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Disaggregative Impacts of Vascular Wall on Platelets of Patients with Arterial Hypertension and Dyslipidemia.

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ABSTRACT

Last years, notwithstanding the significant efforts of medical community, wide prevalence of arterial hypertension very often combined with dislipidemia is still kept among population of industrially developed countries. At the heart of the high frequency of thrombosis of various localizations in this contingent of patients is often the development of vasopathy, the severity of which in recent years has a tendency to increase. Purpose of the study: to determine peculiarities of vascular walls' dis aggregative capacities in respect of platelets in patients with arterial hypertension and dislipidemia. We examined 380 patients of the second mature age (mean age 53.4±1.9 years) with arterial hypertension of the 1st-2nd degree, risk 4 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. There were applied biochemical, hematological and statistical methods of investigation. 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 lipids' peroxidation processes in it leading to alteration of vascular wall, is noted in conditions of arterial hypertension combination with dislipidemia. The persons with arterial hypertension and dislipidemia are detected to have evident weakening of disaggregating vascular impacts of vascular wall on strengthening aggregative ability of platelets. In the result of it given patients get sharply increased risk of thromboses of any localization which can lead to invalidism and lethal outcome.

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

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INTRODUCTION

Last years, notwithstanding the significant efforts of medical community, wide prevalence of arterial hypertension (AH) very often combined with dislipidemia [1,2] is still kept among population of industrially developed countries. This circumstance provides preservation of high frequency of various vascular thromboses' development in able-bodied citizens. These disorders lead to invalidism and mortality [3]. The development of angiopathy (its evidence has a trend to strengthening [4] last years) very often lies in the basis of thromboses' high frequency with various localizations in the given group of patients. The consequence of angiopathy is weakening of vascular control over regular blood elements' aggregation what mostly determines the initiation of hemostasis processes and development of thrombosis [5,6,7]. Synthesis weakening of substances-disaggregants in vascular wall lies in the basis of the given process. Prostacyclin and nitric oxide [8,9] are the most important of these substances. Taking into account wide prevalence of AH with dislipidemia, studying the level of vascular control over the process of platelets' aggregation in the given group of patients [10] is of great scientific and practical interest. We put the following aim in our study: to determine peculiarities of vascular walls' disaggregative capacities in respect of platelets in patients with AH and dislipidemia.

MATERIALS AND METHODS

The research was approved by the Ethics Committee of Kursk Institute of Social Education (branch of 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 1^{st}-2^{nd} degree, risk 4 [11] 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 content/2.2. Received indices of common CS and CS of LDLP were considered as normal, border-line or high in accordance with Russian recommendations (2012) [12].

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) [13]. Antioxidant abilities of liquid part of blood were determined according to the level of its antioxidant activity (AOA) [14].

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 [13]. 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 platelets' aggregation was detected according to its weakening in the test with temporal venous occlusion [15].

Aggregation of platelets (AP) was registered by visual micromethod [16] before and after venous occlusion with the application of ADP (0.5×10^{-4} M, collagen (dilution 1:2 of the basic suspension), thrombin (0.125 un/ml), ristomicin (0.8 mg/ml), adrenaline (5.0×10^{-6} M) and with combinations of ADP and adrenaline; ADP ande collagen; adrenaline and collagen in the same concentrations in rich in platelets plasma with standardized quantity of platelets 200×10^{9} pl. The index of antiaggregatory activity of vascular wall (IAAVW) was calculated by dividing the time of AP development after venous occlusion on the time without it. Diaaggregative capabilities of vascular wall in respect of intravascular aggregate-formation of platelets were determined with the usage of phase-contrast microscope according to the number of little, medium and large

aggregates and to the involvement of platelets into them before and after temporary venous occlusion [17,18].

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 dislipidemia 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

Registrated 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
acylhydroperoxides plasma, 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 platelets		
cholesterol of platelets, mkmol/10^9platelets	1,03±0,005	0,67±0,005 p<0,01
common phospholipids of platelets, mkmol/10^9platelets	0,33±0,004	0,49±0,004 p<0,01
acylhydroperoxides of platelets, D_{233}/10^9platelets	3,25±0,05	2,20±0,04 p<0,01
malonicdialdehyde of platelets, nmol/10^9platelets	1,32±0,06	0,68±0,02 p<0,01
catalase of platelets, ME/10^9platelets	5069,0±16,93	9790,0±20,10 p<0,01
superoxidismutase of platelets, ME/10^9platelets	1101,9±7,29	1650,0±3,00 p<0,01
aggregation of platelets in intact plasma		

aggregation with ADP, s	24,1±0,09	41,0±0,12 p<0,01
aggregation with collagen, s	22,0±0,12	33,2±0,10 p<0,01
aggregation with thrombin, s	35,0±0,14	55,3±0,05 p<0,01
aggregation with ristomycin, s	27,0±0,12	45,2±0,06 p<0,01
aggregation with epinephrine, s	70,7±0,13	93,0±0,07 p<0,01
aggregation with ADP and epinephrine, s	19,5±0,15	34,5±0,04 p<0,01
aggregation with ADPand collagen, s	17,9±0,15	26,6±0,05 p<0,01
aggregation with epinephrine and collagen, s	13,0±0,10	29,2±0,12 p<0,01
The number of platelets in the aggregates, %	11,1±0,10	6,5±0,07 p<0,01
Number of little aggregates (in 100 free thrombocytes)	12,5±0,12	3,1±0,03 p<0,01
Number of medium and large aggregates (in 100 free thrombocytes)	1,47±0,10	0,14±0,03 p<0,01
cardiovascular control of platelet aggregation		
IAAVWwithADP	1,23±0,12	1,53±0,16 p<0,01
IAAVWwith collagen	1,16±0,13	1,48±0,16 p<0,01
IAAVWwith thrombin, s	1,17±0,12	1,44±0,13 p<0,01
IAAVWwith ristomycin, s	1,24±0,12	1,56±0,11 p<0,01
IAAVWwithepinephrine	1,34±0,10	1,62±0,13 p<0,01
IAAVWwithADPandepinephrine	1,25±0,13	1,49±0,12 p<0,01
IAAVWwithADPandcollagen	1,24±0,13	1,51±0,10 p<0,01
IAAVWwithepinephrineandcollagen	1,16±0,12	1,53±0,11 p<0,01
The number of platelets in the aggregatesafter temporary venous occlusion, %	10,4±0,09	4,5±0,15 p<0,01
Number of little aggregates (in 100 free thrombocytes) after temporary venous occlusion	7,1±0,12	2,1±0,15 p<0,01
Number of medium and large aggregates (in 100 free thrombocytes)after temporary venous occlusion	0,18±0,005	0,02±0,005 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 persons with AH and dislipidemia were found to have evident time reduction of AP development with separate inductors and their combinations (Table). AP developed most headlong under the impact of

collagen, a bit slower – with ADP, still slower with ristomicin, thrombin and adrenaline. The process of AP with combinations of inductors was also accelerated. At the same time, the number of platelet aggregates of different sizes freely circulating in patients' blood and the involvement degree of platelets into them in persons with AH and dislipidemia surpassed the control values.

All the patients were noted to have the decrease of vessels' disaggregative impacts on platelets (Table).

The persons with AH and dislipidemia were noted to have lowering of IAAVW with separate agonists (for adrenaline – 1.33±0.14, for ADP – 1.25±0.14, for ristomicin – 1.23±0.10, for collagen and thrombin – 1.15±0.08 and 1.14±0.13, respectively) and with their combinations (for ADP and adrenaline – 1.21±0.15, for ADP and collagen – 1.22±0.16, for adrenaline and collagen – 1.16±0.14). It was accompanied by content increase of platelet aggregates' quantity of different sizes in patients' blood against the background of temporary venous occlusion and surplus involvement of platelets into them.

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 – platelets [19,20]. At combination of AH and dislipidemia the depression of plasma antioxidant activity is formed which provides the increase of LPO activity in it [21,22]. The increase of freely radical processes in liquid part of blood inevitably promotes the damage of platelets' membranes. The development of these manifestations in combination with found in these patients' platelets lipid imbalance leads to their hyperaggregability. The level of disaggregating impacts from the side of vascular wall [23,24] lowers simultaneously with it in respect of platelets.

Lowering of IAAVW with separate inductors and their combinations has simultaneous AP strengthening and weakening of vascular wall's disaggregative impact on them [25,26] in its basis. Most probably, dislipidemia and activation of plasma LPO [27,28] lie in the basis of this situation. AP acceleration in response to ristomicin in patients was conditioned by strengthening of von Willebrand's Factor production [29,30] in vessels' endothelium. Short AP duration with inductors' combinations and numerous platelets' aggregates in blood of patients before and after venous occlusion pointed at evident weakening of vessels' disaggregative impacts on patients' platelets in conditions near to reality [31,32].

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 platelets. 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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