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Dis Aggregative Capabilities of Vascular Wall in Respect of Erythrocytes in Patients with Arterial Hypertension and Dislipidemia.

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ABSTRACT

Frequent thromboses' occurrence of various localizations at arterial hypertension with dislipidemia is mostly connected with the development of angiopathy against their background. Taking into account wide prevalence of the combination of arterial hypertension with dislipidemia in developed countries, studying the state at the given pathology of vascular control over aggregation of the most numerous regular blood elements' population – erythrocytes – is of great scientific and practical interest. The aim of the research is to determine peculiarities of vessels' dis aggregative impacts on erythrocytes of patients with arterial hypertension and dislipidemia. There were observed 380 patients of the second mature age with arterial hypertension of the 1st-2nd degree, risk 4 with dislipidemia of IIb type. The control group was composed of 26 clinically healthy volunteers of the same age. There were applied biochemical, hematological and statistical methods of investigation. The observed patients were noted to have some reliable increase of cholesterol in erythrocytes' membranes which was accompanied by some decrease of common phospholipids in them and activation of lipids' peroxidation. The enrolled into the research patients were registered to have reliable strengthening of spontaneous erythrocytes' aggregation. At that all the patients were noted to have lowering of vascular control over erythrocyte aggregation. Evident weakening of disaggregating vascular impacts on strengthening aggregative capability of erythrocytes is the consequence of developing angiopathy at arterial hypertension with dislipidemia. In the result of it the given patients have sharply increased risk of thromboses of any localization which can lead to invalidism and lethal outcome.

Keywords: arterial hypertension, dislipidemia, vascular wall, anti aggregation, erythrocytes.

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INTRODUCTION

Notwithstanding the serious efforts of modern medicine wide prevalence of arterial hypertension (AH), more and more often in combination with dislipidemia (D) [1,2] is still preserved among population of industrially developed countries. This combination conditions high frequency of vascular complications' development leading to incapacitation and mortality [3,4], in able-bodied citizens.

Frequent occurrence of thromboses of various localizations at AH with dislipidemia is mostly connected with the development of angiopathy [5,6]. It is known that all the regular blood elements show the ability to aggregation what mostly determines the initiation of hemostasis and thrombosis [7,8,9]. Given process is limited by the synthesis of disaggregants' substances in vascular wall and their emission out of it into blood. Prostacyclin and nitric oxide [10,11] are the most important of these substances. Taking into account wide prevalence of the combination of arterial hypertension with dislipidemia, studying the level of vascular control over aggregation of the most numerous regular blood elements' population – erythrocytes – in this group of patients is of great scientific and practical interest.

We put the following aim in our research - to determine peculiarities of vessels' disaggregative impacts on erythrocytes of patients with arterial hypertension and dislipidemia.

MATERIALS AND METHODS

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

We examined 380 patients of the second mature age (mean age 53.4 ± 1.9 years) with AH of the 1st-2nd degree, risk 4 [12] with dislipidemia of IIb type. The control group was composed of 26 clinically healthy people of the same age. All the examined persons gave written informed consent on participation in the research.

We determined the content of common cholesterol (CS) and triglycerides (TG) in blood of all the observed persons by enzymatic colorimetric method with the help of a kit "Vital Diagnostikum" (Russia). CS level of high-density lipoproteins (HDLP) was determined with the help of a kit "OlveksDiagnostikum (Russia) by enzymatic colorimetric method. Common lipids (CL) were estimated with the help of a kit "Erba Russ" (Russia). The quantity of common phospholipids (CPL) in blood plasma was registered according to the content of phosphorus in them. CS levels of low-density lipoproteins (LDLP) were established by calculation according to Freedwald V. CS concentrations of very low-density lipoproteins (VLDLP) was determined according to the formula: $TG \text{ content} / 2.2$. Received indices of common CS and CS of LDLP were considered as normal, borderline or high in accordance with Russian recommendations (2012) [13].

Intensity of lipids' peroxidation (LPO) processes in plasma was estimated according to the content of thiobarbituric acid (TBA)-active products by a kit "Agat-Med" and acylhydroperoxides (AHP) [14]. Antioxidant abilities of liquid part of blood were determined according to the level of its antioxidant activity (AOA) [15].

LPO activity in studied regular blood elements was determined according to the quantity of malondialdehyde (MDA) in reduction reaction of thiobarbituric acid in washed and resuspended cells and the content of AHP in them [14]. In studied washed and resuspended regular blood elements we estimated the levels of cholesterol by enzymatic colorimetric method with the help of a kit "Vital Diagnostikum" and CPL according to the content of phosphorus in them.

Evidence of vascular wall's control over erythrocytes' aggregation was detected according to its weakening in the test with temporal venous occlusion [16]. Spontaneous erythrocytes' aggregation before and after temporal ischemia of vascular wall was determined with the help of a light microscope in Gorjaev's box. We registered there the quantity of erythrocyte aggregates, number of aggregated and non-aggregated erythrocytes [17].

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

RESULTS AND DISCUSSION

The blood of patients was noted to have levels' increase of CL and common CS which surpassed the control values in 1.6 and 1.3 times, respectively, at simultaneous lowering of plasma CPL in 2.3 times (Table). The blood of persons with AH and dyslipidemia was found to have the increase of CS LDLP, CS VLDLP and TG in 1.72, 1.67 and 1.66 times, respectively. It is combined with the lowering of CS HDLP in 1.55 times. The patients were noted to have evident plasma LPO activation – the content of AHP in it surpassed the control value in 2.25 times, TBA-active products – in 1.45 times, being accompanied by suppression of antioxidant plasma activity in 1.38 times (Table).

Table: Registered indicators in the surveyed

Registered parameters	Patients with arterial hypertension and dyslipidemia, n=380, M±m	Control, n=26, M±m
common cholesterol, mmol /l	6.4±0.04	4.8±0.05 p<0.01
CS level of high-density lipoproteins , mmol /l	1.06±0.04	1.60±0.06 p<0.01
CS levels of low-density lipoproteins, mmol /l	4.04±0.06	2.43±0.04 p<0.01
CS concentrations of very low-density lipoproteins, mmol /l	1.03±0.05	0.77±0.05 p<0.01
triglycerides, mmol /l	2.86±0.05	1.70±0.02 p<0.01
common lipids, g/l	9.2±0.12	5.6±0.03 p<0.01
common phospholipids, mmol /l	1.53±0.05	3.54±0.09 p<0.01
acylhydroperoxidesplasma, D ₂₃₃ /1ml	3.23±0.08	1.42±0.09 p<0.01
TBA-compounds, mcmol / l	5.17±0.09	3.56±0.07 p<0,01
antioxidantactivityplasma, %	22.8±0.17	32.9±0.12 p<0.01
biochemical parameters of erythrocytes		
cholesterol of erythrocytes, mkmol/10 ¹² erythrocytes	1.33±0.006	1.04±0.004 p<0.01
common phospholipids of erythrocytes, mkmol/10 ¹² erythrocytes	0.55±0.005	0.75±0.003 p<0.01
acylhydroperoxides of erythrocytes, D ₂₃₃ /10 ¹² erythrocytes	4.53±0.13	3.08±0.10 p<0.01
malonicdialdehyde of erythrocytes, nmol/10 ¹² erythrocytes	1.66±0.12	1.14±0.05 p<0.01
catalase of erythrocytes, ME/10 ¹² erythrocytes	7490.2±12.4	11196.0±22.4 p<0.01
superoxidismutase of erythrocytes, ME/10 ¹² erythrocytes	1576.9±2.32	1986.0±7.01 p<0.01
aggregation of erythrocytes in intact plasma		
sum of all the erythrocytes in an aggregate	68.9±0.12	41.9±0.10 p<0.01

quantity of aggregates	13.1±0.15	9.0±0.06 p<0.01
quantity of free erythrocytes	152.5±1.83	240.0±0.23 p<0.01
aggregation of erythrocytes in plasma after temporary venous occlusion		
sum of all the erythrocytes in an aggregate	57.6±0.13	32.6±0.14 p<0.01
quantity of aggregates	10.6±0.10	7.0±0.07 p<0.01
quantity of free erythrocytes	182.0±1.21	305.3±0.18 p<0.01

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

The observed patients were noted to have increased CS content in erythrocytes' membranes which was accompanied by the decrease of CPL in them and LPO activation on behalf of weakening of their antioxidant protection (Table).

The blood of patients enrolled into the research was registered to have evident strengthening of spontaneous erythrocytes' aggregation (Table). It was pointed at by the increased level of their summary involvement into aggregates (by 64.9%), quantity increase of aggregates themselves (by 46.7%) and the decrease of freely moving red corpuscles (by 57.8%).

All the patients were noted to have the decrease of vessels' disaggregative impacts on erythrocytes (Table). It was found out that the patients' plasma received against the background of temporal venous occlusion was characterized by such summary quantity of erythrocytes in aggregates which surpassed the control value by 76.9%. These aggregates' number was increased by 51.4% being accompanied by quantity decrease of free erythrocytes by 67.9%.

Important significance in the development of rheological disturbances and thrombophilia in persons with AH and dislipidemia belongs to aggregation increase of regular blood elements and especially – erythrocytes [18,19]. At combination of AH and dislipidemia the depression of plasma antioxidant activity is formed which provides the increase of LPO activity in it [20]. The increase of freely radical processes in liquid part of blood inevitably promotes the damage of erythrocytes' membranes [21]. The development of these manifestations in combination with found in these patients' erythrocytes lipid imbalance leads to their hyperaggregability. The level of disaggregating impacts from the side of vascular wall [22,23] lowers simultaneously with it in respect of erythrocytes. It was detected in the examined patients according to strengthening of erythrocytes' aggregative activity which was registered in the test with temporal venous occlusion [24]. Evidently, strengthening of erythrocytes' spontaneous aggregation in vivo in patients with AH and dislipidemia is mostly caused by weakening of vessel wall's disaggregating impacts [25,26] and in less degree by appearing quantity lowering of negatively charged proteins on the outer erythrocyte membrane [27]. Weakening of plasma antioxidant activity leads to generation growth of oxygen active forms in it and to oxidative damage of endotheliocytes, proteins of erythrocyte membranes and plasma globular proteins [28,29]. In conditions of physiological disaggregants' deficiency there takes place strengthening of erythrocytes' binding between each other in already formed aggregates [30,31]. Besides, production weakening of prostacyclin and nitric oxide in vessels leads to imbalance of adenylatecyclase and phosphodiesterase activity [32,33] in erythrocytes. It leads to quantity lowering of cyclic adenosine monophosphate in their cytoplasm and to Ca²⁺ increase what additionally strengthens erythrocytes' aggregation [34,35].

CONCLUSION

High thromboses' frequency of various localizations at arterial hypertension with dislipidemia is closely connected with angiopathy development against their background. Weakening of plasma antioxidant protection with activation of LPO processes in it leading to alteration of vascular wall, is noted in conditions of AH combination with dislipidemia. The persons with AH and dislipidemia are detected to have evident weakening of disaggregating vascular impacts of vascular wall on strengthening aggregative ability of

erythrocytes. In the result of it given patients get sharply increased risk of thromboses of any localization which can lead to invalidism and lethal outcome.

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