Discussion about the nature of red blood cell aggregation depending on ABO blood group

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Abstract. This article provides a brief overview of several own studies with an emphasis on the difference of the electric charge of red blood cells (RBCs) belonging to different ABO blood groups. It was determined that the RBCs of B and AB blood group have the highest velocity of the electrophoretic mobility. The concentration of lanthanum chloride solution required for providing the induced RBCs aggregation of B and AB blood groups also exceeded the one for O and A blood groups. Based on these facts, we can conclude that the RBCs of B and AB blood groups have the largest electric charge. B blood group is more common at patients with ischemic stroke. Among the possible causes of the influence of RBCs electric charge on the vascular thrombosis risk, there is an electrostatic attraction due to Coulomb forces, which may increase when the blood viscosity and the solution ionic strength grow.
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Introduction

Since Landsteiner K. discovered ABO blood groups in 1900, the researchers have been concerned about human predisposition to various diseases, depending on the blood group.

This problem has been the subject of many scientific papers. Due to this, the increased susceptibility of people with different ABO blood groups to certain diseases has been established with a different credibility degree.

Currently, a significant number of human diseases, including infectious diseases, are clearly associated with the ABO blood group. Such a relationship is established for certain types of cancers, Parkinson's disease, cholera and other diseases. The cause of such an association for some diseases is established accurately enough, while it remains a debatable issue for many others. [1, 2, 3, 4, 5, 6, 7]

A significant researchers' attention was devoted to finding the relationship between the blood-group specificity and the development of cardiovascular diseases. Taking into consideration the high mortality rate among patients with myocardial infarction or stroke, this attention looks reasonable. [8, 9, 10, 11]

A reduced level of von Willebrand factor is considered to be one of the possible mechanisms of a lower risk of cardiovascular diseases at people having O blood group. Because of this, the risk of blood clots after myocardial infarction or stroke decreases and the overall recovery prognosis is improved. [12]

Without denying the importance of the other points of view, our study aimed at studying the dependence of human RBCs electric charge on type-specific ABO antigens. The fact is that the aggregation properties of RBCs are modified to a certain extent by changing their electric charge, which has been demonstrated in earlier studies. [13, 14, 15, 16]

This fact has been used to explain the greater incidence of ischemic stroke at carriers of certain ABO antigens.

At the beginning of the 20th century, the presence of negative charge in human RBCs produced by molecules of sialic acid was established. Subsequently, it made it possible to extend the range of techniques for studying the RBCs functioning, such as mobility in an electric field. [17, 18]

Recent studies have indicated unequal distribution of type-specific antigens on the RBCs membrane surface relative to sialic acid molecules. [19, 20]

Methods

Based on the previous work, we made a comparative study of the distribution of blood groups at ischemic stroke patients with cerebral atherosclerosis within the bounds of a neurological department of the city hospital. We found out that the third blood group clearly predominated at patients with ischemic stroke, in comparison with the control group (36.84% and 22.41%, respectively, a significant difference with $p < 0.05$). The obtained data coincide with those of similar works. With regard to the population, this study to a great extent can be considered a survey, because the patients who died at home or did not seek medical help have not been considered. [21]

Next, we conducted a comparative study of the RBCs aggregation properties of different ABO blood groups. With this purpose, we carried out a mixing of the washed RBCs suspension with lanthanum chloride, the ions of which have a positive charge, and, as expected, could inactivate the natural

negative charge of the RBCs membrane. Spontaneous erythrocyte aggregation, which occurred after the exposure to lanthanum chloride, indicated the reduction of its cells charge. According to the results of the experiment, it was found that the RBCs of B and AB blood groups have the greatest surface charge, since aggregation of RBCs required much greater concentration of lanthanum chloride than for other groups. [22]

The next step was to compare the RBC electrophoretic mobility of different blood groups. A special electrophoretic cell, electric current source, a microscope and a video camera were used for this purpose. The calculation of RBCs velocity was performed by analyzing the video. The velocity of RBCs ranged from 0.71 to 1.9 μm*cm*V-1*c-1

It was found that the RBCs of the third and fourth blood groups had the highest velocity in the electric field, leaving the RBCs of the first blood group far behind. The relative RBCs number of the total number of measurements that can reach speeds above 1.6 $\mu m*cm*V-1*c^{-1}$ was compared. The obtained values are 2% of O blood group, and 9.25% and 6.5% for B and AB blood groups respectively (a significant difference at $p < 0.05$). [23]

Based on the fact that the velocity of a charged particle in the electric field depends on its electric charge value, it can be assumed that the RBCs charge of third and fourth group was the highest in the experiment.

Thus, similar data were obtained in two different experiments showing that electrical charge of the RBCs of third and fourth blood group is more than that of RBCs of first and second groups.

Discussion

The question that logically arises is why the highest incidence of ischemic stroke in our first study is associated with the third blood group? Doesn't a higher electric charge of blood cells lead to greater electric repulsion and hence, in the forecast, to the better blood rheology? To answer this question, we must turn to the ischemic stroke physiopathology. It is known that ischemic stroke developing at patients with cerebral atherosclerosis develops more often than any other subtypes. The progression of atherosclerosis leads to morphological changes in the vascular wall and endothelial destruction which normally has a negative electrical charge due to chondroitin sulfate molecules. [24, 25, 26]

The damaged vessel wall loses some of the negative charge, probably until inverting it. Thus, the initially apparent positive factor, a RBCs high electric charge of the third and fourth blood groups, in this situation serves as an additional risk factor for ischemic stroke. The loss of the charge of RBCs with a greater surface charge in the process of aging is less. They aggregate well to the positively charged vascular wall and to each other, causing an increase in the size of a blood clot and the consequent risk of ischemic stroke.

The second variant of thrombosis at people liable to it is based on the characteristic mechanism of electrostatic interaction of charged bodies. It is known that the like-charged bodies placed at a certain distance from each other experience the action of various forces. Both electro-repulsion Coulomb forces and van der Waals forces of interactive attraction act here. The priority of this or that force depends on the solution ionic strength and the distance between the charged particles. Under the conditions of increase in the solution ionic strength, which may occur, for example, by the viscosity growth of the original solution, the diffuse electric layer around the particles thickens. This process leads to reducing the distance between the charged particles. This in its turn inevitably leads to aggregation under the action of the van der Waals forces. The obvious fact, which is worth noting, is that the particles charge has a direct impact on the velocity and aggregation probability due to the polarization of the diffuse electric layer. Thus, the RBCs, the size of which is variable within certain limits, can aggregate with each other, and this process will depend on their initial electric charge. [27, 28]

It is worth noting that the thrombosis of the arterial vessel usually develops in the pathologically changed vessel wall, with a slow flow and a formed elements sludge. Irreversible RBCs aggregation in such conditions can be triggered by various external and internal factors, such as psycho-emotional stresses. Obviously, the overall state of the organism hemostatic system will have little effect on the cells interaction in the local portion of the pathologically changed vasculature.

Summary

The possibility of the dependence of the RBCs electric charge on the blood group is not excluded. The highest charge value was observed in RBCs of B and AB blood groups.

Most patients with ischemic stroke had B blood group.

A higher electric charge of RBCs is probably a risk factor for diseases associated with thrombosis, due to the Coulomb interaction under the conditions of grown blood viscosity, and increase in the solution ionic strength.

The results of the research may be reconsidered in case of updating the data on the RBCs interaction in the bloodstream. Another controversy concerns the priority of the thrombosis electrostatic

mechanism over the other mechanisms. The work in this direction is to be continued.

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