

# Research Journal of Pharmaceutical, Biological and Chemical Sciences

## The State Of Aggregation Properties Of Neutrophils In Patients With Dyslipidemia With Impaired Glucose Tolerance.

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### ABSTRACT

Until now, the prevalence of a combination of dyslipidemia and impaired glucose tolerance has remained high among the adult population of industrially developed countries. This combination is considered very dangerous for the development of thrombosis as a result of pronounced hyperaggregation of blood cells. The aim is to determine the aggregation properties of neutrophils in patients with dyslipidemia with impaired glucose tolerance. We examined 45 patients of the second adulthood (mean age  $47.6 \pm 1.5$  years) with dyslipidemia and impaired glucose tolerance. The control group consisted of 26 clinically healthy people of the same age. All persons under supervision were given written informed consent to participate in the study. Biochemical, hematological and statistical methods of investigation were used. As a result of the conducted studies, it can be argued that a high incidence of thrombosis of various localities with dyslipidemia with impaired glucose tolerance is largely due to the development of excessive aggregation of neutrophils. This disruption is largely facilitated by the weakening of the antioxidant protection of the plasma, leading to activation of the processes of lipid peroxidation in it. The situation in people with dyslipidemia and impaired glucose tolerance is very often aggravated by a weakening of the ability to disaggregate in neutrophils. As a result, patients have a sharply increased risk of thrombosis of any location, which can lead to disability and death.

**Keywords:** neutrophils, dyslipidemia, impaired glucose tolerance, thrombophilia, aggregation.

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## INTRODUCTION

Despite the widespread introduction of new health technologies and regular large-scale routine preventive examinations of the population in industrially developed countries, the prevalence of a combination of dyslipidemia and impaired glucose tolerance is preserved [1,2]. Very often they simultaneously develop in working age and lead to various vascular complications, dangerous early death [3]. High frequency in the population of thromboses with the combination of dyslipidemia and impaired glucose tolerance is largely associated with increased aggregation of blood elements [4,5]. It is recognized that increasing their aggregation necessarily leads to the activation of hemostasis and the development of thrombosis [6,7,8]. This is largely due to a decrease in their sensitivity to vascular disaggregants, including prostacyclin and nitric oxide [9,10]. In view of the high prevalence of dyslipidemia with impaired glucose tolerance and serious significance for microcirculation of neutrophil aggregation, it was important to evaluate the aggregation of neutrophilic leukocytes in these patients [11].

The goal is to determine the aggregation properties of neutrophils in patients with dyslipidemia with 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  $47.6 \pm 1.5$  years) with dyslipidemia and impaired glucose tolerance [12]. 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 2.1 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 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 patients enrolled, neutrophil aggregation in response to applied inductors appeared earlier than in the control group (with lectin 54.5%, concanavalin A 43.9%, phytohemagglutinin 37.9%) (Table).

**Table. Registered indicators in the surveyed**

Registrated parameters	Patients, n=45, M±m	Control, n=26, M±m
acylhydroperoxides plasma, D <sub>233</sub> /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 neutrophils		
cholesterol of neutrophils, µmol/10 <sup>9</sup> neutrophils	0.86±0.014	0.62±0.004 p<0.01
common phospholipids of neutrophils, µmol/10 <sup>9</sup> neutrophils	0.34±0.010	0.51±0.003 p<0.01
acylhydroperoxides of neutrophils, D <sub>233</sub> /10 <sup>9</sup> neutrophils	3.70±0.05	2.36±0.05 p<0.01
malonic dialdehyde of neutrophils, nmol/10 <sup>9</sup> neutrophils	1.49±0.08	0.73±0.03 p<0.01
catalase of neutrophils, ME/10 <sup>9</sup> neutrophils	5100.0±13.17	9950.0±19.77 p<0.01
superoxidismutase of neutrophils, ME/10 <sup>9</sup> neutrophils	1200.0±3.25	1780.0±4.21 p<0.01
aggregation of neutrophils		
Aggregation with lectin, %	24.1±0.18	15.6±0.07 p<0.01
Aggregation with concanavalin A, %	21.3±0.16	14.8±0.04 p<0.01
Aggregation with phytohemagglutinin, %	42.2±0.07	30.6±0.09 p<0.01

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

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 – neutrophils [17,18]. 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 [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, the level of disaggregation ability in neutrophils decreases [21,22,23].

The increase in neutrophil aggregation found in the examined patients is largely due to the depression of their sensitivity to vascular compounds having a disaggregation activity against the background of an increase in the number of glycoprotein receptors to lectins used in the study as inducers [24,25]. The intensification of lectin and concanavalin A-induced aggregation of neutrophils in patients with dyslipidemia and impaired glucose tolerance is associated with an increase in the expression level on the membranes of their neutrophils, the adhesion receptors, which contain a significant number of sites containing N-acetyl-D-glucosamine, N- acetyl-neuraminic acid and mannose [26, 27]. The increase in 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 leukocytes to prostacyclin and NO [30,31,32].

## CONCLUSION

Preservation of a high degree of prevalence in the population of dyslipidemia and violation of glucose tolerance requires further comprehensive study of this pathology. Particular attention to the aggregation of neutrophils is due to the high incidence of thrombosis in this category of patients. In the study, it was found that lipid peroxidation in plasma was significantly enhanced in these patients. This causes the formation of neutrophils with increasing aggregation. The resulting increase in neutrophil aggregation worsens capillary blood flow, disrupts tissue trophism, and makes a significant contribution to the risk of thrombosis in patients with dyslipidemia with impaired glucose tolerance [33,34,35].

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