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STUDY OF INTERACTION OF BLOOD ERYTHROCYTES AND IMMUNE SYSTEM PARAMETERS IN ATHLETES – ADOLESCENT

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ABSTRACT

The aim of this study was to study the interaction of red blood cells and the parameters of the immune system in adolescent athletes. Questioning and interviewing of 125 young athletes at the age of 11 - 17 years of the city of Samarkand was carried out. Among them there were 81 boys (65.1%), 44 girls (34.9%). In all study groups, there was a tendency to a decrease in the level of immunoglobulin G when comparing two study groups: incubation with saline and a sorbent immobilized with heparin. The obtained research results indicate the undoubted contribution of the components of the complement system to the pathogenesis of immunocomplex inflammation. The study of the activity of the classical complement pathway showed significant changes in the studied blood parameters.

KEYWORDS: Erythrocytes, inflammation, immunoglobulins, athletes, immune system.

INTRODUCTION

In the literature of recent years, one of the important health problems, namely anemia of the child and adolescent population, is widely discussed. At the same time, the true prevalence of anemia of various etiologies in the children's population, according to different authors, ranges from 3.8% to76%. This is also noted by the statistics of all countries without exception. Currently, the issues of preserving and strengthening the health of adolescent children are very acute in the Republic of Uzbekistan. Teenagers are the intellectual potential of our republic, the preservation of their health is one of the most important criteria for the well-being of the state as a whole. Over the past 5 years, according to the literature, the

morbidity of children under the age of 14 years has increased by 17.1 %, at the age of 15-17 years - by 19%. At the same time, the highest growth figures were noted for the following classes of diseases: diseases of the blood and hematopoietic organs - by 47%, including anemia (by 78%). Hemic hypoxia in this situation is one of the reasons for the decrease in the activity of a number of enzymatic systems, which leads to a violation of cellular and tissue metabolism. The most common anemia occurs in young athletes who specialize in sports with the manifestation of endurance, with prolonged aerobic and aerobic-anaerobic loads. Overstrain of the blood system in conditions of intense muscle activity is a little-studied phenomenon. Various points of view are expressed about the causes of anemia in athletes: hemolysis of red blood cells in the capillaries of the lower extremities (mainly in runners), increased destruction of red blood cells as a result of an increase in their fragility, systemic changes in protein metabolism in response to additional loads. However, in each specific case of anemia in athletes, first of all, it is necessary to exclude the causes that are not related to strenuous muscle activity, namely, foci of chronic infection. One of the reasons for this condition, in our opinion, is the lack of proper attention to the quality of medical care for children involved in sports and the proper organization of the training process. Based on the above, strengthening and preserving the health of the younger generation are of particular relevance. The above was the basis for once again addressing the problem of disorders in the composition of red blood and linking it with a chronic viral infection in adolescent athletes, aimed at improving the state of health, and therefore sports achievements.

The purpose of this study was to study the interaction of red blood cells and the parameters of the immune system in adolescent athletes.

Material and methods of research: In order to identify biomedical and socio-hygienic factors affecting the health of children and adolescents engaged in children's and youth sports schools, 125 young athletes aged 11-17 years of Samarkand were surveyed and interviewed. Among them, there were 81 boys (65.1%), 44 girls (34.9%).

This age is chosen because 11 years is the age at which sports specialization begins in many sports. In general, in the system of long-term training of young athletes, the following stages are distinguished: preliminary training - at the age of 6-9 years, initial sports specialization - at 10 -12 years, in-depth training in the chosen sport - at 13-15 years, sports improvement - at the age of 16 years and older, taking into account age and individual anatomical and physiological capabilities, Numerous studies have shown that the formation of chronic

diseases in schoolchildren in most cases begins from the age of 12. When forming the sample population, the method of random selection was used. The sample included children and teenagers who have been playing sports for more than one year, performing at competitions, representing such sports as football, basketball, volleyball, tennis, table tennis, athletics. The material collection program provided for the boiling of information from primary medical documentation. All the data were entered into a specially developed "Map of the study of the morbidity of children and adolescents of children's and youth sports schools according to the data of the appeal". At this stage, a comprehensive assessment of the health status of pupils of sports schools, depending on gender and age, was carried out. The analysis of morbidity was carried out in accordance with the International Statistical Classification of Diseases and Health-Related Problems of the 10th revision.

Blood sampling was carried out in the morning on an empty stomach from the ulnar vein of 0.5 ml, blood serum was isolated by centrifugation and freezing for further testing. The concentration of immunoglobulins in the blood serum of classes M and G was determined by the ELISA method. In this case, we used a diagnosticum of the company BCM Adenovirus ELISA IgG/IgM.

The control group, by age, gender and type of sport, consisted of adolescents of the same age without any somatic diseases. The collection of capillary blood for analysis was carried out in the morning on an empty stomach before training. The blood test was carried out on an automatic hematological analyzer Micros 60 (AVX, France). The following parameters were studied: the concentration of hemoglobin in the blood (Hb), the number of red blood cells (Er), hematocrit (Ht), the average volume of red blood cells (MCV), the average content of hemoglobin in the red blood cell (MCH), the average concentration of hemoglobin in the red blood cell (MCHC), the indicator of the degree of anisocytosis (RDV).The content of immunoglobulin G, M components of complement C3 and C4, as well as haptoglobin were studied by the enzyme immunoassay method using HUMAN test kits.

Mathematical and statistical methods were used to process the obtained data at each stage of the study. Relative values, representativeness errors, and the reliability of differences in indicators according to the Student's criterion were calculated (the differences were considered reliable at $p < 0.05$).

Research results and their discussion: When analyzing the obtained research results, it was

revealed that the majority of adolescents had functional disorders of individual organs or systems and so-called borderline states. First of all, these are nosological forms at the stage of subclinical or initial manifestations, i.e. pre-diseases. Behind their appearance is either an increase in pathogenetic factors, or a weakening of sanogenetic mechanisms, a decrease in the adaptability of the body. At the same time, the formation of low-symptomatic conditions occurs, in which general malaise, asthenoneurotic phenomena come to the fore. The analysis of the structure of morbidity in the study of adolescent development maps showed that children's infections were in the first place in terms of frequency of occurrence. 74% of adolescents (92 boys and girls) have a history of children's respiratory viral infections; influenza, adenovirus infection in the anamnesis. Cases of respiratory viral infections are not more often than 1-3 times a year during the traditional seasonal increase in the number of cases of acute respiratory infections and influenza epidemics (winter and spring months). It was revealed that the health status of adolescent girls is consistently at a lower level compared to young men.

When analyzing the results of the studies presented in Table 1, it shows that a decrease in the number of red blood cells below 3, $9x10^{12}$/l was detected mainly in females, they were much more common than in males - 36 people among girls (84%) and 27 people among boys (22%). When analyzing the level of hemoglobin in athletes specializing in various sports, it was revealed that the most common mild anemia occurs in girls in cyclic and game sports. The majority of the examined patients were diagnosed with microcytic anemia-MCV < 75 fl. At the same time, erythrocyte hypochromia (according to MSN < 27pg and MSNS < 32g%) was registered in more than half of the examined patients with anemia. Anisocytosis (RDV>15%) was detected in 74 people (58.9%).

Table 1: Indicators of the red part of the blood in adolescent athletes by sport and gender.

Types of sport	Number of participants		Anemia was detected	
	males	females	males	females
Cyclic	21	8	11	13
Games	11	23	4	14
Martial arts	23	7	9	5
Speed and power sports	26	6	3	4
In total	81	44	27(22%)	36(84%)

Thus, the majority of adolescent athletes with disorders in the red part of the blood had signs (microcytosis, hypochromia, anisocytosis), which, according to numerous data, is much more common than other anemic conditions.

In modern high-performance sports, a number of athletes have a breakdown of adaptive mechanisms, accompanied by a decrease in immunological reactivity and an increase in the sickness rate against the background of violations of both humoral and cellular immunity. At the same time, the sorption capacity of their receptor apparatus also changes. It is noted that in secondary immunodeficiency conditions caused by chronic infections, the ability of cells to bind to immunoglobulins of various classes increases. Immunoglobulins and the main class of these proteins, IgG, play a key role in protecting the body from genetically foreign molecules and microorganisms. The protective role of IgG is combined, due to the variety of effector functions of this protein. The effector functions of IgG are realized when the conformation of the molecule of this protein and the accompanying process of its aggregation change, which serves as the main cause of pathophysiological reactions involving IgG and occur as a result of the interaction of IgG antibodies with antigens or without the participation of the latter. The content of IgG in the circulation also undergoes changes, for example, in infectious and other diseases. As a result of changes in the electric charge of the IgG molecule due to complexation with polyelectrolytes (sulfated and sialated glycoproteins and their cleavage products (proteo - and peptidoglycans). The most important representative of the peptidoglycan family is heparin. The interaction of IgG with heparin has not been studied to date. Meanwhile, the theoretical significance of this problem for understanding the role of IgG in the regulation of homeostasis seems obvious. The aim of the work was to evaluate changes in the properties of reacting biomolecules and to clarify the role of disulfide bonds of the IgG molecule in the interaction of this protein with heparin. In this regard, the sorption activity of red blood cells and specific antibodies to various antigens becomes an important indicator.

Erythrocytes, as highly specific in their organization, have some features in the structure of the shells, while maintaining the general principles of the structure of biomembranes. On their surface, red blood cells have receptors for "Fc" - a fragment of the immunoglobulin molecule, which play a certain role in the implementation of immunochemical functions of blood cells, V. A. Odinokova with co-author, (1985). These cells are able to bind and remove immune complexes from the bloodstream. The mechanism is mediated by the complement

component and the corresponding receptors in the membranes of red blood cells. Although the number of receptors on red blood cells is much smaller, an almost 1000-fold excess of the number of circulating red blood cells over white blood cells leads to the fact that about 95% of the receptors in the blood circulation are accounted for by red blood cells.

Taking into account the important role of heparin in the selective therapy of many disorders, we "vivo" studied its effect on the physiological properties of red blood cells of athletes with anemia, where there is a decrease in the concentration parameters of red blood. The object of research was the intact erythrocytes washed with saline solution of healthy adolescents and athletes with mild anemia.

The effect of heparin "in vitro" on the quantitative content of immunoglobulin G and M was studied in two series of studies

- In the first case, intact red blood cells were incubated in an amount of 2.3-3.0 x 10^{12} cells with an equal volume of physiological [solution at a temperature of 37°C for two hours;
- In the second-with a sorbent immobilized with heparin in saline solution.

This sorbent was obtained together with the staff of the Institute of Biorganic Chemistry of the Academy of Sciences of the Republic of Uzbekistan, according to the following method: cotton lint pulp SI-200 is dissolved in a solution of a copper-ammonia complex, emulsified in a mixture of benzene-chloroform, followed by peri-precipitation with acetone acidified with acetic acid. Next, the resulting sorbent was fractionated on nylon sieves and balls of 70-250 microns were isolated. To immobilize heparin, the sorbent was pre-activated with a 0.01 M solution of epichlorohydrin; 1 part (100 ml) of porous cellulose beads (PCBs) was placed in a drum equipped with a mechanical stirrer and 10 ml of a 3N solution of sodium hydroxide and 1 ml of epichlogydrin were added. The mixture was stirred for 90 minutes at room temperature. After 30 minutes, the glass is placed in a water bath and heated for 1 hour at a temperature of 60C. After washing the sorbent with distilled water, the porous cellulose balls are balanced with 0.1 N carbonate-bicarbonate buffer pH=9 and the same heparin in the same buffer at a concentration of I ml/ml. Inhibit for 18 hours at a temperature of 4°C in the refrigerator. After 18 hours, the sorbent is washed with 0.15M sodium chloride solution. The free epoxy groups are reduced with 0.1 M HCI solution. The amount of immobilized heparin was evaluated by spectrophotometry. The content of heparin per I ml/ 10 ml of PCBs. After incubation of intact erythrocytes in two series of the study, erythrocyte membranes were isolated by osmotic hemolysis and centrifugation at 8000 C for 20 minutes. The precipitate,

after three times washing with a buffer solution of ammonium chloride, was treated with a buffer solution of triton X-IQ0 at pH= 2.0. The quantitative content of immunoglobulins of class G and M was studied by immunochemical method. The analysis of the obtained results indicates the peculiarity of the dynamics of the level of immunoglobulin G. In all study groups, there was a tendency to decrease the level of immunoglobulin G when comparing two study groups: incubation with saline solution and a sorbent immobilized with heparin. In the second group of the study, a significant decrease in the concentration of immunoglobulin M was also noted. It is gratifying to note that the trend of a slight decrease in immunoglobulin G was also noted in the group of healthy adolescents. Apparently, during the incubation of red blood cells with a sorbent immobilized with heparin, the bonds with the surface of red blood cells are broken by reactive groups of heparin. At the same time, heparin is not adsorbed to the surface of red blood cells. The study of the incubation medium, after separation of red blood cells by centrifugation, indicated that the accumulation of immunoglobulin G occurs in this intubation medium and the difference between immunoglobulin M media before and after incubation in terms of the content of immunoglobulin is 1.2-1.5 times. The latter confirms the above version about the rupture of bonds with the surface of red blood cells by immobilized heparin and the release of immunoglobulin G into the incubation medium. A peculiar dynamics was noted in relation to the quantitative content of immunoglobulin M, where an increase in its concentration was observed after incubation of red blood cells with a sorbent immobilized with heparin when compared with the indicators of immunoglobulin G. The noted changes, in our opinion, are associated with the release of "Fab" fragments of immunoglobulin M from protein aggregates or immune complexes when exposed to active polycationic groups of heparin.

Table 2: Dynamics of immunoglobulin G and M in blood plasma and erythrocyte membranes in adolescent athletes.

Patients	ImmunoglobulinGIU/мл			ImmunoglobulinMIU/мл		
	Plasma	Blood erythrocytes		Plasma	Blood erythrocytes	
		Saline solution	Sorbent		Saline solution	Sorbent
Teenage athletes with mild anemia	106,84±9,51	14,62±1,13	9,87±0,84	218,64±11,2	36,93±3,27	48,32±4,34
Healthy children	113,73±8,69	4,63±0,33	3,17±0,27	152,81±9,79	13,29±1,14	11,32±1,06

Thus, the effect of the sorbent immobilized with heparin leads to a decrease in the concentration of immunoglobulin G and M adsorbed on the surface of red blood cells and the release of "Fab" fragments of immunoglobulin G and M from protein aggregates. In our opinion, a decrease in the level of aggregates on the surface of red blood cells, i.e. immune complexes consisting of immunoglobulin G and M aggregates when exposed to heparin is a positive reaction, since the aggregate state of IgG and IgM is the main cause of pathophysiological reactions involving their aggregates on the surface of functionally impaired red blood cells and does not allow adequate oxygen transport during physical exertion. As is known, heparin samples with a high content of sulfate are more active, have a large number of negatively infected sulfuric acid residues and the degree of sulfation of heparin can affect its ability to bind aggregates formed from immune complexes (immunoglobulin+antigen) having a positive charge due to positively infected amino acids. The question arises why teenage athletes who have suffered a viral infection are more likely to have mild anemia, which manifests itself in the form of dysadaptation during physical exertion. To do this, we conducted an additional study, where we studied the level of haptoglobin in blood plasma. The role of the latter is to bind free hemoglobin formed during the destruction of red blood cells by adhesive circulating immune complexes and the complement system.

As is known, immunoglobulins and antigen-antibody complexes belong to the activators of the complement system. In turn, complement proteins opsonize immune complexes for their subsequent phagocytosis and mediate the destruction of various blood cells and microorganisms. The terminal components of the complement cascade-C5b, C6, C7, C8 and C9 bind to each other and form a membrane-attacking complex (MAC), which causes cell lysis, creating a channel that penetrates the cell membrane, disrupts the osmotic balance in the cell, through which ions penetrate into the cell and water enters. The cell swells, the membrane becomes permeable to macromolecules, which then leave the cell. As a result, the lysis of blood cells, in particular red blood cells, occurs, which leads to hemolysis of the cell and the release of free hemoglobin into the bloodstream. Consequently, by binding to antigen-antibody complexes on the surface of blood cells, complement proteins increase their solubility and contribute to their destruction by phagocytes. Therefore, the activation of complement on the surface of the body's cells, where antigen-antibody complexes are formed, can have disastrous consequences for the body.

All of the above indicates the undoubted contribution of the components of the complement system to the pathogenesis of immunocomplex inflammation. The study of the activity of the classical complement pathway showed significant changes in the studied blood parameters.

Table 3: Dynamics of the quantitative content of the complement component of the classical pathway in the blood plasma of athletes (mg/dl).

Indicator	Comparison group	Main group
Complement componentC3	65,92±4,89	126,35±8,24*
Complement componentC5a	2,24+0,13	6,74+0,46*
Haptoglobin content	42,78±3,51	13,89+0,73*

Note: * - the differences relative to the data of group 1 are significant P<0.05

The table shows that all athletes with mild anemia had significant differences in the degree of activity of the classical complement pathway. The high activity of the classical complement pathway in the examined groups may be associated with increased consumption of the complement system for the destruction of immune complexes and blood cells. In this contingent of subjects, the level of activity of the classical complement pathway shows the transition to the formation of immune complexes and, indirectly, the connection of adaptive immune response components to the inflammation process. Relatively high levels of activity of the classical pathway indicates a sufficient severity of the immune response in this category of patients, which, apparently, is associated with the depletion of the reserves of the immune response due to chronic disease. It should be noted that the C5a complement is a multicomponent plasma enzyme system that exhibits lysis and opsonization functions during activation. Thus, in athletes with mild anemia with an immunocomplex etiology of inflammation, higher concentrations of C5a complement were determined, which exceeded those by 2.6 times. It is known that the C5a complement system is always in a state of readiness, but its activity is minimal. This watchdog function is provided by the fixation of the C3 subunit of the complement on pathogens and the host's own tissues. Through this component of the complement, the formation of anaphylactic C5a and the terminal membrane-attacking complex C5B - 9 are realized. Accordingly, high concentrations of C5a, determined in the group by the immunocomplex etiology of inflammation in athletes, are predisposing to the formation of autoagression relative to blood cells, in particular red blood cells, which leads to the destruction of this blood cell. A prolonged increase in the levels of this complement sub-component potentiates the damaging effect of membrane-attacking complexes and leads to an increase in free hemoglobin in the blood. This condition

adaptively enhances the synthesis of a reactive protein-haptoglobin, which binds free hemoglobin and removes it from the body. All this is ultimately accompanied not only by a latent form of anemia, but also by a decrease in the phagocytic activity of the athlete's body and the development of immune complex pathology.

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