

# Research Journal of Pharmaceutical, Biological and Chemical Sciences

## Vascular Antiaggregatory Effects Of Blood Vessels On Erythrocytes In Patients With Impaired Glucose Tolerance.

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### ABSTRACT

The widespread prevalence of thrombosis in patients with impaired glucose tolerance is currently associated with the presence of vasopathy. Because of the high incidence of glucose intolerance in developed countries, it is of great interest to assess the status of this category of patients with the level of vascular control over aggregation by the most numerous cells of the blood, erythrocytes. The aim of the work is to assess the level of disaggregation capacity of blood vessels in relation to erythrocytes in patients with impaired glucose tolerance. 42 patients with impaired glucose tolerance of the second adulthood were examined. The control group consisted of 26 healthy people of the same age. The study uses biochemical, hematological and statistical methods of investigation. In patients in erythrocytes, an excess of cholesterol, a decrease in total phospholipids, and activation of lipid peroxidation processes were detected. High spontaneous aggregation of erythrocytes was also found in patients. Weakened vascular control over erythrocyte aggregation in all patients. The attenuation of disaggregating vascular effects on erythrocytes is a consequence of metabolic disturbances arising in violation of glucose tolerance, a decrease in the lumen of the vessels due to spasm and active lipid peroxidation. The vasopathy present in the examined patients sharply increased their risk of thrombosis leading to disability and death.

**Keywords:** pathology, violation of glucose tolerance, vascular wall, aggregation, erythrocytes.

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## INTRODUCTION

Large-scale medical observations have shown that in high-prevalence countries, the prevalence of impaired glucose tolerance remains high [1,2]. This pathology contributes often in adulthood to a propensity for vascular thrombosis, which sometimes leads to disability and mortality [3,4]. The widespread prevalence of thrombosis in these patients is largely due to the resulting vasopathy [5,6].

It is known that all blood cells are capable of aggregation. This strongly affects the activity of hemostasis and determines the risk of thrombosis [7,8,9]. Aggregation of blood cells is restrained by substances synthesized in blood vessels and called disaggregants. The most powerful of these are prostacyclin and nitric oxide [10,11]. In view of the widespread prevalence of impaired glucose tolerance, studies of the features of vascular control over erythrocyte aggregation in this category of patients are very important.

The goal is to assess the level of disaggregation capacity of blood vessels in relation to erythrocytes in patients with impaired glucose tolerance.

## MATERIALS AND METHODS

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

42 patients with impaired glucose tolerance [12] of the second adulthood (mean age  $49.6 \pm 1.7$  years) were examined. Control consisted of 26 healthy volunteers of the second adulthood. All surveyed gave written information consent to participate in the study according to generally accepted rules [13].

The activity of lipid peroxidation (LPO) processes in plasma was recorded by the level of thiobarbituric acid (TBA) -active products by the Agat-Med (Russia) and acyl hydroperoxides (AGP) kit by the method [14]. The antioxidant protection of blood plasma by [15].

The state of LPO in erythrocytes was assessed by the level of malonic dialdehyde (MDA) and AHP in them after washing and resuspension of erythrocytes. [14] Also in washed and resuspended erythrocytes, the content of cholesterol was determined by enzymatic colorimetry (Russia) and the level of total phospholipids in the content of phosphorus in erythrocytes.

The level of disaggregation capacity of blood vessels with respect to erythrocytes was estimated by its weakening in plasma obtained under conditions of temporary venous occlusion [16]. Activity spontaneous aggregation of erythrocytes in intact plasma and in plasma taken against a background of temporary ischemia of the vessel wall was determined with the aid of a light microscope in Goryaev's chamber. The number of erythrocyte aggregates, the number of aggregated and non-aggregated erythrocytes were recorded [17].

The results were processed by Student's criterion (t). Statistical processing of received information was made with the help of a programme package "Statistics for Windows v. 6.0", "MicrosoftExcel". Differences in data were considered reliable in case of  $p < 0.05$ .

## RESULTS AND DISCUSSION

In the patients studied, activation of LPO in plasma was found - the amount of AGP in it exceeded control by 2.1 times, TBA-active products - 1.4 times. This was due to the weakening of the antioxidant protection of the plasma by a factor of 1.25 (Table).

In the examined patients, an excess of the content of cholesterol in the erythrocyte membranes and reduction in their total phospholipids was found. This was accompanied by activation of lipid peroxidation in their erythrocytes by weakening enzymes of antioxidant protection of erythrocytes (Table).

In all patients, activation of the process of spontaneous aggregation of erythrocytes was found (Table). This was indicated by an increase in their total involvement in aggregates (by 58.7%), an increase in the number of these aggregates (by 34.4%) and a 36.5% decrease in red blood cells not involved in aggregation.

In the examined patients, weakened disaggregation effects of blood vessels on erythrocytes (Table). It was found that in the plasma obtained after temporary venous occlusion, the number of erythrocytes in the aggregates exceeded the control by 69.0%, the number of these aggregates was increased by 38.6%, and the quantity of non-aggregated red blood cells was reduced by 58.9%.

**Table: Hematologic parameters in the examined**

Registrated parameters	Patients, n=42, M±m	Control, n=26, M±m
acylhydroperoxides plasma, D <sub>233</sub> /1ml	2.93±0.07	1.42±0.09 p<0.01
TBA-compounds, umol/l	4.87±0.12	3.56±0.07 p<0.01
antioxidant activity plasma, %	26.2±0.16	32.9±0.12 p<0.01
biochemical parameters of erythrocytes		
cholesterol of erythrocytes, umol/10 <sup>12</sup> erythrocytes	1.29±0.016	1.04±0.004 p<0.01
common phospholipids of erythrocytes, umol/10 <sup>12</sup> erythrocytes	0.59±0.007	0.75±0.003 p<0.01
acylhydroperoxides of erythrocytes, D <sub>233</sub> /10 <sup>12</sup> erythrocytes	4.35±0.14	3.08±0.10 p<0.01
malonic dialdehyde of erythrocytes, nmol/10 <sup>12</sup> erythrocytes	1.46±0.12	1.14±0.05 p<0.01
catalase of erythrocytes, ME/10 <sup>12</sup> erythrocytes	8500.2±13.5	11196.0±22.4 p<0.01
superoxidismutase of erythrocytes, ME/10 <sup>12</sup> erythrocytes	1700.1±1.92	1986.0±7.01 p<0.01
aggregation of erythrocytes in intact plasma		
sum of all the erythrocytes in an aggregate	66.5±0.20	41.9±0.10 p<0.01
quantity of aggregates	12.1±0.16	9.0±0.06 p<0.01
quantity of free erythrocytes	175.8±0.72	240.0±0.23 p<0.01
aggregation of erythrocytes in plasma after temporary venous occlusion		
sum of all the erythrocytes in an aggregate	55.1±0.14	32.6±0.14 p<0.01
quantity of aggregates	9.7±0.16	7.0±0.07 p<0.01
quantity of free erythrocytes	199.7±1.08	305.3±0.18 p<0.01

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

A significant role in the development of rheological disorders and the formation of a risk of thrombosis in individuals with impaired glucose tolerance belongs to the growth of erythrocyte aggregation [18, 19]. When glucose tolerance is impaired, depression of the antioxidant activity of plasma occurs, which causes the growth of LPO activity in it [20]. This inevitably damages the structure of red blood cells [21]. The development of these disorders with lipid imbalance found in the etitrocytes of the examined patients ensures their hyperaggregation. At the same time, the disaggregating capacity of blood vessels in relation to erythrocytes weakens [22,23]. This was diagnosed in the examined patients to increase erythrocyte aggregation in plasma after temporary venous occlusion [24]. Apparently, the increase in erythrocyte

aggregation in patients with impaired glucose tolerance is primarily due to the weakening of the disaggregating capabilities of their blood vessels [25,26] and a decrease in the density of negative proteins on the erythrocyte surface [27]. Depression of antioxidant properties of plasma entails increased lipid peroxidation processes in it, as well as damage to endotheliocytes and globular plasma proteins [28,29]. In conditions of low intensity of synthesis of vascular deagregantov there is an increase in the connection of erythrocytes in aggregates and their number increases [30, 31]. At the same time, the weakening of the synthesis of vascular prostacyclin and nitric oxide creates an imbalance in the erythrocytes of the activity of adenylate cyclase and phosphodiesterase [32,33]. This lowers the level of cyclic adenosine monophosphate in their cytoplasm and increases  $Ca^{2+}$ , which dramatically increases erythrocyte aggregation [34,35].

### CONCLUSION

In patients with impaired glucose tolerance, thromboses of blood vessels are often noted. This required a survey of this contingent of patients. It was revealed that in violation of glucose tolerance, weakened antioxidant protection of the plasma and increased peroxide oxidation of lipids damaging the endothelium of the vascular wall. In patients with impaired glucose tolerance, a decrease in the disaggregating properties of blood vessels was found against the background of spontaneous aggregation of erythrocytes. It can be considered that for a given contingent of patients, there is an inherent increase in the risk of vascular thrombosis, which can lead to disability and early death [36,37,38].

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