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Intensity Control Disaggregation Of Platelets Vessels In Hypertensive Patients With Type 2 Diabetes Mellitus.

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ABSTRACT

The prevalence of the combination of arterial hypertension and type 2 diabetes mellitus is still preserved in society. It becomes clear that the great danger of these diseases is due to the development of frequent thromboses against them in the development of vasopathy, the nature of which has not been adequately studied. The goal is to assess the level of disaggregation capacity of blood vessels in relation to platelets in arterial hypertension and type 2 diabetes mellitus. We examined 42 patients of the second mature age (mean age 49.3±2.9 years) with arterial hypertension of the 1st-2nd degree, risk 4 with type 2 diabetes mellitus. 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 type 2 diabetes mellitus 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 type 2 diabetes mellitus. The persons with arterial hypertension and type 2 diabetes mellitus 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, type 2 diabetes mellitus, vascular wall, antiaggregation.

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INTRODUCTION

In many developed countries, despite the efforts of medical science and practice, there is still a high incidence of a combination of arterial hypertension (AH) with type 2 diabetes mellitus [1,2]. It is noted that this contingent of patients is very threatened by the development of vascular thrombosis, often leading to disability and death [3]. Previous studies have shown that very often the cause of thrombosis in different patients is vasopathy, whose occurrence in patients also increases [4]. It is known that vasopathy is manifested by weakening of vascular control over the degree of aggregation of blood elements and activation of hemostasis mechanisms, which causes the development of thromboses [5,6,7]. One of the manifestations of vasopathy is the depression of the synthesis of vascular deaggregants, the most active of which are prostacyclin and nitric oxide [8,9]. Given the high incidence of hypertension with diabetes mellitus type 2, it seemed important for science and practice to assess the level of vascular control of platelet aggregation in such patients [10].

The goal is to assess the level of disaggregation capacity of blood vessels in relation to platelets in hypertension with diabetes mellitus type 2.

MATERIALS AND METHODS

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

We examined 42 patients of the second mature age (mean age 49.3±2.9 years) with AH of the 1^{st}-2^{nd} degree [11] with type 2 diabetes mellitus. 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. All those surveyed agreed to participate in the study [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 [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].

The severity of platelet aggregation (AT) was assessed using a visual micro-method [16] in plasma obtained after temporary venous occlusion and without it using ADP ($0.5x10^{-4}$ M), collagen (1: 2 dilution of the base suspension), thrombin (0.125 units / ml), ristomycin (0.8 mg / ml), adrenaline ($5.0×10^{-6}$ M) and with combinations of ADP and epinephrine; ADP and collagen; adrenaline and collagen in the same doses in a platelet-rich plasma standardized for platelet count to $200×10^9$ platelets. The magnitude of the vascular wall antiggregational activity index (IAASC) was calculated in the course of dividing the time of onset of AT in plasma taken against the background of venous occlusion for the duration of development of AT in the intact plasma. The level of disaggregation effects of blood vessels on the processes of intravascular aggregation of platelets was determined using a phase contrast microscope and considering the number of small, medium and large aggregates and the degree of involvement of platelets in plasma taken without the use of temporary venous occlusion and in plasma obtained against its background [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 $p<0.05$.

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RESULTS AND DISCUSSION

The patients were noted to have evident plasma LPO activation – the content of AHP in it surpassed the control value in 2.35 times, TBA-active products – in 1.54 times, being accompanied by suppression of antioxidant plasma activity in 1.5 times (Table).

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).

In persons with AH with type 2 diabetes mellitus, acceleration of occurrence of AT with all inducers and their combinations was found (Table). The earliest time the AT developed with collagen, a little later with ADP, even later with ristomycin, thrombin and adrenaline. The onset of AT with the tested combinations of inductors was greatly accelerated. The value of free-flowing patients with platelet aggregates and the degree of involvement of platelets in hypertension with diabetes mellitus type 2 exceeded control figures.

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

Table: Registered indicators in the surveyed

Registered parameters	Patients, n=42, M±m	Control, n=26, M±m
acylhydroperoxides plasma, D_{233} /1ml	3.34±0.09	1.42±0.09 p<0.01
TBA-compounds, mcmol/l	5.47±0.16	3.56±0.07 p<0,01
antioxidantactivityplasma, %	21.3±0.18	32.9±0.12 p<0.01
biochemical parameters of platelets		
cholesterol of platelets, mkmol/10^9 platelets	1.11±0.005	0.67±0.005 p<0.01
common phospholipids of platelets, mkmol/10^9 platelets	0.32±0.011	0.49±0.004 p<0.01
acylhydroperoxides of platelets, D_{233}/10^9 platelets	3.48±0.09	2.20±0.04 p<0.01
malonicdialdehyde of platelets, nmol/10^9 platelets	1.48±0.10	0.68±0.02 p<0.01
catalase of platelets, ME/10^9 platelets	4910.0±24.95	9790.0±20.10 p<0.01
superoxidismutase of platelets, ME/10^9 platelets	1110.0±9.26	1650.0±3.00 p<0.01
aggregation of platelets in intact plasma		
aggregation with ADP, s	23.2±0.16	41.0±0.12 p<0,01
aggregation with collagen, s	21.4±0.17	33.2±0.10 p<0.01
aggregation with thrombin, s	35.0±0.15	55.3±0.05 p<0.01
aggregation with ristomycin, s	27.0±0.14	45.2±0.06 p<0.01
aggregation with epinephrine, s	70.1±0.12	93.0±0.07 p<0.01
aggregation with ADP and epinephrine, s	19.0±0.17	34.5±0.04 p<0.01

aggregation with ADP and collagen, s	15.2±0.16	26.6±0.05 p<0.01
aggregation with epinephrine and collagen, s	12.3±0.22	29.2±0.12 p<0.01
The number of platelets in the aggregates, %	15.0±0.19	6.5±0.07 p<0.01
Number of little aggregates (in 100 free thrombocytes)	18.2±0.21	3.1±0.03 p<0.01
Number of medium and large aggregates (in 100 free thrombocytes)	1.64±0.07	0.14±0.03 p<0.01
cardiovascular control of platelet aggregation		
IAAVWwith ADP	1.21±0.12	1.53±0.16 p<0.01
IAAVWwith collagen	1.16±0.24	1.48±0.16 p<0.01
IAAVWwith thrombin, s	1.17±0.19	1.44±0.13 p<0.01
IAAVWwith ristomycin, s	1.23±0.13	1.56±0.11 p<0.01
IAAVWwith epinephrine	1.30±0.16	1.62±0.13 p<0.01
IAAVWwith ADP and epinephrine	1.25±0.15	1.49±0.12 p<0.01
IAAVWwith ADP and collagen	1.23±0.24	1.51±0.10 p<0.01
IAAVWwithepinephrine and collagen	1.16±0.17	1.53±0.11 p<0.01
The number of platelets in the aggregatesafter temporary venous occlusion, %	10.6±0.11	4.5±0.15 p<0.01
Number of little aggregates (in 100 free thrombocytes)after temporary venous occlusion	7.5±0.14	2.1±0.15 p<0.01
Number of medium and large aggregates (in 100 freethrombocytes)after temporary venous occlusion	0.25±0.012	0.02±0.005 p<0.01

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

Patients with AH and type 2 diabetes showed a decrease in IAAWW with all tested inducers (for adrenaline 1.30±0.16, for ADP 1.21±0.12, for ristomycin 1.23±0.13, for collagen and thrombin 1.16±0.24 and 1.17±0.19, respectively) and with all their combinations (for ADP and adrenaline 1.25± 0.15, for ADP and collagen – 1.23±0.24, for adrenaline and collagen – 1.16±0.17). At the same time, in a plasma obtained against a background of temporary venous occlusion, the number of platelet aggregates in the blood of patients and the excessive involvement of platelets in them decreased little.

Important significance in the development of rheological disturbances and thrombophilia in persons with AH and type 2 diabetes mellitus belongs to aggregation increase of regular blood elements and especially – platelets [19,20]. At combination of AH and type 2 diabetes mellitus 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.

The decrease in the IAAVW values with inducers and their combinations is caused by the growth of AT and depression of the disaggregation capacity of the vessels [25,26]. An important reason for this is the activation of LPO in plasma [27,28]. The early onset of AT in response to ristomycin in patients is associated with increased vWF generation in the vessels [29,30]. The accelerated onset of AT in response to two inducers and an excessive number of platelet aggregates in the blood of patients before and after temporary venous occlusion should be considered a manifestation of increasing depression of the disaggregation capacity of the vessels [31, 32].

CONCLUSION

Mechanisms of vascular hemostasis are very important for the optimal functioning of the body. A serious manifestation of dysfunctions is the depression of desagregation manifestations of blood vessels in relation to platelets. This can be noted especially often in patients with cardiac pathology, including arterial hypertension. Recently, it is often combined with type 2 diabetes mellitus, which is accompanied by a high incidence of thrombosis in this contingent of patients. The study found that in arterial hypertension with type 2 diabetes mellitus, there is often a strong depression of the vascular disaggregation function with respect to platelets. These disorders were a serious cause of activation of hemostasis mechanisms in patients with arterial hypertension and type 2 diabetes and the development of fatal thromboses in them.

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