

Changes in the Rheological Properties of Blood in Kidney Diseases

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Abstract Blood viscosity is one of the defining characteristics of microcirculation and significantly affects hemodynamic parameters. Microcirculation plays a large role in maintaining hemodynamic processes. Violation of microcirculation processes develops hypoperfusion, which causes dystrophic and hypoxic processes in tissues. The main cells that determine the rheological parameters of the blood are erythrocytes and make up 98% of the total volume of blood-shaped elements. The study of the mechanisms of hemorrheological changes that develop in the body serves to shed light on the mechanism of most somatic diseases. Therefore, in the development of pathological processes, great attention is paid to the study of the rheological parameters of the blood. The incidence of glomerulonephritis (GN) in children is much observed in later times, with the disease being a serious medical problem in terms of severity. Primary localization of the pathological process in GN is a violation of microcirculation in the kidneys. Therefore, the study of the rheological properties of blood in patients with glomerulonephritis is one of the pressing problems.

Keywords Blood, Rheological properties of blood, Blood viscosity, Glomerulonephritis, Pathogenesis, Microcirculation, Blood form elements, Hemodynamics, Homeostasis

1. Introduction

Accumulated evidence suggests that variability in the rheological properties of erythrocytes affects the symptoms of diseases and also plays a role in monitoring the effectiveness of treatment for patients. In this regard, studies of the variability of the rheological properties of red blood cells during their life and the study of the factors that determine the variability of rheological properties in the population are of particular relevance. Especially, these changes significantly determine hemodynamics in the microvasculature, causing the flow of the required amount of oxygen to the tissues [4,7,8].

The key role in the formation of the rheological parameters of blood belongs to the formed elements of blood, primarily erythrocytes, which make up 98% of the total volume of formed elements of blood. Blood viscosity is one of the integral characteristics of microcirculation, which significantly affects hemodynamic parameters [2,4].

It is known that blood flow through the microcirculation system is determined primarily by the rheological properties of blood, which change during pathology and especially significantly during terminal conditions. The viscosity of

whole blood is normally about 4-5 cP (1.5 times higher than plasma viscosity), and under pathological conditions it ranges between 1.7-22.6 cP. Violation of the rheological properties of blood often takes on the character of a general pathological reaction and is an important link in the pathogenesis of various diseases. Rheological parameters of blood affect the delivery of oxygen and glucose and make a significant contribution to the formation and progression of ischemic disorders of cerebral circulation. In patients with acute and chronic cerebrovascular accidents, a significant increase in blood viscosity, fibrinogen concentration and erythrocyte aggregation was revealed compared with clinically healthy patients of similar age. [11,12]

Tissue homeostasis and transcapillary exchange determine the functioning of the microvascular bed. Tissue perfusion ensures the balanced functioning of the body as a whole. To maintain adequate perfusion processes in tissues, adequate microcirculation with the metabolism of biologically active substances and gas exchange is necessary [3,5]. Tissue homeostasis and transcapillary exchange determine the functioning of the microvascular bed. Tissue perfusion ensures the balanced functioning of the body as a whole. To maintain adequate perfusion processes in tissues, adequate microcirculation with the metabolism of biologically active substances and gas exchange is necessary [6,8,9].

Microcirculation plays a huge role in maintaining hemodynamic processes. Disruption of microcirculation

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processes initiates hypoperfusion, which induces dystrophic and hypoxic processes in tissues. Microrheological disorders play a significant role in circulatory disorders at the regional level. In connection with the relatively recent study of the mechanisms of regulation of hemorheological changes and their importance in ensuring adequate tissue perfusion, much attention is paid to the study of rheological parameters of blood both in normal and pathological conditions [9,12,13].

Due to hypoxia, metabolic and functional disorders occur [6]. Blood viscosity with intact vessels determines the efficiency of oxygen delivery to tissues. The viscosity itself is influenced by plasma rheological parameters, the degree of aggregation and deformability of erythrocytes, and hematocrit [1,6].

There is evidence of the relationship between blood viscosity and microcirculatory disorders. The optimal hematocrit for good tissue perfusion is 45%; as it increases, oxygen delivery to tissues decreases [1,2,6,14].

In terms of prevalence and severity of outcomes, glomerulonephritis (GN) in children is a serious medical problem. According to a number of authors [6,7], children with various forms of GN make up more than 20% of all nephrological patients. The unfavorable course of GN leads already in childhood to renal failure, early disability of patients and a reduction in life expectancy, which gives the problem social significance. The primary localization of the pathological process in GN is the microvasculature of the kidneys [2,3,5,9].

Blood viscosity determines rheological parameters, including blood fluidity, and depends on the content of plasma protein components, temperature, and fibrinogen [14]. Plasma in the capillaries ensures ease of sliding of moving blood cells through the vessels [13,15]. In small capillaries, interaction occurs between the red blood cell membrane and endothelial cells. In capillaries of small diameter, red blood cells are able to change their shape to be able to move. Under these conditions, the parietal plasma layer retains its functional capacity and prevents the absorption of nitric oxide produced by the endothelium.

The importance of the problems identified above prompted us to conduct this study, the purpose of which was to assess the variability of the rheological properties of human blood.

2. Purpose of the Research

The purpose of the study is to study the state of the viscoelastic properties of blood and the rate of its shift in patients with the nephrotic form of glomerulonephritis.

3. Materials and Methods

To study the state of the viscoelastic properties of blood and the rate of its shift in patients, examinations were carried out in 17 children with the nephrotic form of glomerulonephritis who were treated at the TMA clinic. The control group

consisted of 6 practically healthy children. The rheological properties of blood were studied by determining the viscosity of the blood and its shear rate. Blood viscosity and its shear rate were determined by applying the appropriate hydrostatic pressure (3, 8, 12, 16 mm of water column) according to the modified method of V.M. Udovichenko [10], the range of applied hydrostatic pressures is 2-16 mm of water column, corresponding afferent, exchange and efferent links of the microvasculature.

4. Results and Discussion

Research results and discussion. We analyzed the viscoelastic properties of blood in proactively healthy children and adults in an arid climate. It has been established that in adults, with applied hydrostatic pressure of 4 and 16 mm water column, blood viscosity was 14.9 and 22.5% higher than in healthy children. This caused a lower shear rate in adults than in children - by 18.84% and 21%, respectively. It should be noted that we did not identify any particular differences in the indicators of viscoelastic properties of blood in children depending on gender.

In patients with the nephrotic form of glomerulonephritis, blood viscosity significantly increases compared to healthy children both at minimal and at maximum shear stress. The results of the study showed that in patients with the nephrotic form of acute glomerulonephritis (NF AGN), blood viscosity significantly increases compared to the values of healthy children at both minimum and maximum shear stresses. When applying hydrostatic pressure of 2 mm. It was not possible to determine the viscosity and shear rate of blood in the water column.

Starting from 4 mm water column of hydrostatic pressure, determination of these parameters was possible. However, the studied parameters significantly exceeded the normal values and their severity depended on the degree of activity of the pathological process. At hydrostatic pressure of 4 and 16 mm water column, the determined parameters significantly exceeded the norm and the severity depended on the degree of activity of the pathological process: with UFOGN of II degree of activity, blood viscosity exceeded the values of healthy people by 2.59, 2.70, 1.92 and 1.52 times ($P < 0.05$), respectively, to the applied hydrostatic pressures, then in children with grade III severity of the pathological process this increase was 3.11; 2.98, 2.29 and 1.56 times, respectively ($P < 0.05$). Moreover, there was a clear dependence of the severity of these changes on the magnitude of the applied pressure, since at low values of pressure, characteristic of the exchange and outlet section of the microcirculatory bed, a sharp increase (approximately 3 times) was detected, while at higher values of the applied pressure, characteristic for the adductor link of the microcirculatory bed are less pronounced (approximately 1.5 times).

A sharp increase in blood viscosity in patients with NF AGN led to a slowdown in the shear rate, which was also characterized by a dependence on the degree of the pathological

process. Thus, in sick children with NF AGN II degree, the shear rate at an applied pressure of 2 mm of water column of hydrostatic pressure was not detected. Starting from 4 mm of water column, the shear rate was determined, however, these values were statistically significantly lower than the standard values by 1.67, 2.66, 1.92 and 1.49 times, respectively, at applied pressures of 4.8, 12 and 16 mm of water column hydrostatic pressure. These values in patients with grade III AGN were even more pronounced at 2.03; 3.17; 2.21 and 1.57 times lower, respectively. Moreover, a more pronounced slowdown in the shear rate was characteristic of the efferent and exchange link of the microvasculature (2-3 times) than for the adductor (1.5 times).

A significant increase in blood viscosity under applied hydrostatic pressure slows down the rate of its shear compared to the control. In children with acute glomerulonephritis, the rate of blood shear at applied pressures (4 and 16 mmH₂O) decreases from the norm by 40.3 and 33.27%, respectively, with 2 degrees of activity, by 50.9 and 36.42% ($P < 0.05$) – 3 degrees.

Studies have shown a significant decrease in sick children, while the severity of the change was largely determined by the severity of the pathological process. Thus, if in sick children with NF AGN of the second degree of activity, the indicators of electrophoretic mobility and zeta potential of erythrocytes were lower than the values of practically healthy children by 1.10; 1.4 times, respectively, then in patients with III degree of activity – 1.15; 1.54 times respectively. Moreover, the dependence of these indicators on each other was revealed. Consequently, in children with an acute form of the disease there is a significant increase in blood viscosity and a decrease in its shift. Their severity is directly dependent on the degree of activity of the pathological process.

Therefore, it can be argued that in patients with UFOGN, the formation of red blood cell aggregates in capillaries and small venules will be observed largely, causing the development of congestion and edema, and thereby contributing to the development of tissue hypoxia, especially of the affected organ.

Violations of the viscoelastic properties of blood are mainly caused by significant changes in the charge of erythrocyte membranes, which promotes the adhesion of erythrocytes. The repulsion of negatively charged red blood cells from each other prevents their aggregation, even in a state of blood stasis. These repulsive forces are due to the electrokinetic properties of blood cell membranes, which are characterized by the electrophoretic mobility of red blood cells and the zeta potential. A significant decrease in their charge under pathological conditions contributes to the aggregation of erythrocytes and the development of the sludge phenomenon.

A study of the rheological properties of blood in patients with the nephrotic form of chronic glomerulonephritis (NF CGN) showed a significant increase in blood viscosity and a decrease in its shear. As with AGN, in children with II and III degrees of NF CGN, it was not possible to determine blood viscosity and shear rate at a minimum (2 mm of water column) pressure. With an increase in the applied hydrostatic

pressure, the studied parameters were determined; however, their values differed significantly from normal values and the severity depended on the degree of activity of the pathological process.

Thus, with the II degree of NF CGN activity, blood viscosity at 4.8, 12 and 16 mm water column of applied pressure increased statistically significantly in relation to the values of practically healthy individuals of 3.08; 2.38; 1.98 and 1.53 times, respectively. At the same time, in the third degree of activity of the pathological process, this increase was even more pronounced and amounted to 3.49, respectively; 3.26; 2.42 and 2.5 times.

Along with this, a significant slowdown in the rate of blood shear was noted in all cases in the studied ranges of applied pressure values. At the same time, if when studying blood viscosity we observed a certain dependence of changes on the degree of activity of the pathological process in sick children, then when determining the rate of shift we did not identify this dependence. Thus, the shear rate in stage II NF CGN slowed down statistically significantly by 1.63; 2.540; 1.87 and 1.48 times respectively the applied pressures of 4.8, 12, 16 mm of water column. At the third degree of activity, this decrease was 1.6; 2.80 and 1.50 times respectively.

It should be noted that changes in the viscoelastic properties of blood in children with CGN were somewhat less pronounced than with AGN. In our opinion, this was due to the frequent use of anticoagulants and antiplatelet agents for CGN. At the same time, it should be pointed out that small vessels are more vulnerable: capillaries, precapillaries and postcapillaries, which are characterized by low values of applied pressure. Apparently, we should expect greater aggregation of erythrocytes in these areas of the microvasculature, and as a consequence, a decrease in transcapillary exchange and the development of environmental hypoxia.

As noted earlier, the aggregability of erythrocytes depends on the magnitude of the electrical breakdown, their “zeta” potential and the electrophoretic mobility of the cells. A study of these parameters in children with UFCHN showed their decrease, the severity of which to a certain extent depended on the degree of activity of the pathological process. They, together with changes in the physical parameters of erythrocyte membranes, contribute to the deterioration of blood fluidity, transcapillary exchange of gases and nutrients, causing disruption of cellular homeostasis and activation of membrane- destructive processes.

The results of such studies contribute to a correct assessment of the variability of rheological characteristics in pathology, a more optimal influence on the formation of quantitative characteristics of rheological properties, and at the same time serve as a source of new knowledge about the morphofunctional state of the erythron.

5. Conclusions

Research into many pathological processes currently includes the search for a general mechanism that determines the damage to the body as an integral self-regulating structure.

The progression of any disease is accompanied by functional and structural changes in certain blood cells. Of particular interest are changes in erythrocytes, the membranes of which are a model of the molecular organization of plasma membranes. Their aggregation activity and deformability, which are the most important components in microcirculation, largely depend on the structural organization of red blood cell membranes.

According to the literature when various organs and systems are affected, damage develops not only in the lesion, but also in nearby organs and systems, as well as in functionally and anatomically distant organs [11,12]. On the one hand, this is due to a change in the physicochemical properties of the blood, on the other, to the toxic effect of endo- and exotoxins circulating in the blood from the lesion. The scattered data available in the literature indirectly indicate the leading role of peripheral hemodynamic disorders in the development of pathology. Thus, in various pathological conditions, not only specific damage to the structural components of tissues, organs and systems is observed, but also changes in the blood system and its components. At the same time, studying the characteristics of hemodynamics in patients helps to determine not only a number of pathogenetic aspects of the underlying disease, but also to predict possible complications, develop reliable criteria for early diagnosis and adequate drug correction of the disorders [5].

Numerous studies carried out in pathological processes revealed various disturbances in the mechanical and physico-chemical properties of blood, significant disorders of the microcirculation system, consisting in slowing down blood flow, increasing the degree of aggregation of blood cells, functional and morphological changes in the vascular wall, ultimately leading to tissue hypoxia.

It is known that the movement of blood through vessels of various sizes depends not only on the pressure applied to the blood flow, but also primarily depends on the rheology of the blood. Blood viscosity is not constant, but increases significantly in areas of reduced blood flow rates and low pressure. In this regard, the study of the rheological properties of blood is carried out at different shear rates.

To clarify the general and specific aspects of changes in the rheological properties of blood during pathological processes, acute and chronic forms of glomerulonephritis were selected.

Blood viscosity in patients with the nephrotic form of acute glomerulonephritis at stage II of activity was statistically significantly higher than the values of practically healthy individuals by 159.8%; 170%; 92B54 and 52B 11%; with III degree of activity - by 211.17%, 190%, 129%. Chronicity of the pathological process further increased blood viscosity.

It has been established that "improper blood behavior", i.e. the increase in volumetric flow is disproportionate to the applied pressure, due to the presence of so-called structural viscosity, which sharply decreases with increasing exposure to the blood. It is known that blood viscosity is largely determined by the rheological properties of erythrocytes,

since they are the predominant cellular elements of the suspension. In fast flow, the droplet-like behavior of red blood cells due to internal viscosity is of great importance. In a slow flow, mainly the number determines the viscosity of blood and size of erythrocyte aggregates, since the viscosity of plasma in such areas is significantly lower than the viscosity of the erythrocyte suspension.

Red blood cell aggregation is a spontaneous process of formation of cell conglomerates in the form of coin columns of primary, secondary and tertiary structures. According to the existing biophysical theory, aggregation of erythrocytes occurs due to an imbalance between the van der Waals attractive forces and the repulsive forces between negatively charged blood cells. The latter is due to the carboxyl groups of sialic acid. Fibrinogen is of great importance in the formation of aggregates, which is assumed to form bridges between individual red blood cells. However, it should be noted that moderate aggregation is a normal physiological process. It promotes more efficient transfer of blood cells in axial flow. In precapillary vessels, coin columns of aggregates are oriented at a greater distance from the vascular wall, compared to single erythrocytes. As a result, the speed of movement of the aggregates becomes higher compared to plasma and provides more intense oxygenation of tissues.

Glomerulonephritis is characterized by biochemical changes that cannot but affect the rheological and coagulation properties of the blood, increased levels of beta-lipoproteins and non-esterified fatty acids. The most significant changes are detected in the nephrotic form, which is characterized by the development of hypercholesterolemia. Blood circulation in small, medium and, to a lesser extent, large vessels depends not only on the propulsive activity of the heart, but also on the biophysical properties of the blood itself, which determine its fluidity. At the same time, the fluid properties of blood are determined by the integral value - viscosity, on which the degree of normalization of microcirculation in the organs and tissues of the body largely depends. In this case, the viscosity of the blood decreases with a decrease in the radius of the vessel, during stasis it increases 20 times, and during stasis the blood loses its fluidity and acquires the property of a solid body. In patients with glomerulonephritis, depending on the activity of the pathological process, erythrocyte aggregation was mainly detected in precapillary sphincters, capillaries and postcapillaries, which coincides with the pronounced change we observed in the rheological properties of blood at low values of applied hydrostatic pressure.

Aggregation of erythrocytes in the blood inevitably disrupts the normal structure of blood flow in microvessels. This must be the most important factor causing changes in the normal rheological properties of blood under pathological conditions.

In addition to the aggregation properties of erythrocytes, in hemorheology much attention is paid to the elastic properties of erythrocytes, internal viscosity and ability to deform. Deformability is an important and necessary quality of a red blood cell, since with its own diameter of about 8

microns, it must pass through capillaries with a diameter of 2.5 microns. It has been established that the deformability of erythrocytes is closely related to their internal viscosity, metabolic state, and hemoglobin content and membrane permeability.

Thus, the development of NFGN is characterized by changes in the viscoelastic properties of blood and the associated physicochemical characteristics of erythrocyte membranes. The severity of these changes depends on the severity and degree of activity of the pathological process.

REFERENCES

- [1] Balachandran Nair A. N. et al. A reduced-order model for deformable particles with application in bio-microfluidics // *Computational Particle Mechanics*. – 2020. – T. 7. – pp. 593-601.
- [2] Blumens A. L. et al. Multiscale parareal algorithm for long-time mesoscopic simulations of microvascular blood flow in zebrafish // *Computational Mechanics*. – 2021. – T. 68. – №. 5. – pp. 1131-1152.
- [3] Golubeva M. G. Osmotic resistance of erythrocytes, methods of determination and correction, significance for various pathologies // *Advances in modern biology*. – 2019. – T. 139. – No. 5. – pp. 446-456.
- [4] Miranda E. et al. Role of the left coronary artery geometry configuration in atherosusceptibility: CFD simulations considering sPTT model for blood // *Computer Methods in Biomechanics and Biomedical Engineering*. – 2021. – T. 24. – №. 13. – pp. 1488-1503.
- [5] Ismailov I. Ya., Skvortsov V. V. Chronic glomerulonephritis // *Nurse*. – 2018. – T. 20. – No. 6. – pp. 17-20.
- [6] Mchedlishvidi G.I. The structure of blood flow is the leading factor in the rheological properties of blood in microvessels, the device for estimating the diameters of microvessels // *Materials of the III All-Union. Symposium: "TV microscopy and research of the cardiovascular system."* –L., 1990. –pp. 57-66.
- [7] Mchedlishvidi G.I. Blood microcirculation. –L.: Nauka, 1989. pp.280.
- [8] Thondapu V. et al. Non-Newtonian Endothelial Shear Stress Simulation: Does It Matter? // *Frontiers in Cardiovascular Medicine*. – 2022. – T. 9.
- [9] Mendieta J. B. et al. The importance of blood rheology in patient-specific computational fluid dynamics simulation of stenotic carotid arteries // *Biomechanics and Modeling in Mechanobiology*. – 2020. – T. 19. – pp. 1477-1490.
- [10] Udovichenko V.I. Improved Copley viscometer for determining viscosity in small blood samples under thermostable conditions // *Pat. Physiol*. -1978. - No. 1.-pp. 73-76.
- [11] Paunova S.S., Kucherenko A.G., Markov Kh.M. and others. Platelet nitric oxide in children with kidney diseases // *Pediatrics*. - 2000. - No. 1, - pp. 7-9.
- [12] Tikhonova K.Yu. Bogomolets E.Sh. Alymbaev T.S. Features of the blood coagulation system and its viscosity in glomerulonephritis with nephritic syndrome in children. // *Bulletin of KSMA*.-Vol. 5, No. 5-6. TNIK KGM K.
- [13] Petrov V.N. Glomerulonephritis: principles of diagnosis, treatment, nursing care // *Medical sister*. – 2009. – No. 1. – pp. 3-6.
- [14] Rakhmanova L.K., Daminov B.T., Karimova U.N. Chronic glomerulonephritis in children. – 2017.
- [15] Korovina N.A., Pykov M.I., Korostelova E.A., Tvorogova G.M. Ultrasound examination of renal blood flow in children // *Pediatrics*. -2002. -No. 2. -pp. 33-37.
- [16] Nastaushva G.A., Ryaskina L.V., Volosovets G.G. and others. Chronobiological study of urine parameters in nephrotic syndrome in children with varying sensitivity to steroids // *Russian Pediatric Journal*. - 2005. - No. 6. - pp. 16-22.
- [17] Reshetova T.G., Kurbatova M.V., Khodunova K.A. The state of renal hemodynamics in chronic glomerulonephritis in children // *Bulletin of the Ivanovo Medical Academy*. T. 13., No. 1-2, 2008. pp. 63-67.