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Vasopathy In Patients With Arterial Hypertension 2 Degrees.

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ABSTRACT

The prevalence of arterial hypertension among persons of mature age and the high incidence of its complications dictates the need for continuing research on this contingent of patients. Special attention should be paid to the antiaggregatory properties of the vessels, which in many respects limit the duration and quality of life of patients with a very common arterial hypertension of the 2nd degree. Aim of the present study was to assess the state of the antiaggregatory function of the vascular wall in patients with AH of degree 2.46 patients with arterial hypertension of the 2nd degree of the second adult age were under observation. The control group consisted of 25 healthy people of the second adulthood. The work uses biochemical, hematological and statistical methods of investigation. The examined patients showed a decrease in the antiaggregatory properties of the vessels over significantly enhanced platelet aggregation. These disorders occurred in the presence of a pronounced increase in the peroxide oxidation of plasma lipids, inhibition of production in the walls of vessels of nitric oxide, prostacyclin with a rise in blood levels and endothelia. In patients with arterial hypertension of the 2nd degree against a background of increased aggregation activity of platelets, there is a marked decrease in the ant aggregative capacity of the vessel wall. The development of these disorders is a serious factor in the development of thrombophilia and requires a systematic long-term correction, the approaches to which need to be clarified in future studies.

Keywords: arterial hypertension 2 degrees, vascular wall, platelets, ant aggregation, second mature age.

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INTRODUCTION

The ability of the vascular wall to inhibit platelet aggregation is an important element in maintaining blood in the liquid state in the mammalian organism [1]. This process is realized by the endothelium of the vascular wall, which continuously generates substances possessing disaggregation activity [2, 3]. Earlier studies on vascular homeostasis made it possible to realize the dynamism of its functioning under various conditions, incl. With arterial hypertension (AH). In recent years, this pathology has attracted increasing attention of researchers [5, 6]. This is due to the steady increase in its prevalence among the working population [7] and the need to continue to search for effective options for its treatment [8, 9] and prevention of complications [10]. The greatest danger of hypertension is associated with the very frequent development of various thromboses with it, arising from the weakening of synthesis in the vascular wall of substances that inhibit the activity of homeostasis [11]. The most common is the 2nd degree of AH. In this connection, the state of the synthesis of hemostatically active substances: nitric oxide, prostacyclin, ant thrombin III, tissue plasminogen activators is of great interest in this category of patients [12]. In view of the high risk for hypertension, it is very important to assess the degree of platelet activation in patients with AH of degree 2 [13, 14]. In this connection, the aim of the present study was to assess the state of the antiaggregatory function of the vascular wall in patients with AH of degree 2.

MATERIALS AND METHODS

The research was approved by the Ethics Committee of Russian State Social University (record №5 from 12.05.2014).

There were observed 46 patients of the second mature age (48.5±2.8 years) with AH of the 2rd degree [15]. The criteria for the enrollment into the research were as follows: AH existence for not less than 5 years, it corresponded to the level of the 3rd degree, absence of systematic pharmacological treatment of AH (because of personal beliefs). The existing metabolic, ontological and allergic diseases were the criteria for the expulsion from the group of observation.

The patients didn't consume drugs and alcohol, didn't smoke, had average welfare and good housing conditions. Chronic diseases of 9 persons (chronic pyelonephritis, chronic cholecystitis) were in the stage of persistent clinical remission for not less than 1.5 years. Control group was composed of 25 clinically healthy volunteers of the same age. Chronic diseases of 9 persons (chronic tonsillitis and chronic bronchitis) were in the stage of persistent clinical remission for not less than 1.5 years. All the examined persons signed the informed agreement on taking part in the investigation.

The activity of plasma lipids' peroxidation (LPO) was determined according to the content of thiobarbituricacid (TBA) – active products in it by a set "Agat-Med" (Russia) and aryl hydroperoxides (AHP) [16]. We also estimated the antioxidant potential of liquid part of blood [17]. In plasma of all the examined patients we determined the content of endothelin-1 by radioimmunological method with the help of reagents of the firm "DRG" (USA), the quantity of thromboxane A_2 metabolite – thromboxane B_2 and prostacyclin metabolite – 6-keto-prostaglandin $F_{1\alpha}$ in the course of enzymoimmunoassay with application of sets of the firm "Enzo Life Science" (USA). The summary quantity of nitric acid metabolites in blood of examined patients was determined according to the method by Metelskaya V.A. and co-authors (2005) [18]. The calculation of platelets' quantity in capillary blood was made in Goryaev's box. Platelets' aggregator ability was studied by visual micromethod [19] with the usage of the following inductors – adenosine diphosphate (ADP) (0.5×10^{-4} M), collagen (dilution 1:2 of the basic suspension), thrombin (0.125 un/ml), ristomicin (0.8 mg/ml) and adrenaline (5×10^{-6} M). The antiaggregatory activity of vascular wall was found according to AP weakening in response to all the used inductors in conditions of temporal venous occlusion. It was estimated with the help of index value of the antiaggregatory activity of vascular wall (IAAVW) which was calculated by dividing the period of AP development in plasma, received at temporal venous occlusion, on the period of AP development in blood plasma, taken without application of tourniquet on the vessel.

Statistical processing of received data was made with the help of a programmed package "Statistics for Windows v. 6.0", "Microsoft Excel". The results were processed by Student's criterion (t). Differences in data were considered reliable in case of $p<0.05$.

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RESULTSANDDISCUSSION

We found strengthening of LPO in plasma: concentration of TBA-active products in it was equal to 4.90±0.014mmol/l (in control group – 3.07±0.011mmol/l), the content of AHP – 3.32±0.009 D_{233}/1 ml (in control group – 1.62±0.002 D_{233}/1ml). The examined patients had an evident weakening of antioxidant plasma activity till 25.3±0.16% (in the control group – 36.8±0.03%) (Table).

Table: The indicators considered in the surveyed

Registered parameters		Patients, n=46, M±m	Control, n=25, M±m
AHP, D_{233} /1ml		3.07±0.011	1.62±0.002 p<0.01
TBA-compounds, mcmol / l		4.90±0.014	3.38±0.006 p<0.01
plasmaantioxidantactivity, %		25.3±0.16	36.8±0.03 p<0.01
thromboxaneA_2, pg/ml		208.2±0.52	156.5±0.66 p<0.01
6-keto-prostaglandin $F_{1\alpha}$, pg/ml		74.4±0.48	82.4±0.49 p<0.01
Total metabolites nitrogen oxide, mcmol / l		28.3±0.27	33.6±0.35 p<0.01
endothelin-1, pg/ml		16.2±0.17	8.2±0.15 p<0.01
Aggregation inductor ADP	Aggregation of platelets in intact plasma, s	32.8±0.15	42.9±0.10 p<0.01
	Aggregation of platelets in plasma after temporary venous occlusion, s	45.6±0.19	65.4±0.22 p<0.01
	IAAVW	1.39±0.008	1.52±0.012 p<0.01
Aggregation inductor collagen	Aggregation of platelets in intact plasma, s	27.5±0.15	32.4±0.04 p<0.01
	Aggregation of platelets in plasma after temporary venous occlusion, s	37.4±0.23	48.9±0.09 p<0.01
	IAAVW	1.36±0.004	1.51±0.008 p<0.01
Aggregation inductor thrombin	Aggregation of platelets in intact plasma, s	43.8±0.29	56.9±0.10 p<0.01
	Aggregation of platelets in plasma after temporary venous occlusion, s	58.0±0.37	84.2±0.12 p<0.01
	IAAVW	1.32±0.008	1.48±0.008 p<0.01
Aggregation inductorristomycin	Aggregation of platelets in intact plasma, s	36.2±0.16	45.9±0.12 p<0.01
	Aggregation of platelets in plasma after temporary venous occlusion, s	52.4±0.28	70.8±0.15 p<0.01

	IAAVW	1.44±0.005	1.54±0.009 p<0.01
Aggregation inductor adrenaline	Aggregation of platelets in intact plasma, s	73.6±0.39	99.9±0.09 p<0.01
	Aggregation of platelets in plasma after temporary venous occlusion, s	105.3±0.63	167.6±0.15 p<0.01
	IAAVW	1.43±0.003	1.68±0.010 p<0.01

Symbols: p – reliability of distinctions of indicators between a group of patients and control. In the subsequent table of designation it is similar.

In the blood of patients from the experimentalgroup, we found misbalance of arachidonic acid metabolites: the level of thromboxane B_2 rose on 33.0%, at the level lowering of its functional antagonist's derivative – 6-keto-prostaglandin $F_{1\alpha}$ on 10.7%. It was accompanied by high level of endothelin-1 in the blood (16.2±0.17pg/ml) of examined patients and lowering of the content of summary nitric acid metabolites on 18.7% in it (Table).

The amount of platelets in patients' blood related with the normal level. AP in plasma, taken without venous occlusion, was the most accelerated one under the impact of collagen – 27.5±0.15s (in the control group – 32.4±0.04s) (table). AP developed a bit slower under the impact of ADP and ristomicin. Thrombin and adrenaline AP also developed faster than in the control group – 43.8±0.29s (in the control group – 56.9±0.10s) and 73.6±0.39s (in the control group – 99.9±0.09s), respectively (p<0.01).

In plasma, received on the background of venous occlusion, patients' AP decelerated weaker than in the group for comparison. It provided the patients with the evident lowering of IAAVW values (Table). Therefore, the maximumvalue of IAAVW was noted for adrenaline – IAAVW 1.43±0.003, whereas in the control group this value was equal to 1.68±0.010. A bit less IAAVW was registered with ristomicin and ADP. Values of IAAVW with thrombin and collagen were still lower – 1.32±0.008 and 1.36±0.004, respectively.

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Chronically elevated blood pressure level with AH has a very deleterious effect on blood vessels, disrupting their function, which contributes to the development of thrombophilia [20]. At the same time, the

activity of vascular homeostasis in the given category of patients' needs to be specified. In particular, there is no final clarification about the activity features of basic mechanisms of formation and support of angiopathy in them at AH of the 2rd degree in conditions.

High level of arterial pressure, noted in examined patients, influenced negatively functional features of the vascular wall [21]. Apparently, it was caused by not only evident endothelium alteration but also uncovering of sub-endothelial fibers which could activate platelets by contact [22]. In these conditions, the synthesis of biologically active substances, which can decelerate platelet adhesion and aggregation, weakened in the vascular wall. The synthesis of pro-aggregates strengthened in platelets on this background [23]. It was proved by noted in patients evident intensity of thromboxane synthesis and output lowering of its functional antagonist – prostacyclin. It developed more evident misbalance of arachidonic acid metabolites in their blood than at AH of the 1st degree [24]. It's possible that on the basis of a given situation we had evident activation of platelet thromboxane synthetase and strong activity weakening of vessels' prostacyclin-synthetase. Found disturbances were evidently deepened by an increase of endothelin-1 synthesis in vascular wall and generation weakening of nitric oxide in it. On the basis of these abnormalities, the examined patients had evident activity disturbance of endotheliocytes' enzymes by, probably, surplus plasma LPO and the presence of dyslipidemia what significantly surpassed the situation at AH of the 1st degree on the background [2, 13].

At carrying out the test with temporal ischemia of venous wall the patients were found to have a weakening of vessels' ability to repress adhesive features of platelets with the help of at least two mechanisms [25]. The first mechanism was connected with the evident lowering of control from the side of the vascular wall over the density of collagen receptors- glycoprotein's Ia-IIa and VI on platelets' membranes. It was found according to weak AP deceleration in response to collagen in plasma after temporal venous ischemia. The second mechanism of strong depression of vascular weakening of platelets' adhesion in persons with AH of the 2rd degree was connected with evident strengthening of von Will brand Factor's output by structures of vascular wall and its active binding with receptors to it – (glycoprotein's I b) on platelets' surface in conditions of vascular antiaggregant' deficiency [26]. We managed to judge the level rise of von Will brand Factor by early AP with ristomicin which was like subendothelial vessels' fibers as far as its impact on platelets was concerned. It's known that von Will brand Factor connecting by one end of the molecule with collagen and by the second one through glycoprotein I b – with platelet, formed "adhesion axis": collagen – von Will brand Factor – glycoprotein I b. Synthesis strengthening of von Will brand Factor according to the mechanism of positive feedback increased the amount of receptors to it on platelets' membranes, raising their adhesive readiness [27]. The increase of von Will brand Factor's quantity in patients' plasma, probably, took place in the result of its active release out of endothelium and to some extent, on behalf of secretion by platelets under hemodynamic impacts and metabolic abnormalities. At the same time, the degree of these processes prevailed over the same ones of the patients with AH of the 1stdegree. The first mechanism of vessels' control over platelets' adhesive ability is very important in the provision of homeostasis process in conditions of low shear stress – in large arteries and veins, the second one – at high shear stress in the course of bloodstream in little arteries and arterioles [27, 28].

In conditions of insufficient synthesis of physiological antiaggregant in vessels at AH of the 2rd degree, the strength of fixation of strong aggregation antagonists-collagen and thrombin to their receptors on platelets' membranes rose quickly. It led to evident activation of phospholipase C, stimulation of phospho-inositol way through diacylglycerol and protein kinase C with phospholiririovation of proteins of the contractile system. Forming in these conditions surplus instill triphosphate promoted Ca^{2+} release out of Intra plateletdepo intensifying the involution of act myosin [29]. Being weak inductors of platelets' aggregation ADP and adrenaline also more actively than at AH of the 1stdegree, interacted with their own receptors on their membranes. It took place in conditions of deficiency of prostacyclin and nitric oxide formation in vessels, caused evident expression of fibrinogen receptors (glycoprotein's IIb-IIIa) and stimulated the activity of phospholipase A_2. The last one provided the release of a surplus quantity of arachidonic acid out of platelets' phospholipids. In these conditions,cyclooxygenase and thromboxane synthetase of platelets, activated by metabolic abnormalities and LPO strengthening, increased abundantly thromboxane A_2 formation. In physiological conditions of AH of the 1stdegree thromboxane A_2 and products of instill way still, could stimulate the yield of prostacyclin out of vessels. Prostacyclin limited the impact of thromboxane A_2 [30]. However, at AH of the 2rd degree the secretion of given substances out of vessels weakened to such extent that couldn't already compensate the activity of proaggregants. It's possible that developing deep abnormalities of

hemodynamic in combination with shears in the lipidic range of plasma and strengthening of LPO in it formed all the picture of angiopathy in the given category of patients.

CONCLUSION

Patients with AH of the 2rd degree on the background of strengthened aggregator activity of platelets had an evident lowering of the antiaggregatory ability of vascular wall. We see the basis of these disturbances in shears in lipidic metabolism, activation of plasma lipids' peroxidation, misbalance of arachidonic acid metabolites in blood and synthesis strengthening of von Will brand Factor in the vascular wall. Given disturbances surpass the same ones at AH of the 1st degree and are important factors in the rise of thrombogenic danger for the examined category of patients.

REFERENCES

[1] Kotseva K, Wood D, De Backer G. (2009) Euroaspre Study Group. Cardiovascular prevention guidelines in daily practice: a comparison of Euroaspre I, II, and III surveys in eight European countries. Lancet.373: 929-940.

[2] Kotova OV, ZavalishinaSYu, Makurina ON, KipermanYaV, Savchenko AP, Skoblikova TV, Skripleva EV, Zacepin VI, Skriplev AV, AndreevaVYu. (2017) Impact estimation of long regular exercise on homeostasis and blood rheological features of patients with incipient hypertension. Bali Medical Journal. 6(3): 514-520. doi:10.15562/bmj.v6i3.552

[3] Zamora no J, Edwards J. (2011) Combining antihypertensive and antihyperlipidemic agents - optimizing cardiovascular risk factor management. Integr.Blood Press Control.4: 55-71.

[4] VatnikovYuA, ZavalishinaSYu, Pliushchikov VG, Kuznetsov VI, Seleznev SB, Kubatbekov TS, Rystsova EO, Parshina VI. (2017) Early-changes diagnostics of erythrocytes microrheological features in the model of dyslipidemia development in rats at the late stages of ontogenesis. Bali Medical Journal. 6(1) : 216-222.doi: 10.15562/bmj.v6i1.483

[5] ZavalishinaSYu, VatnikovYuA, Kulikov EV, Yagnikov SA, Karamyan AS, Sturov NV, Byakhova VM, Kochneva MV, Petryaeva AV. (2017) Diagnostics of erythrocytes' microrheological features and early abnormalities of rats in the model of experimental hypertension development. Bali Medical Journal. 6(3): 470-475. doi:10.15562/bmj.v6i3.589

[6] VatnikovYuA, ZavalishinaSYu, Kulikov EV, Vilkovysky IF, Nikishov AA, Drukovsky SG, Krotova EA, Khomenets NG, Bolshakova MV.(2017) Correctional abilities of regular muscle activity in relation to erythrocytes' microrheological features of rats with experimentally developed hypertension. Bali Medical Journal. 6(3): 449-456. doi:10.15562/bmj.v6i3.586

[7] Bikbulatova AA, Karplyuk AA, Tarasenko OV. (2017) Model of Activities of the Resource Training Center of the Russian State Social University in Terms of Professional Orientation and Employment of Persons with Disabilities. Psikhologicheskayanaukaiobrazovanie. 22(1): 26-33.

[8] Bikbulatova AA, Pochinok NB. (2017) Professional Skills Competitions for People with Disabilities as a Mechanism for Career Guidance and Promotion of Employment in People with Special Needs.Psikhologicheskayanaukaiobrazovanie. 22(1) : 81-87.

[9] ZavalishinaSYu. (2012) Platelet activity in newborn calves with iron deficiency anemia.Veterinariya.2 : 51-52.

[10] ZavalishinaSYu, Nagibina EV.(2012) Dynamics of microrheology characteristics of erythrocyte in children 7-8 years with scoliosis with therapeutic physical training and massage.Technologies of Living Systems. 9(4) : 29-34.

[11] Carrizzo A, Puca A, Damato A. (2013) Resveratrol improves vascular function in patients with hypertension and dyslipidemia by modulating NO metabolism. Hypertension.62 : 359-366.

[12] Gurevich VS. (2013) Correction of dyslipidemia with concomitant arterial hypertension from the perspective of an updated paradigm of cardiovascular risk.Systemic hypertension.3 : 54-59.

[13] Skoryatina IA, ZavalishinaSYu. (2017) Ability to aggregation of basic regular blood elements of patients with hypertension anddyslipidemia receiving non-medication andsimvastatin.Bali Medical Journal. 6(3): 514-520.doi:10.15562/bmj.v6i3.553

[14] Sushkevich GN.(2010) Pathological systems of homeostasis and principles of their correction. Krasnodar: Soviet Kuban, 240.

[15] Diagnosis and treatment of hypertension. In the book: National Clinical Recommendations. 3rd edition. Moscow: Silicea-Polygraph, 2010: 463-500.

[16] ZavalishinaSYu.(2011) Fibrinolysis blood activity at calves in the first year of life. Zootekhniya.2 : 29-31.
[17] Volchegorskiy IA, Dolgushin II, Kolesnikov OL, Tseilikman VE. (2000) Experimental modeling and laboratory evaluation of adaptive reactions of the organism. Chelyabinsk, 167.
[18] Metelskaya VA, Gumanova NG. (2005) Nitric oxide: a role in the regulation of biological functions, methods of determination in human blood. Laboratory medicine.7 : 19-24.
[19] ZavalishinaSYu.(2010) Anticoagulative and fibrinolitic activity of plasma of blood at calves. Veterinariya.11: 41-43.
[20] Sossdort M, König V, Gummert J. (2008) Correlations between platelet-derived micro vesicles and thrombin generation in patients with coronary artery disease. Platelets. 19(6) : 476-477.
[21] Folsom AR.(2013) Classical and novel biomarkers for cardiovascular risk prediction in the United States. J Epidemiol.2013; 23: 158-162.
[22] ZavalishinaSYu. (2012) Dynamics of homeostasis system at newborn calves with iron deficiency by use ferroglucin and glycerin. Zootekhniya.7 : 14-16.
[23] ZavalishinaSYu.(2012) vascular homeostasis at calves in milk-and-vegetable phase of feeding. Zootekhniya.2 : 21.
[24] ZavalishinaSYu. (2011) Functional condition of system of a homeostasis at newborn calves.Veterinariya.6 : 42-45.
[25] ZavalishinaSYu.(2012) Activity of a vascular homeostasis at calfs of a dairy food. Russian Agricultural Sciences. 4 : 49-51.
[26] ZavalishinaS.Yu. (2012) Hemostatic activity of a vascular wall at newborn calfs. Russian Agricultural Sciences.1 : 37-39.
[27] ZavalishinaSYu. (2011) Coagulation activity of plasma of blood at calves of a vegetative feeding. Veterinariya.4 : 48-49.
[28] Stang D, Kriston L, von Wolff A. (2013) Reducing cardiovascular medication complexity in a German university hospital: effects of a structured pharmaceutical management intervention on adherence. JMCP. 19:396-407.
[29] Burnier L, Fontana P, Kwak BR, Andelillo-Scherrer A. (2009) Cell-derived micro particles in haemostasis and vascular medicine. Thromb.Haemost.101 : 439-451.
[30] Koniari I, Mavrilas D, Papadaki H. (2011) Structural and biochemical alterations in rabbit thoracic aorta are associated with the progression of atherosclerosis. Lipids in Health and Disease. 10: 125-134.