

the brain. The small vessels tonus in patients with ON is higher by 77.7% according to the DKI indicator and by 62.1% according to the DSI indicator, compared to acute AION.

Conclusions. The use of the indicators: the eye volume blood filling (RQ), the speed of volume pulse blood filling V (Om/s), the tone of large blood vessels of the eye $\alpha 1/T$ (%) is proposed for the differential diagnosis of optic neuropathies such as ON and AION.

Key words: ischemic neuropathy of the optic nerve, the optic neuritis, blood supply to the eye and brain, speed of blood supply, vascular tone of the eye and brain.

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RESVERATROL MORE SIGNIFICANTLY THAN QUERCETIN IMPROVES CENTRAL HEMODYNAMICS IN PATIENTS WITH ISCHEMIC HEART DISEASE

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The leading cause of death in the world remains coronary heart disease (IHD), despite the numerous treatments being developed. Therefore, the search for new effective methods of treatment of IHD is extremely relevant. One of the pathogenetic mechanisms for the progression of atherosclerosis, which is the morphological basis of coronary heart disease, is chronic systemic inflammation. Anti-inflammatory activity at different levels of proinflammatory signaling have polyphenols of plant origin.

The purpose of the work is to assess the impact of polyphenols of resveratrol and quercetin on the indicators of central hemodynamics in patients with IHD.

A prospective open randomized controlled trial was conducted with the participation of 230 people with IHD, I-II functional class (FC), with heart failure not higher than II FC. After assessing hemodynamics, according to echocardiography (echo), patients are randomized into 2 groups of study and a comparison group. Along with the basic therapy of ICH, the study group And assigned 100 mg of resveratrol per day, group II –120 mg of quercetin per day. After 2 months, the results of echo were evaluated.

In patients with IHD, signs of diastolic dysfunction by type And by type – relaxation disorder have been identified. The presence of heart failure by diastolic type was confirmed by the the left ventricle isovolumetric relaxation time and the left ventricle deceleration time, and the size of the left atrium.

Systolic function in the vast majority of patients corresponded to the limits of the norm, but was significantly less than in the group of healthy individuals. Under the influence of both polyphenols, more significantly than with the use of standard therapy, the systolic and diastolic functions of LV have improved, with the advantage of resveratrol.

The use of resveratrol and quercetin in complex therapy of patients with IHD had a positive effect on the central hemodynamics, especially on the diastolic function of the left ventricle, with the advantage of resveratrol efficiency, which makes it possible to recommend it for wide use in the treatment of IHD.

Key words: ishemic heart disease, central hemodynamics, diastolic heart failure, polyphenols, resveratrol, quercetin.

Connection of the publication with planned research works.

This work is a fragment of the SWR "Peculiarities of the course of cardiovascular pathology in patients of different age categories depending on the presence of

components of the metabolic syndrome and comorbid conditions, ways of correcting the detected disorders and prevention", (state registration number 0119U1028)

Introduction.

Cardiovascular diseases (CVD) are the leading cause of disability and mortality of the population. For more than a decade, according to the WHO, the list of leading causes of death from all factors in the world is headed by coronary heart disease (coronary heart disease). Almost a third of this number are persons of working age 28.3% [1]. Among CVDs, about 35% of people have primary IHD disability, and an even greater percentage is determined in people of working age (37.4%) [1, 2].

Similar statistics are also observed in Ukraine, where the main cause of death of the population is CVD, among which the first place is occupied by the IHD (64.3%) [3]. The situation is much worse under the conditions of war. Data have been obtained that the long-term state of anxiety is the basis for increasing the risk of IHD by 26-41%, and other CVD by 52% [4]. Also affects post-traumatic stress disorder, which is a predictor of a number of pathological conditions, including CVD.

Despite the wide system of preventive and medical measures, the epidemiological situation in the world with respect to IHD is not improved [1]. The problem in Ukraine is especially urgent, which requires active research in this direction. Therefore, the search for new effective pathogenetically based means for the treatment and prevention of this disease is extremely important.

Clinical manifestations of coronary heart disease are based on pathophysiological changes – myocardial perfusion disorder with central hemodynamics disorder and chronic heart failure (CHF) formation [2].

It is known that the morphological basis of IHD is atherosclerosis (AS), and its leading pathogenetic component is chronic systemic inflammation (CSI). In conditions of inflammatory activation, a large number of reactive molecules are formed, which leads to the oxidation of low-density lipoproteins (LDL) [5]. It has been found that in the areas of atherosclerotic lesions, T-cells CD4+ accumulate, which cause progression of AS, increasing the expression of receptors for oxidized LDL, chemokines and the products of proinflammatory cytokines (CK) mediated by the nuclear factor Kappa B (NF- κ B) with subsequent activation of endothelial cells [6, 7].

Therefore, the influence on the molecular mechanisms of proinflammatory activation can be a promising direction for the development of hemodynamic and perfusion disorders in IHD and AS.

A special place among the applicants for the role of such means is occupied by polyphenols. It is a wide group of natural plant components that have anti-inflammatory, antioxidant activity and a number of positive biological effects in relation to various organs and systems of the body. With a wide range of biological activity, low toxicity, high bioavailability, polyphenols have taken a prominent place in modern clinical practice. Among the famous representatives are silymarin, diosmin, eupatilin, quercetin, resveratrol and others. The property of polyphenols has been proven to block the proinflammatory signal transduction, which determined the focus of our scientific interest [8].

The aim of the study.

To investigate the effect of resveratrol and quercetin polyphenols on central hemodynamics in patients with stable ischemic heart disease.

Object and research methods.

To implement this task, a prospective open randomized controlled trial was conducted with the participation of 230 people of both sexes aged 55+7.2 years, patients with IHD: Stenocardia of tension stable, II FC, SN 0-I. 30 healthy individuals formed a control group.

On the eve of the examination, all patients personally signed an informed consent to participate in the study, in accordance with the requirements of the Helsinki Declaration of 1975, the order of the Ministry of Health of Ukraine No. 690 of 23.09.2009 "On approval of the procedure for conducting clinical trials of medicines and examination of clinical trial materials" and "Model Regulations on the Ethics Commission".

The criteria for inclusion in the study were the age of men and women 40-74 years, the presence of a verified by means of cycling ergometry IHS: Angina tension II FC in the absence of destabilization of the course for at least two months, the presence of compliance.

The criteria for non-inclusion were the presence of hypertension above the II stage of rhythm disturbance in the form of a constant form of atrial fibrillation or extrasystole high gradations for Lown, nodular blockades above the II stage, complete blockades of the legs of the bundle of His, myocardial infarction in anamnesis, heart defects, rheumatic diseases, anemia, diabetes and other endocrine diseases, given obesity, chronic liver and kidney diseases with insufficient function, oncological diseases, inflammatory diseases of the musculoskeletal system in the acute stage.

All the studied patients were examined in accordance with the Unified Clinical Protocol of primary, secondary (specialized) and tertiary (highly specialized) medical care "Stable ischemic heart disease" [9].

Among the instrumental studies before and after the therapy, patients underwent echocardiography (echo). On the eve of the Echo, patients were tested with a 6-minute walk with the definition of the functional class (FC) of chronic heart failure (CHF) according to the classification of the New York Association of Cardiology (NYHA) [10].

Echo was performed on the ultrasound scanner "Fukuda UF 750-XT" (Japan) according to the standard technique. The linear dimensions in M- and B-mode were determined: left ventricle (LV) end-diastolic dimension (EDD), LV end-systolic dimension (ESD), diameter of the left atrium (LA). LV end-diastolic volume (EDV) and LV end-systolic volume (ESV) were determined by the modified Simpson method. Global contractility of the LV was assessed by stroke volume (SV) and ejection fraction (EF) [11].

The diastolic function of LV in pulse-wave Doppler mode (PWD) was estimated by the maximum speed of early (E) and late (A) diastolic filling of LV, their ratio (E/A), the time of early diastolic filling – deceleration time (DT), the LV isovolumetric relaxation time (IVRT), blood flow velocity in the LV outflow tract (v_{LVOT}) [11].

All patients with IHD received standard therapy (β -blockers, statins, acetylsalicylic acid, nitrates as needed) for at least 2 months to stabilize the clinical condition [2].

At the end of this period, patients were randomized into the study group by envelope method. 30 patients were included in the study groups I and II. 55 patients were included in the comparison group.

Table – Parameters of central hemodynamics in patients with stable IHD under the therapy

Group/ Parameter, X±σ	The control group, n=30	Group comparison, n=55		Group And (resveratrol), n=30		Group II. (quercetin), n=30	
		before the treatment.	after the treatment.	before the treatment.	after the treatment.	before the treatment.	after the treatment.
EDD LV, cm	4,7+0,3	5,0+0,3	4,9+0,3	4,9+0,3	4,8+0,2	4,9+0,3	4,9+0,3
ESD LV, cm	3,1+0,2	3,7+0,3	3,6+0,3	3,5+0,3	3,4+0,2	3,6+0,3	3,5+0,2
EDV LV, ml	104,8+12,0	117,1+13,8	119,5+18,1	113,0+14,7	113,4+14,5	115,9+17,5	112,6+16,1
ESV LV, ml	42,5+11,5	55,0+9,4	51,9+9,3	54,1+8,4	48,6+8,0*	55,5+11,3	52,9+9,0
SV LV, ml	66,0+8,3	63,0+8,4	62,7+6,7	59,0+8,1	64,6+8,7*	59,0+11,4	60,8+10,3
LVEF, %	62,0+3,6	53,2+4,2	55,9+4,0■	52,3+2,7	57,3+2,7#	52,6+4,9	54,9+3,5■
LA, ml	3,2+0,2	3,6+0,4	3,7+0,4	3,7+0,4	3,5+0,3■	3,8+0,3	3,7+0,2*
IVRT, ms	70,4+8,2	91,4+8,43	89,4+8,5*	90,8+7,6	87,2+6,2■	93,5+8,4	90,8+9,2*
DT, ms	154,0+18,8	207,3+19,0	206,5+16,5	217,7+23,4	187,4+28,2#	217,1+22,88	210,9+18,5■
E/A, RVU	1,63+0,24	0,76+0,12	0,82+0,12	0,87+0,18	0,97+0,16#	0,78+0,17	0,84+0,16*

Notes: * – Reliable difference before and after treatment (p<0.05), ■ – reliable difference before and after treatment (p<0.01), # – reliable difference before and after treatment (p<0.001).

After examination of the patients of the study group I to standard treatment, resveratrol at a dose of 100 mg per day per os is additionally prescribed, patients of the II study group – quercetin at a dose of 120 mg per day per os. Patient comparison groups continued to take standard therapy. 2 months after the start of therapy with these polyphenols. all patients were re-examined

Statistical processing of the results of the study was carried out using the KyPlot program (version 6.0). The hypothesis of the normality of the distribution was tested using the Shapiro-Wilk criterion. The belonging of samples to one population was determined using the rank criterion of Crazell – Wallis. To compare the data of the examination of patients before and after treatment, the even T-criterion of Student was used, when comparing the data between three independent groups with a normal distribution, an odd T-criterion of Student with the Bonferoni correction was used. The data was represented as X±σ, where X is the mean, σ is the mean square deviation. The differences in data were considered reliable under the conditions of the level of significance p value <0.05 [12].

Results of the research and their discussion.

According to the results of the test, 6-minute walking, 62.6% of patients with IHD on the test with determined I FC of CHF (overcome the distance from 435 to 520 meters), 21.7% – II FC CHF (332 – 420 meters). The rest of the patients went a distance of more than 550 meters, which did not confirm the presence of clinical signs of CHF. Lwithin 45-49%, the rest of this figure was 50% or more.

In the vast majority of patients with coronary heart disease (96.1%), a change in the ratio of the phases of the transmitral blood flow was determined, which corresponded to diastolic dysfunction by type I (relaxation disorder). 1.3% of patients had signs of diastolic dysfunction by the type of pseudonormalization (II type), which was verified with the Valsalva sample [11].

The diameter of the LA, which to a certain extent characterizes the diastolic function of the LV, was greater than that of the healthy individuals, the IVRT and DT were greater than the established physiological norm.

After the course of therapy with resveratrol and quercetin, a comparative assessment of the central

hemodynamics indicators was carried out according to the Echo (**table**). During the treatment of the studied patients, complications, allergic reactions, individual intolerance of medicinal products in patients was not detected.

As indicated in **table**, after treatment, the systolic function of LV improved in all study groups. In patients of the group of study II, taking quercetin, as in the comparison group, the LV EF increased by 4.5% and 3.2% respectively, but the value of this indicator between the

groups probably did not differ (p>0.05). In patients of the study group I under the influence of resveratrol LV EF increased by 9.7% and probably differed from the value of the comparison group and the group taking quercetin (p<0.05). Also, in the research group, not only the FV LH has probably changed, but the UO LSH has also increased (p<0.05), and, accordingly, the CSO LSH (p<0.05) has decreased (**table**).

LV EF is an important predictor of survival of patients with CVD, this shortness index is included in the criteria used to calculate the risk of mortality according to known estimates. In the case study, it was shown that a decrease in LV EF for every 10% is accompanied by a probable increase in mortality [13].

At the heart of the disorder of the systolic function of LH are structural-functional remodeling, activation of neurohumoral systems and reactions with the participation of inflammatory molecules. Remodeling is a consequence of a combination of metabolic and structural changes in the myocardium in response to violations of hemodynamic conditions. In case of IHD, this is, first of all, a violation of microcirculation in the myocardium.

The biomechanical reconstruction of the heart causes changes in the expression of genes mediating CVD, apoptotic reactions, etc. An important role in myocardial dysfunction and remodeling in IHD is played by ATII, endothelin-I and TNFα [14]. Also, increased activity of ACE leads to ATII mediated effects, including IL-6 dependent JAK/STAT induced activation of monocytes with increased expression of inflammation genes. The role of ACE inhibitors in preventing myocardial contractility is confirmed in well-known clinical studies SOLVD and SONSENSUS [15].

It is known that under the conditions of stretching of the LV, compensatory mechanisms are activated – the Beebringer reflex, the Frank-Starling law and the increase in the activity of the renin-angiotensin-aldosterone system (RAAS), the sympathoadrenal system (CAS) and the effect of vasopressin [13, 15]. However, in patients with stable IHD, we have not identified the probable differences between the EDD LV and the ESD LV from the indicators of healthy individuals.

The diastolic function of LV, in terms of the ratio of the phases of the transmission flow E/A, improved in all groups, however, more significantly in patients taking resveratrol ($p < 0.001$). The value of E/A was close to normal ($E/A > 1.0$), and significantly differed from that in the comparison group ($p < 0.001$) and in the study group II ($p < 0.05$) (table).

In all study groups the value of IVRT ($p < 0.05$) decreased, the value of DT significantly decreased under the influence of resveratrol (13%) and quercetin (2.9%), in the comparison group – has not changed. At the same time, under the influence of resveratrol, the decrease of DT was more significant ($p < 0.05$).

Indirect but hemodynamically justified confirmation of the improvement of the diastolic function of LV was the decrease in the diameter of LA, which was found in the study groups I and II ($p < 0.01$ and $p < 0.05$, respectively) (table).

Diastolic load is formed by increasing pressure in the chambers of the heart, increasing their volume, reducing the ability of the myocardium to relaxation and increasing its stiffness, as well as changes in the myocardium that occur during systole, which, in particular, depends on the state of coronary blood circulation. Myocardial stiffness develops as a result of prolonged relaxation of the myocardium due to hemodynamic disorders, metabolic and ischemic changes of the myocardium, which leads to dystrophy, apoptosis or necrosis of cardiomyocytes, the restructuring of the components of the extracellular matrix, fibrosis and cardiosclerosis [16].

Also, the accumulation of calcium causes excessive activation of the contractile apparatus of cardiomyocytes to form contractures of myofibrils, which leads to impaired contractile ability and relaxation of the myocardium [16].

In the conditions of ischemia, the function of mitochondria is disturbed with a decrease in ATP production and an increase in the formation of oxygen active species (OAS). OAS is also formed in inflammation reactions, when iNOS is activated, which depletes the antioxidant systems of myocardiocytes and activates apoptosis [17].

Episodes of ischemia lead to activation of calcium-dependent phospholipase A with release from the membranes of arachidonic acid with subsequent cascade of reactions and formation of leukotrienes, prostaglandins, thromboxane A₂, which cause the migration of neutrophils into ischaemia zones with products of OAS and biologically active molecules. Recruitment of monocytes and lymphocytes into the areas of atherosclerotic lesions with the formation of inflammatory metabolites deepens pathological changes in IHD – endothelial dysfunction, vasoconstriction, platelet activation and microcirculation disorders in the myocardium [6, 16].

According to the analysis, under the influence of both polyphenols more significantly than with the use of standard therapy, systolic and diastolic functions of LV have improved, with the advantage of resveratrol.

Taking into account the data of our previous studies, the increase in the levels of pro-inflammatory CK and the inflammatory activation of ET are independent predictors of systolic-diastolic dysfunction of LV in patients with IHD [18, 19]. Therefore, the obtained

effects of polyphenols can be considered directly related to the anti-inflammatory action detected in them.

In our opinion, in the comparison group, the improvement of cardiac hemodynamics could occur, mainly due to the action of β -blockers, as well as anti-inflammatory and angioprotective effects of statins. However, patients taking resveratrol and quercetin also used basic standard therapy, similar to the comparison group. Therefore, the revealed advantages in these groups should be attributed to the action of the studied polyphenols.

Our findings are consistent with the results of other researchers. Thus, according to Parkhomenko A.N., the use of parenteral form of quercetin improved the systolic function of LV in patients with CHF [20]. According to clinical and experimental data, quercetin increased the bioavailability of NO. and improved myocardial blood circulation. Also, according to Sheng R. and colleagues, quercetin warned apoptosis of cardiomyocytes, preventing the shortening of telomeres [21].

The cardioprotective properties of resveratrol found in our study are also established by different authors. In experimental studies, resveratrol increased the survival rate of cardiomyocytes by activating sirtuin 1 (SIRT1) and reduced apoptosis by inhibiting angiotensin II induction [22]. According to Das S. and colleagues, cardioprotection under the influence of resveratrol was provided by the induction of hemoxygenase-1 through the activation of nuclear erythrocyte-2-linked transcription factor (Nrf2) and activation of r38 kinase and phosphoinositide-3-kinase (PI3K) [23]. The properties of resveratrol have been found to inhibit the proliferation of fibroblasts in the myocardium [24].

It is important to note that both resveratrol and quercetin inhibit the activity of metalloproteinases of the intercellular matrix, reducing pro-inflammatory effects and the development of fibrosis [25, 26]. And, as already noted, the blockade by polyphenols of the transcriptional activity of NF- κ B and other signal pro-inflammatory cascades helps to reduce the formation of inflammation molecules and inhibit the effects mediated by them, which plays a key role in cardioprotection and improving cardiac hemodynamics, which is fully consistent with the results of our studies [27].

Conclusions.

Thus, the use of resveratrol and quercetin in the complex therapy of patients with IHD had a positive effect on the parameters of central hemodynamics.

The effectiveness of resveratrol prevailed over such quercetin, which makes it possible to recommend it for wide use in clinical practice in the complex therapy of IHD.

Prospects for further research.

The predominance of the positive effects of resveratrol in comparison with quercetin in relation to the indicators of central hemodynamics in patients with coronary artery disease may be the result of its more significant anti-inflammatory effect and endothelioprotection, which is the basis for further research in this direction.

References

1. Ievropeiska baza danykh statystychnoi informatsii «Zdorovia dlia vsikh». Dostupno: <http://medstat.gov.ua/ukr/normdoc.html>. [in Ukrainian].
2. Kovalenko VM, Lutai MI, Sirenko YuM, Sychov OS. Sertsevo-sudynni zakhvoriuvannia: klasyfikatsiia, standarty diahnozyky ta likuvannia. Kiev: Morion; 2019. 239 s. [in Ukrainian].
3. Sakhandia IV, Nehoda TS, Siatynia ML. Faktory ryzyku vynykennia, struktura i dynamika rozvytku sertsevo-sudynnoi zakhvoriuvanosti naselennia Ukrainy. *Liky Ukrainy*. 2015;4(25):116-8. [in Ukrainian].
4. Kovalenko VM. Stres i sertsevo-sudynni zakhvoriuvannia i umovakh voiennoho stanu. Kyiv; 2022. 267 s. [in Ukrainian].
5. Fan J, Watanabe T. Atherosclerosis: Known and unknown. *Pathol Int*. 2022 Mar;72(3):151-160.
6. Hedrick CC. Lymphocytes in Atherosclerosis. *Arterioscler. Thromb. Vasc. Biol*. 2015;35(2):253-7.
7. Brunetti ND, Correale M, Pellegrino PL, Munno I, Gennarj LD, Cuculo A, et al. Early inflammatory cytokine response: A direct comparison between spontaneous coronary plaque destabilization vs angioplasty induced. *Atherosclerosis*. 2014;236(2):456-60.
8. Sobhani M, Farzaei MH, Kiani S, Khodarahmi R. Pharmaceutical Science Immunomodulatory; Anti-inflammatory/antioxidant Effects of Polyphenols: A Comparative Review on the Parental Compounds and Their Metabolites. *Food Reviews International*. 2021;37(3):759-811.
9. Unifikovanyi klinichniy protokol pervynnoi, vtorynnoi (spetsializovanoi) ta tretynnoi (vysokospetsializovanoi) medychnoi dopomohy. Stabila ishemična khvoroba sertsia. *Novyny medytsyny i farmatsii. Kardyolohiia i revmatolohiia (tematychnyi nomer)*. 2016;572:27-60. [in Ukrainian].
10. Enright PL, Sherrill DL. Reference equations for the six-minute walk in healthy adults. *Am. J. Respir. Crit. Care Med*. 1998;158(5.1):1384-7.
11. Galderisi M, Cosyns B, Edvardsen T, Cardim N, Delgado V, Salvo GD, Donal E. et al. Standardization of adult transthoracic echocardiography reporting in agreement with recent chamber quantification, diastolic function, and heart valve disease recommendations: an expert consensus document of the European Association of Cardiovascular Imaging. *European Heart Journal-Cardiovascular Imaging*. 2017;18(12):1301-10.
12. Riffenburgh RH, Gillen DL. *Statistics in Medicine*. 4th ed. Oxford, UK: Academic Press; 2020. 795 p.
13. Hallstrom A, Pratt CM, Greene H, Huther M, Gottlieb S, DeMaria A, et al. Relationship between heart failure, ejection fraction, arrhythmia suppression and mortality: analysis of the cardiac arrhythmia suppression trial. *JACC*. 1995;13(1):1250-7.
14. Paulus WJ, Zile MR. From systemic inflammation to myocardial fibrosis. The heart failure with preserved ejection fraction paradigm revisited. *Circ Res*. 2021 May 14;128(10):1451-1467.
15. Schulman IH, Raji L. The angiotensin II type 2 receptor: what is its clinical significance. *Curr. Hypertens. REP*. 2008;10:188-93.
16. Frangogiannis NG. The inflammatory response in myocardial injury, repair and remodelin. *Nat. Rev. Cardiol*. 2014;11(5):255-65.
17. Christa A, Bekkering S, Latza E, Riksen NP. Long-term activation of the innate immune system in atherosclerosis. *Seminars in Immunology*. 2016;28(4):384-93.
18. Chekalina NI, Shut SV, Trybrat TA, Burmak YuG, Petrov YeYe, Manusha YI, et al. Effect of quercetin on parameters of central hemodynamics and myocardial ischemia in patients with stable coronary heart disease. *Wiadomosci lekarskie*. 2017;70(4):707-11.
19. Chekalina NI, Kazakov YM, Mamontova TV, Vesnina LE, Kaidashev IP. Resveratrol more effectively than quercetin reduces endothelium degeneration and level of necrosis factor α in patients with coronary artery disease. *Wiadomosci lekarskie*. 2016;69(3):475-9.
20. Parkhomenko AN, Kozhukhov SN. Rezultaty otkrytoho randomyzyrovannoho yssledovannia po yzuchenyiu perenosymosti y efektyvnosti preparata Korvytyn u patsyentov s zastoinoi serchednoi nedostatochnosti u systolycheskoi dysfunktsyi levoho zheludochka. *Ukrainskyi. med. chasopys*. 2014;4(102):71-6. [in Ukrainian].
21. Sheng R, Gu ZL, Xie ML. Epigallocatechin gallate, the major component of polyphenols in green tea, inhibits telomere attrition mediated cardiomyocyte apoptosis in cardiac hypertrophy. *Int. J. Cardiol*. 2011;162:199-209.
22. Singh NP, Singh UP, Hegde VL, Guan H, Hofseth L, Nagarkatti M, et al. Resveratrol (trans-3,5,4'-trihydroxystilbene) suppresses EL4 tumor growth by induction of apoptosis involving reciprocal regulation of SIRT1 and NF- κ B. *Mol. Nutr. Food. RES*. 2011;55(8):1207-18.
23. Das S, Fraga CG, Das DK. Cardioprotective effect of resveratrol via HO-1 expression involves p38 map kinase and PI-3-kinase signaling, but does not involve Nf κ B. *Free radical research*. 2006;40(10):1066-75.
24. Olson ER, Nougale JE, Zhang X, Zhang X, Bomser JA, Meszaros JG. Inhibition of cardiac fibroblast proliferation and myofibroblast differentiation by resveratrol. *Am. J. Physiol. Heart. Circ. Physiol*. 2005;288:1131-8.
25. Andriantsitohaina R, Auger C, Chataigneau T. Molecular mechanisms of the cardiovascular protective effects of polyphenols. *BR. J Nutr*. 2012;108(9):1532-49.
26. Voskresensky ON, Zhutaev IA, Bobyrev VN, Bezugly YuV. The antioxidant system, ontogenesis and ageing. *Voprosy Meditsinskoj Khimii*. 1982;28(1):14-27.
27. Kaidashev IP. Aktyvatsiia NF- κ B pry metabolichnomu syndromi. *Fiziol. zhurnal*. 2012;58(1):93-101. [in Ukrainian].

РЕСВЕРАТРОЛ БІЛЬШ СУТТЄВО, НІЖ КВЕРЦЕТИН, ПОКРАЩУЄ ПОКАЗНИКИ ЦЕНТРАЛЬНОЇ ГЕМОДИНАМІКИ У ХВОРИХ НА ІШЕМІЧНУ ХВОРОБУ СЕРЦЯ

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Резюме. Ішемічна хвороба серця (ІХС) очолює список причин смертності населення у всьому світі вже багато років поспіль. Попри численні методи лікування, що розробляються та впроваджуються у клінічну медицину, проблема залишається незмінною, тому пошук нових ефективних патогенетично обґрунтованих методів лікування ІХС є край актуальним. ІХС призводить до порушення структури та функції міокарда, формування його жорсткості та прогресування гемодинамічних розладів. Одним з механізмів прогресування атеросклерозу – морфологічної основи ІХС – є хронічне системне запалення. Протизапальною активністю на різних рівнях прозапальної сигналізації володіють поліфеноли рослинного походження.

Мета роботи – оцінити вплив поліфенолів ресвератролу та кверцетину на показники центральної гемодинаміки у хворих на ІХС.

Проведено проспективне відкрите рандомізоване контрольоване дослідження за участю 230 осіб, хворих на ІХС, I-II функціональний клас (ФК), із серцевою недостатністю не вище II ФК за Нью-Йоркською Асоціацією Кардіологів (NYHA). Після оцінки показників гемодинаміки за даними ехокардіографії (Ехо), хворі рандомізовані у I та II групи дослідження, 55 осіб обрано у групу порівняння. Поряд з базисною терапією ІХС, I групі призначено 100 мг ресвератролу на добу, II групі – 120 мг кверцетину на добу. Група порівняння отримувала базисну терапію. Через 2 місяці оцінено результати Ехо.

У переважній більшості хворих на ІХС визначалася зміна співвідношення фаз трансмітрального кровотоку, що відповідало діастолічній дисфункції за I типом (порушення релаксації). Наявність серцевої недостатності за діастолічним типом підтверджували час ізовольметричного розслаблення та час уповільнення раннього діастолічного наповнення лівого шлуночку, розміри лівого передсердя. Систолічна функція у переважній більшості хворих відповідала межах норми, але була достовірно меншою, ніж у групі здорових осіб.

За даними проведеного аналізу, під впливом обох поліфенолів більш суттєво, ніж при застосування стандартної терапії, покращилася систолічна та діастолічна функція ЛШ, з перевагою дії ресвератролу.

Висновки. Застосування ресвератролу та кверцетину в комплексній терапії хворих на ІХС позитивно вплинуло на показники центральної гемодинаміки, особливо щодо діастолічної функції лівого шлуночка, з перевагою ефективності ресвератролу, що є основою для його широкого впровадження в клінічну практику для лікування ІХС.

Ключові слова: ішемічна хвороба серця, центральна гемодинаміка, діастолічна серцева недостатність, поліфеноли, ресвератрол, кверцетин.

RESVERATROL MORE SIGNIFICANTLY THAN QUERCETIN IMPROVES CENTRAL HEMODYNAMICS IN PATIENTS WITH ISCHEMIC HEART DISEASE

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Abstract. Ischemic heart disease (IHD) has topped the list of causes of death in the population worldwide for many years in a row. Despite the numerous methods of treatment that are being developed and implemented in clinical medicine, the problem remains unchanged, so the search for new effective pathogenetically justified methods of treatment of IHD is extremely urgent. IHD leads to disruption of the structure and function of the myocardium, the formation of its stiffness and the progression of hemodynamic disorders. One of the mechanisms of progression of atherosclerosis – the morphological basis of IHD – is chronic systemic inflammation. Plant polyphenols possess anti-inflammatory activity at different levels of pro-inflammatory signaling.

The purpose of the work is to assess the effect of polyphenols resferatrol and quercetin on central hemodynamic parameters in patients with IHD.

A prospective open-label randomized controlled trial was conducted in 230 people with IHD, I-II functional class (FC), with heart failure not higher than II FC according to the New York Heart Association (NYHA). After the evaluation of hemodynamic parameters according to echocardiography (Echo), patients randomized in the I and II groups of the study, 55 people were selected in the comparison group. Along with the basic therapy of IHD, group I was prescribed 100 mg of resveratrol per day, group II – 120 mg of quercetin per day. The comparison group received basic therapy. After 2 months, Echo results were evaluated.

In the vast majority of patients with IHD, a change in the phase ratio of transmitral blood flow was determined, which corresponded to type I diastolic dysfunction (impaired relaxation). The presence of heart failure according to the diastolic type was confirmed by the time of isovolumetric relaxation and the time of slowing the early diastolic filling of the left ventricle, the size of the left atrium. Systolic function in the vast majority of patients corresponded to the limits of the norm, but was significantly less than in the group of healthy individuals. The presence of heart failure by diastolic type was confirmed by the the left ventricle isovolumetric relaxation time and the left ventricle deceleration time, and the size of the left atrium.

Systolic function in the vast majority of patients corresponded to the limits of the norm, but was significantly less than in the group of healthy individuals. Under the influence of both polyphenols, more significantly than with the use of standard therapy, the systolic and diastolic functions of LV have improved, with the advantage of resveratrol.

Conclusions. The use of resveratrol and quercetin in complex therapy of patients with IHD had a positive effect on the central hemodynamics, especially on the diastolic function of the left ventricle, with the advantage of resveratrol efficiency, which makes it possible to recommend it for wide use in the treatment of IHD.

Key words: ischemic heart disease, central hemodynamics, diastolic heart failure, polyphenols, resveratrol, quercetin.

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