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Aggregational Capacity Of Platelets In Patients With Dyslipidemia With Impaired Glucose Tolerance.

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ABSTRACT

In a large number of works, there is still an increase in the number of patients suffering from a combination of dyslipidemia and impaired glucose tolerance. For these patients, there is a high frequency of vascular thrombosis, which is caused by hyperaggregation of blood cells. All aspects of this process have so far not been adequately investigated. The goal is to find out the aggregation capacity of platelets in patients with dyslipidemia with impaired glucose tolerance. In the work, 45 patients of the second adult age (mean age 47.6 ± 1.5 years) with dyslipidemia and impaired glucose tolerance were examined. The control group consisted of 26 clinically healthy people of the same age. When taking under observation, all the examinees gave written informed consent to participate in the study. Biochemical, hematological and statistical methods of investigation were used. There are reasons to believe that a high incidence of thrombosis of various localizations with dyslipidemia and violation of carbohydrate metabolism is closely related to the development of platelet hyperaggregation. A serious cause of this disorder may be a weakening of the antioxidant defense of blood plasma with the activation in it of processes of lipid peroxidation leading to an increase in platelet activity. People with dyslipidemia and impaired glucose tolerance also showed a pronounced weakening of platelet capacity for disaggregation. As a result of his patients, the risk of thrombosis of any localization increases sharply, which can lead to disability and death.

Keywords: platelets, dyslipidemia, impaired glucose tolerance, thrombophilia, aggregation.

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INTRODUCTION

Until now, in many countries there is a high prevalence of dyslipidemia, which is increasingly combined with a violation of glucose tolerance [1,2]. This combination is always accompanied by a very high risk of developing vascular thrombosis in such patients, often leading to disability and mortality [3]. It is recognized that the basis for the mechanisms of thrombosis of any localization often lies the onset of hyperaggregation of blood cells [4]. In this case, it always comes when the sensitivity of blood cells to vascular disaggregants decreases. This situation strongly stimulates the mechanisms of hemostasis, thereby leading to thrombosis [5,6,7]. In this regard, hyperaggregation of blood cells is caused by a weakening of the sensitivity of blood cells to disaggregant substances, the most important of which are prostacyclin and nitric oxide [8,9]. In view of the wide prevalence of the combination of dyslipidemia with impaired glucose tolerance, it was especially important to evaluate the state of platelet aggregation in these patients [10].

The goal is to clarify the aggregation capacity of platelets in patients with dyslipidemia and impaired glucose tolerance.

MATERIAL AND METHODS

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

We examined 45 patients of the second mature age (mean age 47.6 ± 1.5 years) with dyslipidemia with impaired glucose tolerance [11]. 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 malon dialdehyde (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 total phospholipids 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 level of platelet aggregation (AP) was assessed by visual micromethod [16] in plasma obtained without and using venous occlusion using ADP (0.5×10^{-4} M), collagen (1:2 dilution of the base suspension), thrombin (0.125 U/ml), ristomycin (0.8 mg/ml), epinephrine (5.0×10^{-6} M) and with combinations of ADP and epinephrine; ADP and collagen; epinephrine and collagen at the same concentrations in the platelet-rich plasma as standardized for the platelet count of 200×10^9 platelets. The value of the index of antiaggregatory activity of the vascular wall was calculated during the division of the time of development of AP in the plasma after venous occlusion during the time of this process in intact plasma. The severity of disaggregation capacity of blood vessels with respect to intravascular aggregation of platelets was determined using a phase contrast microscope by recording the number of small, medium and large aggregates and the degree of platelet involvement in them in plasma obtained without temporal 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 $p < 0.05$.

RESEARCH RESULTS AND DISCUSSION

The patients were noted to have evident plasma LPO activation – the content of AHP in it surpassed the control value in 2.1 times, TBA-active products – in 1.4 times, being accompanied by suppression of antioxidant plasma activity in 1.33 times (Table).

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

Table. Registered indicators in the surveyed

Registered parameters	Patients, n=45, M±m	Control, n=26, M±m
acylhydroperoxides plasma, D ₂₃₃ /1ml	3.02±0.09	1.42±0.09 p<0.01
TBA-compounds, µmol/l	4.99±0.16	3.56±0.07 p<0,01
antioxidant activity plasma, %	24.8±0.22	32.9±0.12 p<0.01
biochemical parameters of platelets		
cholesterol of platelets, µmol/10 ⁹ platelets	1.09±0.014	0.67±0.005 p<0.01
common phospholipids of platelets, µmol/10 ⁹ platelets	0.34±0.008	0.49±0.004 p<0.01
acylhydroperoxides of platelets, D ₂₃₃ /10 ⁹ platelets	3.51±0.05	2.20±0.04 p<0.01
malonic dialdehyde of platelets, nmol/10 ⁹ platelets	1.39±0.13	0.68±0.02 p<0.01
catalase of platelets, ME/10 ⁹ platelets	5200.0±26.11	9790.0±20.10 p<0.01
superoxidismutase of platelets, ME/10 ⁹ platelets	1100.0±8.36	1650.0±3.00 p<0.01
aggregation of platelets		
aggregation with ADP, s	25.7±0.14	41.0±0.12 p<0.01
aggregation with collagen, s	23.4±0.12	33.2±0.10 p<0.01
aggregation with thrombin, s	36.2±0.13	55.3±0.05 p<0.01
aggregation with ristomycin, s	27.4±0.05	45.2±0.06 p<0.01
aggregation with epinephrine, s	71.5±0.12	93.0±0.07 p<0.01
aggregation with ADP and epinephrine, s	20.3±0.16	34.5±0.04 p<0.01
aggregation with ADP and collagen, s	16.5±0.07	26.6±0.05 p<0.01
aggregation with epinephrine and collagen, s	13.0±0.12	29.2±0.12 p<0.01
The number of platelets in the aggregates, %	13.1±0.15	6.5±0.07 p<0.01
Number of little aggregates (in 100 free thrombocytes)	17.4±0.18	3.1±0.03 p<0.01

Number of medium and large aggregates (in 100 free thrombocytes)	1.54±0.09	0.14±0.03 p<0.01
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Note: p - reliability of differences in the indices of a group of patients and a control group.

In the patients with dyslipidemia and impaired glucose tolerance, the development of AP with inductors and their combinations was revealed (Table). The earliest time AP came with collagen, a little later with ADP, even later with ristomycin, thrombin and adrenaline. The development of AP with combinations of inductors was further accelerated. The number of platelet aggregates and the level of platelet involvement in patients with dyslipidemia and impaired glucose tolerance exceeded the control figures.

Important significance in the development of rheological disturbances and thrombophilia in persons with dyslipidemia and impaired glucose tolerance belongs to aggregation increase of regular blood elements and especially – platelets [19,20]. At combination of dyslipidemia and impaired glucose tolerance 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. At the same time, the level of their disaggregation is reduced in platelets [23,24].

The acceleration of AP with individual inducers and their combinations is caused not only by the strengthening of AT mechanisms, but also by the weakening of disaggregation mechanisms [25,26]. Apparently, an important role in this is the activation of LPO in plasma [27,28]. Acceleration of the process of AP with ristomycin in patients is associated with increased synthesis in the walls of vessels of von Willebrand factor and an increase in the sensitivity of platelets to it [29,30]. The rapid onset in patients with AP in response to combinations of two inducers and the presence of a large number of platelet aggregates in their blood is a consequence of severe depression of disaggregation mechanisms in platelets [31, 32].

CONCLUSION

The state of aggregation properties of blood cells is extremely important for maintaining homeostasis in the body. A dangerous manifestation of its disorders is considered to be an increase in the aggregation capacity of platelets. These disorders are very common in any metabolic pathology, including dyslipidemia and impaired glucose tolerance. This dictates the need to clarify the aggregation capacity of platelets in this contingent of patients. It was found that with dyslipidemia with a violation of glucose tolerance, there is a marked increase in platelet aggregation. These disorders in this contingent of patients are a serious cause of activation of hemostasis in them and development of a risk of thrombosis of any localization [33,34,35].

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