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Реферати

ВЛИЯНИЕ КОМПЛЕКСНОГО ЛЕЧЕНИЯ АРТЕРИАЛЬНОЙ ГИПЕРТЕНЗИИ НА ПОКАЗАТЕЛИ СИСТЕМНОЙ ИММУНОВОСПАЛИТЕЛЬНОЙ АКТИВАЦИИ У БОЛЬНЫХ АРТЕРИАЛЬНОЙ ГИПЕРТЕНЗИЕЙ С ОЖИРЕНИЕМ И ПОДАГРОЙ

Вацеба М.О.

Целью исследования было оценить эффективность влияния лозартана и мельдонию дигидрата на показатели СИА у больных эссенциальной артериальной гипертензией с ожирением и подагрой. Обследовано 80 больных ЭАГ II стадии 2 степени в сочетании с ожирением и подагрой. Показатели СИА под влиянием стандартной терапии в динамике достоверно не менялись. Лозартан на фоне стандартной терапии достоверно снижал уровень IL-6. После 6 месячного лечения его концентрация в крови уменьшилась на 10,81% (р <0,05), а уровень СРП - на 17,31% (р <0,05). Мельдонию дигидрат достоверно снижал уровень СРП уже после 1 месяца лечения на 9,22% (р <0,01), а после 6 месяцев - на 11,48% (р <0,001). Следует отметить, что динамика показателей СИА была наиболее выраженной при сочетании лозартана и мельдонию дигидрата. Об этом свидетельствует снижение уровня СРП в сыворотке крови на 23,39% (р <0,001) через 1 месяц лечения, а через 6 месяцев - на 35,01% (р <0,001), а содержания IL-6, соответственно, на 40, 15% (р <0,001) и 62,10% (р <0,001). Таким образом, установлено, что сочетанное применение лозартана и мельдонию дигидрата на фоне стандартной терапии мало значительно большую эффективность по снижению СИА по сравнению с раздельным приемом данных препаратов.

Ключевые слова: артериальная гипертензия; ожирение; подагра; системная иммуновоспалительная активация.

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INFLUENCE OF THE COMPLEX TREATMENT OF ARTERIAL HYPERTENSION ON THE INDICATORS OF THE SYSTEMICAL IMMUNOINFLAMMATORY ACTIVATION IN PATIENTS WITH ARTERIAL HYPERTENSION WITH OBESITY AND GOUT

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The aim of the study was to evaluate the effect of losartan and meltedonium dihydrate on the parameters of systemic immune activation in patients with essential hypertension with obesity and gout. The study involved 80 patients with essential hypertension II stage 2 degrees combined with obesity and gout. Indicators of systemic immune activation under the influence of standard therapy in the dynamics did not significantly change. Losartan on the background of standard therapy significantly lowered the level of IL-6. After 6 months of treatment, its concentration in the blood decreased by 10.81% (p<0.05), and the level of CRP - by 17.31% (p<0.05). Meldonium dihydrate significantly reduced the CRP level after 1 month of treatment by 9.22% (p <0.01), and after 6 months - by 11.48% (p<0.001). It should be noted that the dynamics of systemic immun activation rates was most pronounced while combination losartan and meltedium dihydrate. This is evidenced by a decrease level of the CRP in the blood in 23.39% (p<0.001) after 1 month of treatment, and after 6 months - by 35.01% (p<0.001) and IL-6 content, respectively, by 40,15% (p<0.001) and 62.10% (p<0.001). Thus, it has been found that the combined use of losartan and meltedonium dihydrate against the background of standard therapy was much more effective in reducing the systemic immune activation compared with the separate administration of these drugs.

Key words: arterial hypertension; obesity; gout; systemic immunoactive activation.

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MULTIPARAMETRIC APPROACHES TO DIAGNOSING FUNCTIONAL STATUS OF THE CARDIOVASCULAR SYSTEM IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND SYSTEMIC SCLERODERMA

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It has been established that among the visceral pathology in systemic scleroderma and systemic lupus erythematosus, the key role is played by the heart damages. For early diagnosis of heart failure in these pathologies, the most informative are electrocardiography and echocardioscopy with the transmitral blood flow study. At the same time, in the vast majority of patients, the specific features of the left ventricle structural-geometric changes are normal cavities with the walls hypertrophy and the preserved pumping function, but the diastolic function is significantly disordered. Development of the chronic heart failure in such patients is due to the natural evolution of the transmitral blood flow spectrum from the normal type through hypertrophic and pseudonormal to the decompensated (restrictive) one.

Key words: systemic scleroderma, systemic lupus erythematosus, heart failure, diastolic dysfunction.

The study is a fragment of the research project "Clinical and immunological aspects of the internal organs major diseases course and their correction", state registration No. 0114U002040.

Systemic connective tissue diseases (SCTD) is a serious disabling pathology, which is based on the shift of immunological tolerance to the body's own cells with development of the systemic inflammatory process [7]. Regarding their incidence, they occupy the 3rd place in the overall somatic diseases structure together with other rheumatic diseases after the pathology of the hematopoiesis organs and the gastrointestinal tract, covering over 4 million (8%) of the world's population [3]. In recent years, there has been a significant growth in the incidence of systemic scleroderma (SSD) and systemic lupus

erythematosus (SLE), which are relatively frequent and severe SCTD by their course. Thus, the incidence of SLE varies from 4 to 250 cases per 100,000 of population. Its peak amounts to the age of 15-25 years. Women suffer by 8-10 times more frequently than men [5]. Mortality from SLE is by 3 times higher than the overall mortality in the population from various causes [3]. Infections, diseases of the cardiovascular system, kidneys and the central nervous system are the most common causes of death in such patients [4]. SSD ranks the third among all the SCTD, and among the rheumatologic profile diseases it accounts for about 2% [9]. Over the past decade, a growth in the SSD incidence has been observed up to 0.6-19 cases per 1 million people per year. Women suffer by 3-8 times more frequently than men, and most often at the age of 45-54 years [6].

Irrespective of the progress in modern rheumatology, the forecast for SLE and SSD remains quite serious. This is primarily associated with numerous complications of the internal organs. A significant place among the viscerites, which affect the clinical picture of the disease, the nature of its course and prognosis, belongs to the cardiovascular pathology [8].

The purpose of the study was to determine the features of the cardiac pathology in patients with SLE and SSD.

Materials and methods. We have examined 115 patients with SCTD (91 with SSD and 24 with SLE) with the chronic heart failure (CHF) manifestations who underwent inpatient treatment in the Rheumatology Department of Ivano-Frankivsk Regional Clinical Hospital. The correctness of the SSD and SLE diagnosis was confirmed by the unified diagnostic criteria developed by the American College of Rheumatology (ACR / EULAR, 2013), agreed by the Association of Rheumatologists of Ukraine. The stage and severity of CHF were established in compliance with the guidelines of the European Society of Cardiology (ESC, 2016) and the Ukrainian Association of Cardiology (2013).

All patients underwent the `12-lead electrocardiography (ECG) by means of the Yukard ECG-recorder (Ukraine) and echocardioscopy (EchoCS) in M- and B-modes with pulsed wave myocardial Doppler sonography by means of the "SIEMENS ACUSON Antares Premium EDITION" doppler (Germany) in compliance with the guidelines of the American Society of Echocardiography (ASE 2015). To assess the nature of the left ventricle (LV) diastolic filling, transthoracic Doppler sonography was performed with the transmitral blood flow study. The following parameters were determined: the left ventricle diastolic filling early peak maximum velocity (VmaxPeakE), the transmitral blood flow maximum velocity during the left atrium (LA) systole (VmaxPeakA), the time of the LV early diastolic filling velocity deceleration (DT), the LV isovolutium relaxation time (IVRT).

All calculations were carried out using the Microsoft Excel spreadsheet data software using the "Statistica 8.0" statistical software package. The arithmetic mean values (M), mean values errors (m), mean square deviation (σ), Student's t-test for pair measurements were calculated. The data are presented in the form ($M \pm m$). The statistically reliable difference was considered to be $p < 0.05$.

To determine the normal parameters of all the indices, a group of healthy persons was examined in parallel, including 20 persons who constituted a control group (CG).

Results of the study and their discussion. Among the SCTD patients, the majority were women - 101 person (87.8% of cases). The age of the examined patients varied from 21 to 72 years and averaged 46.5 ± 2.3 years. In 48 (41.7%) patients (8 with SLE and 40 with SSD), the pathology went on with the symptoms of HF stage I, and in 67 (58.3%) patients (16 with SLE and 51 with SSD) - with those of HF stage II A. The duration of the disease varied from 1 to 28 years and averaged 7.4 ± 3.1 years.

All patients were diagnosed with an active phase of the disease. The minimum activity of the inflammatory syndrome is established in 81 (70.4%) patients with SSD and SLE, among which 37 persons with HF stage I. and 44 patients with HF stage II A, a moderate degree of activity was detected in 27 (23.5%) of the examined patients, among which 10 patients with HF stage I. and 17 patients with HF stage II A, the maximum expressed inflammatory pathology component was in 7 patients, among them - 1 person with HF stage I and 6 patients with HF stage II A.

The initial stage of the SSD and SLE development was diagnosed in 6 patients with HF stage I, and the generalized stage - in 109 (94.8%) patients, among which 42 patients with HF stage I and 67 - with HF stage II A. In 5 patients, the disease was consistent with the subacute version of the course, patients with the chronic course of SCTD amounting 110 (95.7%) persons constituted the absolute majority.

In the examined patients, changes in the ECG were recorded in 78 (67.8%) persons. Among them, various forms of rhythm disorders prevailed - 43 (37,4%) cases and the conduction disorders - 23 (20,0%) cases. The most common forms of rhythm disorders were extrasystoles - in 10 (8.7%) patients and sinus bradycardia - in 16 (13.9%) of the examined patients. Among the extrasystoles, the premature ventricular beat was detected in 6 patients, premature atrial contraction - 2, atrioventricular extrasystoles - 2; single -

in 7, group - in 3 patients. The intraventricular conduction disorders were observed very often - in 20 (17.4%) persons, in 13 of them there was the His bundle right branch blockade. These changes correlated with the duration of the disease, but did not depend on the SCTD activity.

In assessing the results of EchoCS, it became clear (Tables 1, 2) that the mean indices of the LV function in patients with SSD and SLE were not significantly different from those of healthy individuals. But it was established that individually they fluctuate both towards the growth and towards the reduction. The deterioration of the left ventricular parameters grows with the increase in the SCTD duration and at stage II of the disease.

The individual analysis of the data obtained showed that only 14 (12.2%) patients had the increased LV size and volume compared to those in the control group, which was observed, particularly, in patients with heart defects (except for mitral stenosis) and with pronounced prolapse of the mitral valve leaflets with flow regurgitation (++). Instead, 19 (16.5%) of the patients examined showed a reduction in the LV size and volume, which is explained not by systolic dysfunction but by the cardiosclerosis development and disorders in the processes of LV myocardial relaxation, particularly expressed with the disease duration of more than 6 years.

Table 1

Results of the left ventricle volumetric characteristics analysis in patients with systemic scleroderma and systemic lupus erythematosus

Group	EDV, ml	ESV, ml	SV, ml	EF, %
Healthy persons, (n=20)	97.54±4.04	36.81±1.76	60.24±1.31	62.75±2.12
Patients with SSD and SLE, (n=115)	92.82±2.69	37.46±1.64	54.86±1.53*	59.51±1.69

Note: 1. EDV – LV end diastolic volume, ESV – LV end systolic volume, SV – stroke volume, EF – ejection fraction; 2. *p<0.05 – indices difference reliability compared to healthy persons.

The thickening of interventricular septum (IVS) and LV posterior wall (LVPW) was by 1.1 times was detected in patients with SCTD, as well as the increased value of the LA index (p <0.05), possibly compensatory, aimed at maintaining the LV systolic function under the conditions of primary diffuse cardiosclerosis development.

Table 2

Results of the left ventricle linear characteristics analysis in patients with systemic scleroderma and systemic lupus erythematosus

Group	EDD, cm	LA, cm	LVPVTd, cm	IVSTd, cm
Healthy persons, (n=20)	4.56±0.37	2.81±0.05	0.86±0.02	0.84±0.02
Patients with SSD and SLE, (n=115)	4.41±0.28	3.5±0.04*	0.98±0.01*	0.96±0.02*

Note: 1. EDD – LV end-diastolic dimension; LA – left atrium anterior-posterior dimension; LV PVTd -LV posterior wall thickness, diastolic; IVSTd – interventricular septum thickness, diastolic; 2. *p<0.05 - indices difference reliability compared to healthy persons.

Analysis of the study results shows that there is no change in the LV systolic function in the majority of patients with SSD and SLE, taking into account that LV EF was above 45% and averaged 59.51 ± 1.69%, which does not differ significantly (p> 0. 05) from its value in the control group, and also there is no dilatation of LV (EDV amounts to 92.82 ± 2.69 ml at the normal of 97.54 ± 4.04 ml).

Comparing the parameters of intracardiac hemodynamics in patients with SCTD having different manifestations of HF, it was found that CHF stage I is characterized by normal values of linear and volumetric indices, thickening of the LV walls and moderate LA increase, and for patients with CHF stage II A, there is a significant growth in the anterior-posterior LA size by 28.1%, LVPVT - by 15.1%, IVST - by 15.5%, reduction of EDV - by 8.37% and EF - by 6.71%.

Parameters of LA, IVST and LVPVT in patients with CHF stage I and CHF stage II A differed from each other with the reliability of p <0.05, while EDV with the CHF progression reduced unreliably, although the tendency towards its reduction was clearly observed and amounted to 6.63%. The LV EF was lower in patients with CHF of both stages compared to the control group and amounted to 60.68 ± 0.86% at CHF stage I and 58.54 ± 1.01% in CHF stage II A, but the reliable difference was only with the clinical stage II of CHF.

Taking into account the little changed LV myocardium systolic function values in patients with SLE and SSD, the absence of noticeable LV dilatation in the presence of left ventricular failure symptoms, physical data indicating the presence of concentric LV hypertrophy in some patients, we excluded in the examined patients the predominant significance of the LV systolic dysfunction in the CHF development, which correlates with the literature data [1, 2].

In the majority of patients - 83 (72.2%), in the analysis of individual indices values, changes in the LV diastolic function were established (table 3). In 67 (80.7%) patients, hypertrophic type (insufficient relaxation type) of diastolic dysfunction (DD), in 12 (14.5%) patients - pseudo-normal, in 4 (4.8%) - restrictive type was detected. Obviously, DD resulted in a reliable increase of the LA diameter ($p < 0.05$), which was observed in the majority of patients with SSD and SLE.

DD at the initial stage of development (hypertrophic type) was manifested in the increased contribution of LA systole to the LV filling, as evidenced by the reduction in VmaxPeakE to 0.63 ± 0.03 m/s, the increase in VmaxPeakA to 0.72 ± 0.04 m/s, the reduction of VmaxPeakE / VmaxPeakA ratio to 0.88 ± 0.03 m/s, the IVRT extension to 102.42 ± 10.21 m/s, and the moderate LV DT prolongation ($p < 0.05$).

This can be explained by the fact that at this stage there is still no growth in the LV end-diastolic pressure (EDP) ($p > 0.05$) and in the LA pressure; with the LA volume just before its reduction beginning, i.e. at the end of the diastole, is significantly growing [10]. The time characteristics analysis of diastolic blood flow with the hypertrophic type compared to that in the control group indicates that the periods of active filling (Te and Tl intervals) were prolonged, with the Tl duration (late diastolic filling time) increased and amounted about 44% of the Te duration (early diastolic filling time) .

Table 3

Results of Doppler-EchoCS indices analysis in patients with SSD and SLE with different types of diastolic filling

Index, units	Normal type (healthy), (n=20)	Hypertrophic (type I), (n=67)	Pseudo-normal (type II), (n=12)	Restrictive (type III), (n=4)
VmaxPeakE, m/s	0.76±0.02	0.63±0.03*	0.72±0.05°	0.73±0.02°
VmaxPeakA, m/s	0.51±0.02	0.72±0.04*	0.57±0.04°	0.30±0.03*°□
VmaxPeakE/ VmaxPeakA	1.49±0.04	0.88±0.03*	1.26±0.05*°	2.43±0.06*°□
IVRT, ms	75.54±4.07	102.42±10.21*	78.25±7.92°	50.01±5.63*°□
DT, ms	165.76±5.13	180.40±8.37*	167.41±11.81	138.74±14.02*°□
EDP, mm Hg	6.64±0.55	7.33±0.35	8.68±0.31*°	10.34±0.47*°□
EDP/EDV, mm Hg/ml	0.07±0.01	0.08±0.01	0.09±0.01*	0.11±0.01*°
Te, ms	230.65±7.19	273.94±4.36*	252.36±9.41*°	182.72±6.23*°□
Tl, ms	115.18±5.74	121.17±10.09	131.78±8.52*	99.66±6.94*°□

Note: 1. * – $p<0.05$ indices difference reliability compared to healthy persons; 2. ° – $p<0.05$ indices difference reliability compared to type I; 3. □ – $p < 0.05$ indices difference reliability compared to type II.

Analyzing the subsequent changes that occurred during the DD progression, we observed the acceleration of VmaxPeakE to 0.72 ± 0.05 m/s with simultaneous VmaxPeakA reduction to 0.57 ± 0.04 m/s, apparently due to growing LA pressure and the atrium - ventricular gradient pressure increase during the rapid filling phase (pseudo-normalization of LV diastolic filling) [1, 10]. At the same time, the VmaxPeakE / VmaxPeakA, IVRT and DT indices were close to the norm ($p > 0.05$), and EDP and EDP/ EDV reliably increased ($p < 0.05$), indicating a significant increase of the myocardial stiffness. The interval Tl was approximately 52% of the Te interval duration.

Further heart diastole disorders were accompanied by an even more reliable EDP increase ($p < 0.01$) in the LV cavity, which contributed to an even greater limitation of blood flow during the atrial systole, resulting in the increased VmaxPeakE / VmaxPeakA ratio up to 2.43 ± 0.06 m/s, reduced IVRT by 36.1% and reduced DT by 17.1% (restrictive type). The EDP and EDP/ EDV indices acquired the highest values ($p < 0.01$ and $p < 0.05$). [5]

The Te interval was reduced to its minimum among patients of the comparison groups due to the shortened time of reducing the VmaxPeakE velocity (DT interval). The VmaxPeakE index was close to that of the patients group with pseudo-normal type diastolic filling and was reliably higher ($p < 0.05$) than with DD type I. Indices of VmaxPeakA and Tl were the lowest among the comparison groups. The Tl interval sharply reduced compared to the previous groups and amounted approximately 55% of the Te duration.

The analysis of diastolic function in patients with SCTD was carried out depending on the CHF stage. Both in patients with CHF stage I and with CHF stage II A, compared to healthy persons, a reliable reduction of VmaxPeakE, an increase of VmaxPeakA, a reduction of VmaxPeakE / VmaxPeakA, an increase of Tl, Te, and EDP were determined. The index of myocardium stiffness (EDP/EDV) was reliably higher only in patients with CHF stage II A ($p < 0.05$). [7]

Thus, the cardiovascular pathology in SSD and SLE largely determines the prognosis and quality of life in patients, requires assessment of the myocardium functional state, correction of the revealed disorders following the treatment principles used in modern cardiology. Instrumental research methods along with clinical data permit to reveal features of cardiac pathology in patients with SLE and SSD, to perform an early diagnosis of LV DD.

Conclusions

1. In patients with SSD and SLE, the characteristic features of structural and geometric changes in the LV are normal cavities with the walls hypertrophy and the preserved pump function.

2. The development of CHF in SLE and SSD is due to the natural evolution of the transmitral blood flow spectrum from the normal type through the hypertrophic and pseudo-normal to the restrictive type.

Prospects for further research lie in studying the possibility of the heart functional state disorders medical correction in patients with SLE and SSD.

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Реферати

МУЛЬТИПАРАМЕТРИЧНІ ПІДХОДИ ДО ДІАГНОСТИКИ ФУНКЦІОНАЛЬНОГО СТАНУ СЕРЦЕВО-СУДИННОЇ СИСТЕМИ У ХВОРИХ НА СИСТЕМНИЙ ЧЕРВОНИЙ ВОВЧАК І СИСТЕМНУ СКЛЕРОДЕРМІЮ

Дрогомерецька О.І., Курилів Г.М., Гриджук Т.І., Герич П.Р., Дідушко О.М.,.

Встановлено, що серед вісцеральної патології при системній склеродермії та системному червоному вовчаку провідне місце належить ураженню серця. Для ранньої діагностики серцевої недостатності при цих патологіях найінформативнішими є електрокардіографія та ехокардіоскопія з дослідженням трансмітрального кровотоку. При цьому у переважної більшості пацієнтів характерними особливостями структурно-геометричних змін лівого шлуночка є нормальні порожнини із гіпертрофією стінок та збереженою насосною функцією, проте суттєво порушується діастолічна функція. Розвиток хронічної серцевої недостатності у таких хворих обумовлений закономірною еволюцією спектра трансмітрального кровотоку від нормального типу через гіпертрофічний і псевдонормальний до декомпенсованого (рестриктивного).

Ключові слова: системна склеродермія, системний червоний вовчак, серцева недостатність, діастолічна дисфункція.

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МУЛЬТИПАРАМЕТРИЧЕСКИЕ ПОДХОДЫ К ДИАГНОСТИКЕ ФУНКЦИОНАЛЬНОГО СОСТОЯНИЯ СЕРДЕЧНО-СОСУДИСТОЙ СИСТЕМЫ У БОЛЬНЫХ СИСТЕМНОЙ КРАСНОЙ ВОЛЧАНКОЙ И СИСТЕМНОЙ СКЛЕРОДЕРМИЕЙ

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Установлено, что среди висцеральной патологии при системной склеродермии и системной красной волчанке ведущее место принадлежит поражению сердца. Для ранней диагностики сердечной недостаточности при этих патологиях наиболее информативными являются электрокардиография и эхокардиоскопия с исследованием трансмитрального кровотока. При этом у подавляющего большинства пациентов характерными особенностями структурно-геометрических изменений левого желудочка есть нормальные полости с гипертрофией стенок и сохраненной насосной функцией, однако существенно нарушается диастолическая функция. Развитие хронической сердечной недостаточности у таких больных обусловлено закономерной эволюцией спектра трансмитрального кровотока от нормального типа через гипертрофический и псевдонормальный к декомпенсированному (рестриктивному).

Ключевые слова: системная склеродермия, системная красная волчанка, сердечная недостаточность, диастолическая дисфункция.

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