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Vascular Disaggregative Control Over Neutrophils In Patients With Arterial Hypertension And Dyslipidemia.

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ABSTRACT

Intensification of modern life is accompanied by preservation of wide prevalence of arterial hypertension and dislipidemia among population of industrially developed countries. Modern researches connect frequent occurrence of thromboses of various localizations at arterial hypertension and dislipidemia with the disturbance of vessels' functions, especially in respect of their control over regular elements. Purpose of the study: to determine peculiarities of vessels' disaggregative capabilities in respect of neutrophils 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 neutrophils. 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: neutrophils, arterial hypertension, dislipidemia, vascular wall, antiaggregation.

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INTRODUCTION

Intensification of modern life is accompanied by preservation of wide prevalence of arterial hypertension (AH) and dislipidemia [1,2] among population of industrially developed countries. Their frequent combination provides high rate of vascular complications' development in significant part of able-bodied population. These complications cause invalidism and high mortality [3]. Modern researches connect frequent occurrence of thromboses of various localizations at AH and dislipidemia with the disturbance of vessels' functions, especially in respect of their control over regular elements [4,5]. It is known that hyperaggregation of regular blood elements takes place in conditions of vascular dysfunctions leading to the initiation of hemostasis and thrombosis [6,7,8]. Given process is mostly caused by synthesis' complication of substances-disaggregants in vascular wall. Prostacyclin and nitric oxide [9,10] are two of them which are the most important ones from physiological point of view. Taking into account wide prevalence of AH with dislipidemia and great signification of neutrophils for microcirculation, studying the level of vascular control over aggregation of neutrophil leucocytes in the given group of patients [11] is really interesting from scientific and practical points of view.

The following aim was put in the research: to determine peculiarities of vessels' disaggregative capabilities in respect of neutrophils 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 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 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) [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 neutrophils' aggregation was detected according to its weakening in the test with temporal venous occlusion [16].

The state of vascular wall's control over neutrophils' aggregation was estimated in plasma which was received after temporary venous occlusion and without it with the help of photoelectron-colorimeter. As inductors there was used wheat germ lectin in the dose of 32 mkg/ml, concanavalin A – 32 mkg/ml and phytohemagglutinin – 32 mkg/ml. The inhibition index of neutrophils' aggregation by vascular wall (IINAVW) was calculated in all the patients by dividing the degree of neutrophils' aggregation in plasma received without a cuff on its degree in plasma received with application of a cuff.

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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

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
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
Antioxidant activity plasma, %	22.8±0.17	32.9±0.12 p<0.01
biochemical parameters ofneutrophils		
cholesterol of neutrophils, mkmol/10^9neutrophils	0.83±0.006	0.62±0.004 p<0.01
common phospholipids of neutrophils, mkmol/10^9neutrophils	0.36±0.004	0.51±0.003 p<0.01
acylhydroperoxides of neutrophils, D_{233}/10^9neutrophils	3.51±0.06	2.36±0.05 p<0.01
malonicdialdehyde of neutrophils, nmol/10^9neutrophils	1.44±0.05	0.73±0.03 p<0.01
catalase of neutrophils, ME/10^9neutrophils	5243.4±20.01	9950.0±19.77 p<0.01
superoxidismutase of neutrophils, ME/10^9neutrophils	1238.3±4.88	1780.0±4.21 p<0.01
aggregation of neutrophilsin intact plasma		

Aggregation with lectin, %	24.5±0.08	15.6±0.07 p<0.01
Aggregation with **concanavalin A**, %	19.6±0.10	14.8±0.04 p<0.01
Aggregation with phyto hemagglutinin, %	42.±0.05	30.6±0.09 p<0.01
vascular control of aggregation neutrophils		
Aggregation with lectin after temporary venous occlusion, %	21.6±0.11	11.8±0.06 p<0.01
Aggregation with **concanavalin A**after temporary venous occlusion, %	17.2±0.06	11.0±0.07 p<0.01
Aggregation with phyto hemagglutinin after temporary venous occlusion, %	39.2±0.09	24.1±0.03 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).

Neutrophils' aggregation with all the applied inductors developed in the observed patients earlier than in the control group (with lectin – by 57.7%, with concanavalin A – by 32.4%, with phytohemagglutinin – by 38.6%) (Table).

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

In the test with temporary venous occlusion the patients were noted to have evident redundancy of neutrophils' aggregation exceeding the control values with all the applied inductors (with lectin – by 82.2%, with concanavalin A – by 57.3%, with phytohemagglutinin – by 61.8%). It conditioned depression of IINAVW for lectin – by 18.9%, for concanavalin A – by 19.6%, for phytohemagglutinin – by 14.4%.

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 – neutrophils [17,18]. At combination of AH and dislipidemia the depression of plasma antioxidant activity is formed which provides the increase of LPO activity in it [19]. The increase of freely radical processes in liquid part of blood inevitably promotes the damage of neutrophils' membranes [20]. The development of these manifestations in combination with found in these patients' neutrophils lipid imbalance leads to their hyperaggregability. The level of disaggregating impacts from the side of vascular wall [21,22] lowers simultaneously with it in respect of neutrophils [23].

Detected increase of neutrophils' aggregation in the examined patients is, evidently, mostly connected with production decline of substances-disaggregants in vascular wall against the background of negative changes of leucocytes' glycoprotein receptors to lectins used as inductors in the research [24,25]. Strengthening of lectin- and concanavalin A-induced neutrophils' aggregation in patients with AH and dislipidemia against the background of temporary venous occlusion was caused by the expression increase of adhesion on the membrane of neutrophil receptors with the increase of sites in their composition which contained N-acetyl-D- glucosamine, N-acetyl-neuraminic acid and mannose [26,27]. Redundancy of neutrophils' aggregation induced by phytohemagglutinin, the authors are inclined to connect with the increase of glycoproteins' sites in their receptors which contain bD-galactose [28,29] at level lowering of prostacyclin and NO [30,31,32] in blood of patients.

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 neutrophils. 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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