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## Vascular Disaggregation Effects On Erythrocytes In Patients With Arterial Hypertension With Type 2 Diabetes Mellitus.

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### ABSTRACT

It was noted that patients with arterial hypertension with type 2 diabetes mellitus often have vasopathy. The prevalence in the developed countries of a combination of arterial hypertension with type 2 diabetes mellitus provides a high interest for researchers. Great attention in this pathology deserves vascular control over aggregation by the most numerous population of blood cells - erythrocytes. The purpose of the study was to study the severity of disturbances in the disaggregation properties of blood vessels in relation to erythrocytes in patients with arterial hypertension with type 2 diabetes mellitus. 42 patients with arterial hypertension of 1-2 degrees and type 2 diabetes mellitus of the second adult age were examined. The control consisted of 26 healthy persons of the second adult age. The study uses biochemical, hematological and statistical methods. In the group of patients, an increase in the cholesterol content in erythrocyte membranes, a decrease in total phospholipids in them, and activation of lipid peroxidation were found. In patients, excessive activity of spontaneous aggregation of erythrocytes was found. This was accompanied by a weakening of the vascular disaggregation control over them. The changes found in the examined category of patients should be considered as a consequence of metabolic abnormalities arising on the background of arterial hypertension and diabetes mellitus 2, expressed vasospasm and activation of lipid peroxidation. Patients with this contingent of vasopathy dramatically increased their risk of fatal thrombosis.

**Keywords:** arterial hypertension, diabetes mellitus, vascular wall, aggregation, erythrocytes.

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## INTRODUCTION

Continuous examination and health improvement measures in industrially developed countries could not yet significantly affect the widespread prevalence of a combination of hypertension (AH) and type 2 diabetes in the society [1,2]. It is believed that the combination of these two conditions greatly contributes to an increase in episodes of vascular thrombosis in persons of mature age, which often leads to disability and mortality [3,4]. The high incidence of thrombosis in patients with type 2 diabetes mellitus is largely related to the formation of vasopathy [5,6]. This aggravates the aggregation processes in the blood of these patients. Under these conditions, hemostasis can be strongly activated, causing thrombosis [7-9]. It is known that the aggregation of blood cells is inhibited by substances of vascular origin and called desaggregants. The most powerful of these are prostacyclin and nitric oxide [10,11]. Given the high risk of thrombosis in hypertension with diabetes mellitus type 2, it seemed important to assess the level of vascular control over erythrocyte aggregation in this category of patients. The aim of the study is to study the severity of disturbances in the disaggregation properties of blood vessels in relation to erythrocytes in patients with type 2 diabetes mellitus.

## MATERIALS AND METHODS

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

42 patients with AH of 1-2 degree, risk 4 [12] with type 2 diabetes, the second adult age (mean age 49.3 ± 2.9 years) were examined. Control consisted of 26 healthy people of the second adulthood. The examinees gave written information consent to participate in the conducted research according to the generally accepted procedure [13]. The severity of lipid peroxidation (LPO) in plasma was taken into account in terms of the level of thiobarbituric acid (TBA) -active products with the help of the Agat-Med (Russia) and acyl hydroperoxides (AGP) kit. [14] The state of antioxidant plasma protection was estimated by the method of [15].

The intensity of LPO in erythrocytes was determined by the level of malonicdialdehyde (MDA) in them and the content of AGP in them after washing and resuspension. [14] In addition, in washed and resuspended erythrocytes, the cholesterol content was assessed by the enzymatic colorimetric method (Russia) and taking into account the total phospholipids in the content of phosphorus in erythrocytes. The severity of disaggregation of vascular effects on erythrocytes was assessed by its decrease in plasma taken after temporary venous occlusion [16]. The activity of spontaneous aggregation of erythrocytes in a plasma obtained after a temporary ischemia of the vessel wall and without it was determined by means of a light microscope in the Gorjaev chamber. The number of erythrocyte aggregates, the number of aggregated and non-aggregated erythrocytes were taken into account [17].

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

## RESULTS AND DISCUSSION

In the patients examined, pronounced activation of LPO in plasma was found - the content of AGP in it exceeded the level of control 2.35 times. The quantity of TBA-active products is 1.54 times. This occurred as a result of attenuation of the antioxidant protection of the plasma by a factor of 1.5 (Table).

In patients, an excess of the amount of cholesterol in the erythrocyte membranes was found while reducing the total phospholipids in them. At the same time, activation of LPO due to depression of their antioxidant protection was found in erythrocytes (Table). In patients, a strong activation of spontaneous erythrocyte aggregation was noted (Table).

This was indicated by an increase in their overall inclusion in aggregates (by 66.8%), an increase in the number of these aggregates (by 74.4%) and a decrease in 64.8% of non-aggregated red blood cells.

In patients, a decrease in the disaggregation properties of blood vessels with respect to erythrocytes was found (Table).

**Table: Registered indicators in the surveyed**

| Registered parameters   | Patients, n=42, M±m | Control, n=26, M±m     |
|---|---------------------|------------------------|
| acylhydroperoxides plasma, D <sub>233</sub> /1ml                                    | 3.34±0.09           | 1.42±0.09<br>p<0.01    |
| TBA-compounds, umol / l   | 5.47±0.16           | 3.56±0.07<br>p<0.01    |
| antioxidant activity plasma, %  | 21.3±0.18           | 32.9±0.12<br>p<0.01    |
| biochemical parameters of erythrocytes  |                     |                        |
| cholesterol of erythrocytes, umol/10 <sup>12</sup> erythrocytes                     | 1.35±0.011          | 1.04±0.004<br>p<0.01   |
| common phospholipids of erythrocytes, umol/10 <sup>12</sup> erythrocytes            | 0.53±0.009          | 0.75±0.003<br>p<0.01   |
| acylhydroperoxides of erythrocytes, D <sub>233</sub> /10 <sup>12</sup> erythrocytes | 4.79±0.27           | 3.08±0.10<br>p<0.01    |
| malonic dialdehyde of erythrocytes, nmol/10 <sup>12</sup> erythrocytes              | 1.72±0.10           | 1.14±0.05<br>p<0.01    |
| catalase of erythrocytes, ME/10 <sup>12</sup> erythrocytes                          | 7210.0±14.7         | 11196.0±22.4<br>p<0.01 |
| superoxidismutase of erythrocytes, ME/10 <sup>12</sup> erythrocytes                 | 1450.0±2.12         | 1986.0±7.01<br>p<0.01  |
| aggregation of erythrocytes in intact plasma  |                     |                        |
| sum of all the erythrocytes in an aggregate   | 69.9±0.17           | 41.9±0.10<br>p<0.01    |
| quantity of aggregates  | 15.7±0.22           | 9.0±0.06<br>p<0.01     |
| quantity of free erythrocytes   | 145.6±0.99          | 240.0±0.23<br>p<0.01   |
| aggregation of erythrocytes in plasma after temporary venous occlusion              |                     |                        |
| sum of all the erythrocytes in an aggregate   | 59.7±0.26           | 32.6±0.14<br>p<0.01    |
| quantity of aggregates  | 12.5±0.17           | 7.0±0.07<br>p<0.01     |
| quantity of free erythrocytes   | 181.3±1.25          | 305.3±0.18<br>p<0.01   |

Note: p - reliability of differences in the indices of a group of patients and a control group.

It was noted that in plasma taken against a background of temporary venous occlusion, the number of erythrocytes in the aggregates exceeded the control by 83.1%, the number of aggregates themselves was increased by 78.6%, and the number of non-aggregated red blood cells was reduced by 68.4%. Growth of erythrocyte aggregation plays a significant role in increasing the risk of thrombosis in individuals with AH and type 2 diabetes mellitus [18, 19]. When AG is combined with type 2 diabetes mellitus, depression of the antioxidant protection of the plasma develops, which ensures the growth of LPO processes in it [20]. This inevitably worsens the structure and function of erythrocyte membranes [21]. All this leads to hyperaggregation of erythrocytes. The oncoming weakening of the disaggregating effects of blood vessels on erythrocytes aggravates the situation [22,23]. This was observed in the patients observed for the growth of erythrocyte aggregation in plasma after temporary venous occlusion [24]. It is clear that the growth of erythrocyte aggregation in patients with AH with type 2 diabetes is caused by a weakening of the disaggregating properties of their vessels [25,26] and a decrease in the level of negatively charged proteins on erythrocytes [27]. Weakening of antioxidant plasma parameters promotes intensification of lipid peroxidation processes in it, and, consequently, marked oxidative damage of endotheliocytes and plasma proteins [28,29]. In conditions of deficiency of vascular dezagregantov there is an intensification of erythrocyte communication

among themselves in aggregates and an increase in their number [30,31]. At the same time, a decrease in the level in the blood of prostacyclin and nitric oxide forms a functional imbalance in the erythrocytes of adenylatecyclase and phosphodiesterase [32, 33]. As a result, the amount of cyclic adenosine monophosphate decreases and the level of  $Ca^{2+}$  increases, which additionally stimulates the expression of erythrocyte aggregation [34,35].

### CONCLUSION

It is known that for patients with arterial hypertension and type 2 diabetes mellitus, a high platelet count is characteristic. This required an additional examination of this contingent of patients. It was revealed that in arterial hypertension with type 2 diabetes mellitus, the antioxidant activity of the plasma is weakened and the peroxidation of lipids, which adversely affects the vascular wall, is enhanced in it. In this contingent of patients, a decrease in the disaggregating properties of the vessels was found with respect to the spontaneous aggregation of erythrocytes increasing under these conditions. Expressed vasopathy in this contingent of patients is an important basis for the high risk of thrombosis in any localization, sometimes with fatal consequences.

### 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 hemostasis and blood rheological features of patients with incipient hypertension. *Bali Medical Journal*. 6(3): 514-520. doi:10.15562/bmj.v6i3.552
- [3] Zamorano 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] Vorobyeva NV, Skripleva EV, Makurina ON, Mal GS. (2018) Physiological Reaction of The Ability of Erythrocytes to Aggregate to Cessation of Prolonged Hypodynamia. *Research Journal of Pharmaceutical, Biological and Chemical Sciences*. 9(2) : 389-395.
- [6] 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
- [7] 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
- [8] VatnikovYuA, ZavalishinaSYu, Kulikov EV, Vilkovsky 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
- [9] Bikbulatova AA. (2018) The Impact of Daily Wearing of Medicinal-Prophylactic Clothes on The Evidence of Clinical Manifestations of Osteochondrosis Of The 2nd Degree and Platelet Activity in Persons Of The Second Mature Age. *Research Journal of Pharmaceutical, Biological and Chemical Sciences*. 9(1) : 677-683.
- [10] Folsom AR.(2013) Classical and novel biomarkers for cardiovascular risk prediction in the United States. *J Epidemiol*.2013; 23: 158-162.
- [11] ZavalishinaSYu. (2012) Dynamics of hemostasis system at newborn calves with iron deficiency by use ferroglicin and glicopin. *Zootekhniya*.7 : 14-16.
- [12] Diagnosis and treatment of hypertension. In the book: National Clinical Recommendations. 3rd edition. Moscow: Silicea-Polygraph, 2010: 463-500.

- [13] Diagnostics and correction of lipid disorders for the prevention and treatment of atherosclerosis. Russian guidelines (V revision). Cardiovascular Therapy and Prevention. 2012; 4(1) : 31.
- [14] ZavalishinaSYu. (2012) Platelet activity in newborn calves with iron deficiency anemia. Veterinariya.2 : 51-52.
- [15] Volchegorskiy IA, Dolgushin II, Kolesnikov OL, Tseilikman VE. (2000) Experimental modeling and laboratory evaluation of adaptive reactions of the organism. Chelyabinsk, 167.
- [16] ZavalishinaSYu. (2012) Vascular hemostasis at calves in milk-and-vegetable phase of feeding. Zootekhniya.2 : 21.
- [17] 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.
- [18] 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.
- [19] Bikbulatova AA. (2018) Restoration Of Microcirculatory Processes In Persons Of The Second Mature Age With Osteochondrosis Of Lumbar Spine In The Course Of Daily Wearing Of Medicinal Prophylactic Clothes For Half A Year. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 2018; 9(2) : 620-630.
- [20] ZavalishinaSYu. (2010) Anticoagulative and fibrinolytic activity of plasma of blood at calves. Veterinariya. 11: 41-43.
- [21] Bikbulatova AA. (2018) Comparative analysis of rehabilitation efficiency in persons of the second mature age with spinal column osteochondrosis with the help of regular medicinal physical trainings and daily wearing of medicinal prophylactic clothes. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 2018; 9(2) : 997-1007.
- [22] ZavalishinaSYu. (2011) Functional condition of system of a hemostasis at newborn calves. Veterinariya.6 : 42-45.
- [23] ZavalishinaSYu. (2012) Activity of a vascular hemostasis at calves of a dairy food. Russian Agricultural Sciences. 4 : 49-51.
- [24] ZavalishinaS.Yu. (2012) Hemostatic activity of a vascular wall at newborn calves. Russian Agricultural Sciences.1 : 37-39.
- [25] ZavalishinaSYu. (2013) State of the system in neonatal calves in hemostasis with iron deficiency. Russian Agricultural Sciences. 3 : 43-46.
- [26] ZavalishinaSYu. (2013) Vascular hemostasis in newborn calves with ferrum deficiency treated with ferroglucin. Zootekhniya.8 : 24-26.
- [27] ZavalishinaSYu. (2014) State regulation-vascular interactions in newborn piglets with iron with ferroglucin and glikopin. Russian Agricultural Sciences.1 : 57-59.
- [28] ZavalishinaSYu. (2013) Hemostatic activity of thrombocytes in calves during the phase of milk feeding. Agricultural Biology.4 : 105-109.
- [29] ZavalishinaSYu. (2013) Gemostatical activity of vessels piglets vegetable nutrition. Veterinariya.8 : 43-45.
- [30] ZavalishinaSYu. (2010) Activity of curtailing of blood plasma in calves of a dairy feed. Veterinariya. 8 : 49-51.
- [31] ZavalishinaSYu. (2010) Activity of blood coagulation system at healthy calves at phase of milk-vegetable feeding. Zootekhniya. 9 : 13-14.
- [32] Skorjatina IA (2018) Therapeutic Possibilities Of Rosuvastatin In The Medical Complex In Relation To Disaggregation Vascular Control Over Erythrocytes In Persons With Arterial Hypertension And Dyslipidemia. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(2) : 977-983.
- [33] Epel ES, Lin J, Wilhelm FH. (2006) Cell aging in relation to stress arousal and cardiovascular disease risk factors. Psychoneuroendocrinology. 31(3) : 277-287.
- [34] Konari 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.
- [35] ZavalishinaSYu. (2011) Fibrinolysis blood activity at calves in the first year of life. Zootekhniya.2 : 29-31.