ischemic heart disease (IHD) and arterial hypertension (AH) [6].

The laboratory tests that are used to evaluate the possibility of prescribing one or another treatment, determine the causes of CHF and concomitant diseases that may affect on its course, include the definition of: hemoglobin and leukocytes, natrium, potassium, blood urea, creatinine, functional liver parameters (bilirubin, AsAT, AlAT, GGTP), glucose, glycosylated hemoglobin, lipid profile, TTG, ferritin, general ability binding of iron (class of recommendations I) [3].

It should be emphasized that to make the diagnosis of CHF are necessary parameters of functional diagnosis: electrocardiography, chest X-ray and echocardiography. The purpose of instrumental diagnostics is obtaining objective evidence of the presence of cardiac dysfunction in a patient with suspected of having CHF.

At the same time, on the background of hemodynamic overload of the heart, coronary insufficiency and arterial hypertension, the hypoxic phenomena are formed, which modify metabolic processes in the direction of activation of endogenous intoxication, which are reflected in hematological and biochemical indices. Therefore, the laboratory data reflecting these violations are essential and useful for assessing the patient's condition.

However, in many literary sources there are mostly the peculiarities of clinical and functional parameters that are characteristic of CHF, and, at all, there are no definite comparative characteristic of complex clinical and laboratory studies based on the stages (HF 2A and HF 2B) and their dependence on the prescribed treatment, at that time as the analysis of survival in CHF patients in subgroups, conducted in the framework of multicenter studies SAVE, SOLVD, TRACE, etc., clearly indicates the adverse effects of nitrates on the course and prognosis of CHF [1].

**Objective.** To conduct a comparative analysis of laboratory parameters in course of treatment of patients with ischemic heart disease and hypertension complicated by HF 2A and 2B when the various vasodilators (nitrates and amlodipine) are prescribed on the background of standard therapy of CHF.

**Material and methods.** The research was conducted in the cardiology department of the Military Medical Clinical Center of the Southern Region. We examined 84 patients with ischemic heart disease in combination with hypertension, complicated HF 2A: 18 patients were prescribed nitrates and 18 - amlodipine; and 2B: 22 patients were prescribed nitrates and 24 - amlodipine on a background of standard complex therapy of CHF of a corresponding degree. The average age was  $72.29 \pm 1.66$  years, by gender, men dominated (86.7%).

The screening program complied with the recommendations of the Association of Cardiologists of Ukraine in 2011 [9] and included: the standard WHO questionnaire, filling in

questionnaires containing anamnestic and socio-demographic data, anthropometry, reflecting the quality of life of patients; objective research; laboratory methods (general clinical, biochemical); measurement of blood pressure, registration of an electrocardiogram, echocardiography, ultrasound examination of central and peripheral blood flow, radiography and statistical processing of the data.

The study included patients with IHD and AH with signs of HF 2A and CH 2B who had inpatient treatment before and received standard therapy with ACE inhibitors,  $\beta$ -adrenoblockers, saluretics, cardiac glycosides (mainly with HF 2B), receptor blockers angiotensin II, which are prescribed in intolerance to ACE inhibitors, aldosterone antagonists, intravenous sympathomimetics (dopamine and / or dobutamine for patients with HF 2B), anticoagulants or antiplatelet agents, antiatherogenic preparations, and so on. The resulting effect was saved in them from 1 to 3 months.

The study did not include patients with HF-III according to N.D. Strazhesko and V. Kh. Vasilenko, IV FC according to NYHA classification, unstable angina pectoris, secondary arterial hypertension, kidney disease with excretion of nitrogen, valvular defects and inflammatory heart disease, hyperthyroid and hypothyroidism, other chronic somatic diseases in a state of decompensation.

An extensive clinical analysis of blood, determination of concentration of electrolytes of blood, assessment of serum creatinine and urea, determination of blood glucose, liver enzymes, lipidograms of blood, general urine analysis, evaluation of glomerular filtration rate were studied in this work.

The need to determine the markers of inflammation (CRP, rheumatoid factor (RF), fibrinogen) is substantiated by the presence of endogenous intoxication in patients with heart failure syndrome of ischemic genesis, in connection with which heart failure is considered from the position of chronic inflammation [3].

Additional studies included: the international normalized ratio (INR) (its definition is an international standard for dispensary monitoring of patients taking an indirect anticoagulant); studying the level of thyroid stimulating hormone and T4 in the blood was advised only in the presence of atrial fibrillation, symptoms of thyroid disease or in patients over 65 years of age in order to exclude hyperthyroidism or hypothyroidism on the background of long-term administration of amiodarone [2, 6]. Cardio specific enzymes were determined in cases of sudden deterioration of hemodynamic parameters in order to exclude myocardial infarction [8].

**Research results and their discussion.** According to the result of general blood analysis, patients with HF 2A had all hemograms before and after treatment remained in normal limits. However, in patients with HF 2B the lymphopenia, accelerated erythrocyte sedimentation rate (ESR) and elevated endogenous intoxication index were determined before treatment (Table 1).

Table 1

**Indicators of the general analysis of blood of patients with ischemic heart disease in association with hypertension, depend on the severity of heart failure**

Indicators	Norm	HF 2A, n=18 (nitrates) (1 group)		HF 2A, n=18 (amlodipine) (2 group)	
		before treatment	after treatment	before treatment	after treatment
HGB, g/l	130-160	131,3±7,67	132,0±5,78	130,5±5,23	128,4±6,39
RBC, T/l	4,0-5,0	4,09±0,41	4,14±0,25	4,15±0,19	4,01±0,24
PLT, G/l	180-320	205,1±14,5	226,9±6,38**	197,4±16,70	233,9±10,75*
WBC, G/l	4,0-9,0	6,76±0,90	7,09±0,85	7,72±0,68	7,01±0,45
- BANDS, %	1-6	4,75±1,28	5,00±1,27	5,22±1,45	3,74±0,81
- NEUT, %	47-72	67,50±4,56	67,71±5,71	68,78±2,38	67,96±2,05
- EOS, %	0,5-5,0	1,81±0,52	1,71±0,51	1,96±0,45	2,07±0,41
- LYM, %	19-37	21,06±3,14	19,86±5,42	19,19±2,29	21,30±2,17
- MON, %	3-11	4,81±1,14	5,71±1,10	4,85±0,83	4,93±0,81
ESR, mm/h	1-10	16,00±3,24	13,86±3,69	16,21±2,12	12,16±2,04
LII	0,3-1,5	0,99±0,26	1,05±0,31	1,04±0,38	0,89±0,25
Indicators	Norm	HF 2B, n=22 (nitrates) (3 group)		HF 2B, n=24 (amlodipine) (4 group)	
HGB, g/l	130-160	126,1±4,24	129,91±3,91	121,2±9,94	120,37±10,22
RBC, T/l	4,0-5,0	3,97±0,15	4,07±0,13	3,98±0,35	3,95±0,32
PLT, G/l	180-320	203,0±12,37	214,88±18,38	200,9±18,92	191,47±22,48
WBC, G/l	4,0-9,0	7,56±0,81	8,69±0,92*	8,07±0,91	7,23±0,70*
- BANDS, %	1-6	4,97±0,98	4,10±1,44	5,67±0,95	4,07±1,06*
- NEUT, %	47-72	70,35±3,44	69,20±2,21	73,07±3,16	69,87±4,59
- EOS, %	0,5-5,0	1,74±0,53	1,33±0,17	2,00±0,63	2,13±0,93
- LYM, %	19-37	16,82±1,90	19,38±1,06*	14,87±1,32	19,07±2,19**
- MON, %	3-11	4,62±0,85	6,30±0,82	4,67±1,14	4,73±1,28
ESR, mm/h	1-10	18,29±1,26	16,07±1,01*	18,67±1,68	16,33±0,97*
LII	0,3-1,5	1,86±0,07	1,34±0,08*	1,87±0,58	1,48±0,03*

Note: \* - the reliability of the differences between the groups ( $p < 0.05$ ), \*\* -  $p < 0.01$ .

After treatment, the level of lymphocytes (LYM) in patients (with HF 2B) of group 3 increased significantly from  $16.82 \pm 1.90\%$  to  $19.38 \pm 1.06\%$  ( $p < 0.05$ ), and of group 4 - from  $14.87 \pm 1.32\%$  to  $19.07 \pm 2.19\%$  ( $p < 0.01$ ). This occurred simultaneously with a decrease in ESR: from  $18.29 \pm 1.26$  mm / h to  $16.07 \pm 1.01$  mm / h ( $p < 0.05$ ) in patients who consumed



nitrates and from  $18.67 \pm 1.68$  mm / h to  $16.33 \pm 0.97$  mm / h ( $p < 0.05$ ) - who received amlodipine.

The erythrocyte sedimentation rate is reliable indication of the presence of inflammatory processes in the body [4]. In the majority of examined patients, moderate acceleration of ESR was determined, which decreased simultaneously with a decrease in the hemodynamic load of the heart after treatment (Table 1).

In addition, the leukocyte index of endogenous intoxication (LII), which was elevated in patients of the 3rd and 4th groups with HF 2B before treatment, reached to the normal level in both groups ( $p < 0.05$  and  $p < 0.05$ ).

The nature of the corresponding changes in hemograms was confirmed by the correlation of an increase in the leukocyte index of endogenous intoxication with hemodynamic overload, which is accompanied by the formation of hypoxic phenomena and the accumulation of metabolic substances, and they had not connection with the type of vasodilating agent.

According to the biochemical studies of serum before treatment of patients with HF 2A, most of the indices of both groups had normal values, except for gamaglutamyltranspeptidase (GGTP), which was exceeded slightly ( $68.38 \pm 7.61$  and  $65.67 \pm 6.76$  U/L 1 and 2 groups, respectively, at a rate up to 61 U/L) the reference values, that indicates initial, latent intrahepatic cholestasis (Table 2).

After the course of therapy there were a normalization of GGTP levels ( $p < 0.001$ ,  $p < 0.05$ ) in patients of both groups. Nevertheless, it was determined that in 1.59 times ( $p < 0.01$ ) increased aspartate aminotransferase (AsAt) in patients receiving nitrates and in 1.29 times ( $p < 0.05$ ) taking amlodipine.

At the same time, the level of some indicators has increased moderately: glucose in the 1st group from  $6.88 \pm 1.55$  to  $7.63 \pm 1.52$  mmol / l, and in the 2nd one - from  $6.97 \pm 0.81$  to  $7.51 \pm 1.18$  mmol / l; the urea content - in comparison with the norm increased in 37.4% in the 1st group of patients and in 16.6% - in the 2nd. The level of creatinine slightly exceeded the norm ( $p > 0.05$ ) in patients receiving nitrates, and remained at the upper limit of normal after treatment with amlodipine.

That is, on the background of a decrease in hemodynamic load, which was accompanied by a decrease in clinical signs of HF 2A due to the appointment of diuretic, vasodilating and metabolic drugs, the moderate increase was observed in a number of parameters that are responsible for the functional state of the liver, moreover, more pronounced in patients who consumed nitrates (table 2).

Table 2

**Biochemical parameters of blood of patients with ischemic heart disease in association with hypertension, depend on severity of heart failure**

Biochemical parameters	Norm	HF 2A, n=18 (nitrates) (1 group)		HF 2A, n=18 (amlodipine) (2 group)	
		before treatment	after treatment	before treatment	after treatment
Bilirubin total, mkmol/l	1,7-20,5	15,23±2,89	14,49±2,69	14,31±2,94	12,85±3,18
Bilirubin direct, mkmol/l	0,86-4,4	3,09±2,41	1,60±0,95	2,45±0,99	2,28±1,36
Bilirubin indirect, mkmol/l	1,7-16,1	12,14±1,81	12,89±2,20	12,57±1,85	10,66±1,85
Alkaline phosphatase, U/L	to 129	75,58±5,77	72,64±5,13	73,26±9,08	69,17±4,33
GGTP, U/L	to 61	68,38±7,61	45,08±2,41** *	65,67±6,76	58,07±4,17*
AsAT, U/L	to 37	29,68±4,74	47,42±6,04**	31,80±4,51	40,96±2,52*
AlAT, U/L	to 40	33,29±8,65	34,86±4,02	36,98±3,79	31,83±2,61*
Amylase, U/L	to 95	67,46±11,08	62,80±9,07	67,32±6,16	66,56±5,50
Glucose, mmol/l	3,3-6,1	6,88±1,55	7,63±1,52	6,97±0,81	7,51±1,18
Protein total, g/l	60-85	69,34±4,80	77,10±2,98*	69,14±2,92	69,67±1,93
Urea, mmol/l	1,7-8,3	7,16±0,86	11,40±4,01	6,49±0,86	9,68±0,95*
Creatinine, mmol/l	0,044-0,104	0,078±0,01	0,110±0,04	0,070±0,01	0,101±0,01
Biochemical parameters	Norm	HF 2 Б, n= 22 (nitrates) (3 group)		HF 2Б, n=24 (amlodipine) (4 group)	
Bilirubin total, mkmol/l	1,7-20,5	21,61±2,23	19,57±1,83	21,40±4,67	17,38±2,29
Bilirubin direct, mkmol/l	0,86-4,4	4,46±1,40	5,11±0,84	5,01±1,27	3,37±0,47*
Bilirubin indirect, mkmol/l	1,7-16,1	17,16±1,28	14,49±0,88**	16,39±2,07	14,01±1,47*
Alkaline phosphatase, U/L	to 129	87,94±7,52	103,3±13,16*	85,40±9,64	46,07±3,64***
GGTP, U/L	to 61	124,2±7,87	116,6±5,94	119,5±4,03	94,14±3,67
AsAT, U/L	to 37	40,62±5,28	47,03±3,28*	40,68±7,44	41,28±8,62
AlAT, U/L	to 40	48,53±6,53	64,36±6,47*	49,73±5,40	42,87±3,67*
Amylase, U/L	to 95	68,78±8,69	69,55±8,30	66,20±9,64	58,29±9,30
Glucose, mmol/l	3,3-6,1	5,86±0,57	6,16±0,50	5,99±0,89	6,16±0,67
Protein total, g/l	60-85	70,53±3,48	65,73±0,99	71,37±3,78	70,11±2,55
Urea, mmol/l	1,7-8,3	10,14±1,53	16,22±1,95** *	9,81±1,44	8,21±0,79*
Creatinine, mmol/l	0,044-0,104	0,104±0,01	0,118±0,01	0,107±0,03	0,092±0,01

Note: \* - the reliability of the differences between the groups ( $p < 0.05$ ), \*\* -  $p < 0.01$ , \*\*\* -  $p < 0.001$ .

Biochemical studies performed before treatment of patients with HF 2B reflected congestion in a large circle of blood circulation, accompanied by a slight increase in the total

bilirubin level (while maintaining the normal ratio of direct to indirect), AsAT, AlAt, and more pronounced increase in GGTP (in 2 times), insignificant increase in urea, on the background of normal level of creatinine (Table 2).

After complex treatment of patients with HF 2B, the following changes were observed. The total bilirubin reached the physiological level, both in the 3rd and 4th groups of patients, but the ratio of direct to indirect bilirubin has changed: in patients who were prescribed nitrates - from 1: 3.85 to 1: 2.99 ( $p < 0.05$ ), in case of prescribed amlodipine - from 1: 3.27 to 1: 4.1 ( $p < 0.05$ ). This means that the ratio of direct to indirect bilirubin fractions in patients from the 3rd group increased the content of direct bilirubin, and in patients from the 4th group - this correlation improved by reducing both direct and indirect bilirubin, which is more physiologically.

The content of alkaline phosphatase was maintained in the norm in both groups, but in patients from 3rd there was an increase in this index (from  $87.94 \pm 7.52$  to  $103.3 \pm 13.16$ ;  $p < 0.05$ ), while in the 4th group - there was a decrease (from  $85.40 \pm 9.64$  to  $46.07 \pm 3.64$ ;  $p < 0.001$ ).

In patients from the third group the AsAT level slightly increased ( $p < 0.05$ ), and the changes in the content of this enzyme in patients in group 4 were not valid.

At the same time, the content of AlAT in patients who consumed nitrates increased in 33% (from  $48.53 \pm 6.53$  to  $64.36 \pm 6.47$ ;  $p < 0.05$ ), and the presence of a tendency to normalize the content of AlAT in patients (decrease from  $49.73 \pm 5.40$  to  $42.87 \pm 3.67$ ,  $p < 0.05$ ) whom amlodipine was prescribed.

The level of amylase, glucose, protein in serum remained in the physiological range.

The content of urea in patients of the 3rd group increased from  $10.14 \pm 1.53$  to  $16.22 \pm 1.95$  mmol / l ( $p < 0.001$ ), while in patients of the 4th group decreased from  $9.81 \pm 1.44$  to  $8.21 \pm 0.79$  mmol / l ( $p < 0.05$ ).

The obtained dynamics of biochemical indicators showed a moderately pronounced negative effect of nitrates on the functional state of the liver.

After treatment, there was a preservation of a stable normal blood lipidogram, a significant decrease in inflammation rates, but a tendency to increase the level of INR in patients of both groups was determined.

Patients with HF 2B had more distinct changes of the levels of INR, fibrinogen A, CRP, and RF before treatment than with HF 2A. The prescribed therapy contributed to a significant ( $p < 0.05$ ), but not to norm, reduction of CRP in patients of the 3rd group (from  $11.01 \pm 2.82$  to  $6.14 \pm 0.74$  U / ml) and normalization ( $p < 0.001$ ) in the 4th (from  $12.47 \pm 3.41$

to  $2.23 \pm 1.36$  U / ml). The RF decreased up to physiological values ( $p < 0.05$ ) and more significantly in patients taking amlodipine ( $p < 0.01$ ) (Table 3).

Table 3

**Indicators of lipidogram, hemostasis and inflammatory markers of patients with ischemic heart disease and hypertension, depend on the severity of heart failure**

Biochemical parameters	Norm	HF 2A, n=18 (nitrates) (1 group)		HF 2A, n=18 (amlodipine) (2 group)	
		before treatment	after treatment	before treatment	after treatment
Cholesterol total, mmol/l	3,1-5,2	4,7±0,62	4,53±0,73	5,16±0,54	5,09±0,43
Triglycerides, mmol/l	0,45-1,86	1,44±0,31	1,57±0,39	1,63±0,22	1,59±0,18
Beta lipoproteins, U	35-55	48,19±6,01	48,00±5,77	51,22±8,64	54,33±8,07
INR	to 1,4	1,43±0,22	1,72±0,30	1,44±0,13	1,66±0,20
Fibrinogen A, g/l	2,0-4,0	4,14±0,48	4,09±0,47	4,32±0,59	4,00±0,68
Fibrinogen B	negative	negative	negative	negative	negative
CRP, U/ml	0-6	4,5±1,64	3,1±0,33	4,52±0,56	2,41±0,64***
RF, U/ml	0-3	0,44±0,04	0,22±0,04	0,45±0,08	0,22±0,01
Biochemical parameters	Norm	HF 2B, n= 22 (nitrates) (3 group)		HF 2B, n=24 (amlodipine) (4 group)	
Cholesterol total, mmol/l	3,1-5,2	4,19±0,36	4,14±0,28	4,03±0,33	4,01±0,43
Triglycerides, mmol/l	0,45-1,86	1,21±0,17	1,36±0,20	1,12±0,22	1,03±0,07
Beta lipoproteins, U	35-55	43,29±5,07	43,67±5,85	42,33±3,19	33,86±2,46**
INR	to 1,4	1,54±0,13	1,65±0,12	1,59±0,25	1,45±0,16
Fibrinogen A, g/l	2,0-4,0	4,86±0,55	5,12±0,61	4,47±0,46	4,07±0,90
Fibrinogen B	negative	negative	negative	negative	negative
CRP, U/ml	0-6	11,01±2,82	6,14±0,74*	12,47±3,41	2,23±1,36***
RF, U/ml	0-3	0,71±0,28	0,32±0,21*	0,67±0,40	0,13±0,19**

Note: \* - the reliability of the differences between the groups ( $p < 0.05$ ), \*\* -  $p < 0.01$ , \*\*\* -  $p < 0.001$ .

The INR in patients who took nitrates tended to increase, while in patients received amlodipine, this parameter was close to normal. The same trend occurred in the dynamics of fibrinogen A.

In the study of the functional state of the kidneys according to the general analysis of urine and Reberg test, it was determined that for patients with HF 2A it was characteristically: acidic reaction, normal urine density, normal protein content and diuresis with the preserved velocity of glomerular filtration (GFR) (Table 4). After treatment, a few increased the level of protein in the urine, from  $0.033 \pm 0.010$  to  $0.132 \pm 0.009$  g / l in patients from 1st group and from  $0,033 \pm 0,006$  to  $0,066 \pm 0,008$  g / l in the 2nd. Stable acidic urine showed a lack of

infectious inflammatory process in the kidneys (in which urine pH has an alkaline reaction). Diuresis increased in both groups (more clearly in the 2nd) on the background of increased GFR (Table 4).

Table 4

**Indices of urography of patients with ischemic heart disease and hypertension, depend on the severity of heart failure**

Indices	Norm	HF 2A, n=18 (nitrates) (1 group)		HF 2A, n=18 (amlodipine) (2 group)	
		before treatment	after treatment	before treatment	after treatment
Color	light yellow	light yellow	light yellow	light yellow	light yellow
Transparency	clear	clear	clear	clear	clear
Relative density	1017-1024	1016,6±2,66	1015,5±2,23	1015,5±2,23	1012,8±1,82
Reaction, pH	acid	acid	acid	acid	weakly acid
Protein, g / l	≤ 0,033	0,033±0,010	0,132±0,009	0,033±0,006	0,066±0,008
Leukocytes	0-3	6,69±4,98	7,00±2,51	7,00±1,72	3,44±1,19**
Erythrocytes	single	2,13±1,59	2,96±1,84	2,96±1,84	1,78±1,07
Diuresis, l	1,0 – 1,5	1,09 ± 0,02	1,32±0,08	1,05±0,06	2,78±0,067
Indices	Norm	HF 2B, n=22 (nitrates) (3 group)		HF 2B, n=24 (amlodipine) (4 group)	
		before treatment	after treatment	before treatment	after treatment
Color	light yellow	light yellow	light yellow	light yellow	light yellow
Transparency	clear	clear	clear	clear	clear
Relative density	1017-1024	1012,9±15,33	1012,6±11,82	1012,2±14,61	1013,1±12,12
Reaction, pH	acid	acid	weakly acid	acid	weakly acid
Protein, g / l	≤ 0,033	0,106±0,02	0,152±0,10	0,098±0,02	0,0350±0,01
Leukocytes	0-3	12,79±6,51	4,22±1,28*	9,80±4,25	4,50±2,24
Erythrocytes	single	5,24±2,07	1,78±1,07	4,53±3,17	0,83±0,74*
Diuresis, l	1,0 – 1,5	0,86 ± 0,05	1,28±0,07*	0,83 ± 0,09	1,48±0,06*

Note: \* - the reliability of the differences between the groups ( $p < 0.05$ ), \*\* -  $p < 0.01$ .

Before the treatment in patients with HF 2B was recorded a decrease in the relative density of urine by type of hypoisostenuria (in the study of Zimnitsky test), a increase in three times the protein content, and a reduced diuresis which not reaching 900 ml with slow GFR (Table 4).

After therapy, moderate increase in the protein content was determined - from  $0.106 \pm 0.02$  to  $0.152 \pm 0.10$  g / l in patients of the 3rd group and its decrease from  $0.098 \pm 0.02$  to  $0.0350 \pm 0.01$  g / l patients in the 4th group, which can be explained by the metabolism of nitrates in the liver and kidneys, and amlodipine - only by the kidneys [5, 7]. In addition, a significant ( $p < 0.05$ ) increase in diuresis in both groups was determined, but positive changes were more significant in patients receiving amlodipine (Table 4).

Thus, the conducted studies allowed drawing the following **conclusions**:

1. According to hematological and biochemical studies before treatment, more definite changes of inflammatory and intoxication character in patients with ischemic heart disease and hypertension are in groups with HF 2B than HF 2A, which is associated with a more significant endogenous intoxication of the body caused by hemodynamic overload of small and large blood circulation circles.

2. The prescription of amlodipine, according to most of the studied parameters, was more physiologically than with nitrates, despite their high vasodilating ability.

3. The obtained dynamics of biochemical indicators showed a moderately expressed negative effect of nitrates on the functional state of the liver and kidneys, which makes it advisable to narrow the indications for their appointment to patients with CHF.

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