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Severity Of Aggregation By Neutrophils In Patients With Impaired Glucose Tolerance And Abdominal Obesity.

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ABSTRACT

In adulthood, a combination of abdominal obesity and impaired glucose tolerance is increasingly occurring around the world. With this combination, thromboses of vessels of different severity become very frequent. Their development is associated with the emergence of hyperaggregation of the main blood cells. The goal is to clarify the aggregation activity of neutrophils in patients with abdominal obesity with impaired glucose tolerance. In the study, 39 patients of the second adulthood (mean age 50.1 ± 1.8 years) were examined with impaired glucose tolerance and abdominal obesity. The control group consisted of 26 clinically healthy people of the same age. All informed persons received written informed consent to participate in the study. Biochemical, hematological and statistical methods of investigation were used. It became clear that a high incidence of thrombosis of various localizations in abdominal obesity with impaired glucose tolerance is closely related to the development of neutrophil hyperaggregation against their background. This disorder occurs as a result of the weakening of the antioxidant defense of blood plasma, which leads to the activation of lipid peroxidation processes in it. In people with hypertension and impaired glucose tolerance, the evolving situation is aggravated by a marked weakening of the ability to disaggregate in neutrophils. As a result of his patients, the risk of thrombosis of any localization increases sharply, which can lead to disability and death.

Keywords: neutrophils, abdominal obesity, impaired glucose tolerance, thrombophilia, aggregation.

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INTRODUCTION

Achievements achieved by modern medicine can not yet contain the increase in prevalence among the adult population of a combination of abdominal obesity and impaired glucose tolerance [1,2]. Very often, their combination contributes to the occurrence of vascular complications leading to disability and early mortality [3]. It was noted that a high incidence of thrombosis among people with abdominal obesity and impaired glucose tolerance is associated with an increase in aggregation of blood elements [4,5]. It is recognized that the increase in the aggregation of blood cells occurs necessarily with metabolic disturbances, accompanied by activation of hemostasis and the emergence of thrombophilia [6,7,8]. This is largely due to a decrease in the sensitivity of blood cells to disaggregants, including prostacyclin and nitric oxide [9,10]. In view of the high prevalence of abdominal obesity with impaired glucose tolerance and serious significance for microcirculation of neutrophil aggregation, it was important to assess the level of aggregation of neutrophilic leukocytes in these patients [11].

The aim of the study is to clarify the aggregation activity of neutrophils in patients with abdominal obesity 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 39 patients of the second mature age (mean age 50.1 ± 1.8 years) with impaired glucose tolerance and abdominal obesity. 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 participants in the study gave their written consent to participate in it [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 [15].

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 [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 total phospholipids according to the content of phosphorus in them.

Aggregation of neutrophils was assessed on a photoelectrocolorimeter [16]. Inductors were the lectin of wheat germ at a concentration of 32 $\mu\text{g/ml}$, concanavalin A - 32 $\mu\text{g/ml}$ and phytohemagglutinin - 32 $\mu\text{g/ml}$.

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 2.2 times, TBA-active products – in 1.4 times, being accompanied by suppression of antioxidant plasma activity in 1.32 times (Table).

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

In the examined patients it was revealed that neutrophil aggregation in response to applied inductors appeared earlier than in control (with lectin 35.2%, concanavalin A 27.7%, phytohemagglutinin 30.1%) (Table).

Important significance in the development of rheological disturbances and thrombophilia in persons with abdominal obesity and impaired glucose tolerance belongs to aggregation increase of regular blood elements and especially – neutrophils [17,18]. At combination of abdominal obesity and impaired glucose tolerance 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. At the same time, platelets reduced the ability to disaggregate [21,22,23].

Table. Registered indicators in the surveyed

| Registered parameters | Patients, n=39, M±m | Control, n=26, M±m |
|---|------------------------|------------------------|
| acylhydroperoxides plasma, D ₂₃₃ /1ml | 3.10±0.06 | 1.42±0.09 p<0.01 |
| TBA-compounds, µmol/l | 5.08±0.12 | 3.56±0.07 p<0,01 |
| antioxidant activity plasma, % | 24.8±0.17 | 32.9±0.12 p<0.01 |
| biochemical parameters of neutrophils | | |
| cholesterol of neutrophils, µmol/10 ⁹ neutrophils | 0.81±0.012 | 0.62±0.004 p<0.01 |
| common phospholipids of neutrophils, µmol/10 ⁹ neutrophils | 0.37±0.007 | 0.51±0.003 p<0.01 |
| acylhydroperoxides of neutrophils, D ₂₃₃ /10 ⁹ neutrophils | 3.47±0.05 | 2.36±0.05 p<0.01 |
| malonic dialdehyde of neutrophils, nmol/10 ⁹ neutrophils | 1.38±0.06 | 0.73±0.03 p<0.01 |
| catalase of neutrophils, ME/10 ⁹ neutrophils | 5550.0±9.25 | 9950.0±19.77 p<0.01 |
| superoxidismutase of neutrophils, ME/10 ⁹ neutrophils | 1250.0±3.86 | 1780.0±4.21 p<0.01 |
| aggregation of neutrophils | | |
| Aggregation with lectin, % | 21.1±0.17 | 15.6±0.07 p<0.01 |
| Aggregation with concanavalin A, % | 18.9±0.14 | 14.8±0.04 p<0.01 |
| Aggregation with phytohemagglutinin, % | 39.8±0.05 | 30.6±0.09 p<0.01 |

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

The increase in neutrophil aggregation found in the examined patients is largely due to the depression of their sensitivity to vascular deaggregants. In addition, an increasing role in this was played by an increase in the number of glycoprotein receptors on the surface of leukocytes to lectins used in the study as inducers [24,25]. The intensification of lectin- and concanavalin A-induced aggregation of neutrophils in plasma after temporary venous occlusion in patients with abdominal obesity with impaired glucose tolerance is associated with an increase in the level of expression on the membranes of their neutrophils, adhesion receptors, which include a significant number of sites containing N-acetyl- D-glucosamine, N-acetyl-neuraminic acid and mannose [26,27]. Activation of neutrophil aggregation in response to the appearance of phytohemagglutinin in the plasma is caused by the growth in their receptors of sites of glycoproteins containing bD-galactose

[28,29] under conditions of depression of the sensitivity of neutrophil receptors to prostacyclin and NO [30,31,32].

CONCLUSION

The widespread prevalence in the world of a combination of abdominal obesity and a violation of glucose tolerance requires further in-depth study of this pathology. Particular attention in these patients deserves the aggregation of neutrophils, contributing to thrombosis of different localization. In these patients, the processes of lipid peroxidation in plasma are significantly intensified, which leads to an increase in the aggregation of neutrophils and disrupts tissue trophism, making a significant contribution to the risk of thrombosis in them [33,34,35].

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