

Functional Dynamics of Hemostasis and Hemorheology in Young Men at Risk of Arterial Hypertension

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Of great medical and social importance in modern conditions is the increase in the effectiveness of preventing the development of arterial hypertension at a young age. Purpose of the work: to evaluate the impact of systematic dosed jogging on the parameters of the homeostasis system and the rheological properties of blood in adolescents with a predisposition to the development of arterial hypertension. The study included 60 young men with high normal blood pressure and the risk of developing arterial hypertension with normal body weight. They were divided into 2 groups. The first of them (31 people) began regular jogging for 1 hour a day, 6 times a week for 1 year. The second group (29 young men) kept their previous inactive way of life. The work took into account the level of blood pressure, the amount of fibrinogen in the blood, plasminogen activity, the amount of soluble fibrin-monomer complexes, activated partial thromboplastin time, international normalized ratio, platelet aggregation, blood viscosity. Student's t-test was calculated. As a result of regular jogging in young men with a predisposition to the formation of arterial hypertension, it was possible to normalize the level of blood pressure, homeostasis parameters and hemorheology parameters taken into account. The changes achieved had a very positive effect on microcirculation, providing a general recovery. Long-term low physical activity in young men at risk of developing arterial hypertension contributed to the preservation of elevated blood pressure numbers, aggravation of homeostasis disorders and deterioration of blood rheology.

Keywords: Adolescence; Arterial hypertension; Blood rheology; Hemostasis; Muscle activity; Physical training.

Unfortunately, arterial hypertension (AH) is becoming more and more common in modern society. In recent years, this disease has been widely affecting the population of young and mature age in the economically developed countries of the world. For this reason, it is an important cause of the physical weakening of people of working age, their disability and mortality¹. Even in the case of

a stable course of hypertension, the incidence of sudden vascular thrombosis of any localization, which has a risk of death, is high^{2,3}.

An important goal of hypertension therapy is the stable normalization of blood pressure with an increase in the overall quality of life, minimizing the risk of vascular complications and increasing life expectancy. Currently, various options for drug

therapy are being actively improved, designed to provide an organ-protective effect and reduce the risk of thrombotic manifestations⁴. It has been noted that drugs from the group of calcium antagonists, drugs from the group of angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, diuretics and statins, which are used to treat different categories of patients with hypertension, can weaken the mechanisms of hemostasis^{5,6,7}.

Of great importance for science and practice is the continued search for options for preventing the development of hypertension with the help of non-pharmacological agents that can weaken and sometimes level out many manifestations of this pathological process^{8,9,10}. Of these, regular physical activity is very effective¹¹. Previously, they showed their ability to provide general health improvement and strengthening of the cardiovascular system¹², the ability to inhibit the progression of arterial hypertension¹³, and sometimes they could normalize blood pressure levels, making it unnecessary to take antihypertensive drugs^{14,15}. At the same time, in previous works, no attention was paid to the possibilities of regular aerobic exercise in relation to the prevention of the development of arterial hypertension and the appearance of various hematological disorders that accompany it in young men with high normal blood pressure. For this reason, it was of interest to evaluate the impact of regular jogging on hemostatic and rheological disorders present in young men at risk of developing hypertension.

Purpose of the work: to evaluate the impact of systematic dosed jogging on the parameters of the homeostasis system and the rheological properties of blood in adolescents with a predisposition to the development of arterial hypertension.

MATERIALS AND METHODS

The performed study was approved by the ethical committee of the Russian State Social University in Moscow (Russia) (protocol No. 4 dated April 17, 2017). The study included 60 males of adolescence (19.8 ± 1.3 years) at risk of developing arterial hypertension (AH was present in both parents) with normal body weight. All young men at the time of taking the study had high

normal blood pressure. All surveyed gave written, informed, voluntary consent to their participation in the study. All the observed were divided into 2 observation groups. Boys of the 1st group (31 people) began to voluntarily perform regular aerobic exercise of moderate intensity in the form of jogging at a free pace for 1 hour a day, 6 times a week for 1 year. The criterion for inclusion in the first observation group was the desire to cooperate with the researchers and the agreement to strictly follow their recommendations. The second observation group consisted of 29 young men who refused to change their lifestyle and increase the level of their daily physical activity. All surveyed in both groups were given standard recommendations on the importance and necessity of changes in their lifestyle: reducing the daily intake of table salt with food, the danger of overeating, the need to reduce psycho-emotional stress, and explained the great importance of increasing daily physical activity. The control group consisted of 34 healthy young men (mean age 19.1 ± 0.8 years). The persons who made up both observation groups were under constant control of their condition. They were examined, according to the methods used in the work, twice - when taken into the study and after 1 year. The control group was examined once.

The examination included a dynamic measurement of blood pressure. In all cases, the amount of fibrinogen in the blood was assessed using the Claus method¹⁶. For this, human thrombin with an activity of 100 U/ml, Tris buffer, 0.05 M pH 7.3-7.4, standard calibration plasma with a known fibrinogen content, and a coagulometer were used. The reagents and equipment used in this method were manufactured by Technology Standard (Russia).

Plasminogen activity was assessed using the kinetic method using an FP-901 device (LabSystems, Finland). In this case, standard chromogenic substrates DadeBehring (Germany) were used. Using a standard set of reagents manufactured by Technology-standard (Russia), the amount of soluble fibrin-monomer complexes was determined visually¹⁶. For this purpose, the following reagents were used: ortho-phenanthroline hydrochloride, 70 mg (the reagent was packaged in 96 wells of the tablet); control-minus (lyophilized human blood plasma, not containing soluble fibrin-monomer complexes),

per 1 ml; control-plus (lyophilized human plasma containing soluble fibrin-monomer complexes), per 1 ml; stirring stick - 1 piece, scarifying spear - 1 piece.

The value of activated partial thromboplastin time was recorded using a coagulometer HumaClot manufactured by HUMAN GmbH (Germany) using a standard HemoStat aPTT-EL reagent kit. The international normalized ratio was estimated using the standard Quick method¹⁶. The platelet aggregation ability was monitored by a turbidimetric method on a Biola two-channel laser platelet aggregation analyzer (Russia). As an aggregation inducer, 0.5 μ M ADP was used, manufactured by Technology Standard (Russia)¹⁷. Blood viscosity was assessed using a rotational viscometer AKR-2 (Russia). The blood viscosity was recorded at shear rates of 200 s^{-1} and 20 s^{-1} with further standard calculation of the erythrocyte aggregation index and the erythrocyte deformability index. The results obtained were statistically processed using Student's t-test.

RESULTS

When included in the study, the young men of both observation groups had a stable increase in blood pressure values to a high normal level. In patients of the first observation group, against the background of regular physical activity, by the end of the study, normalization of blood pressure levels was achieved. The surveyed, who avoided physical training and made up the second group, maintained an elevated level of blood pressure (Table 1).

At the beginning of the study, no statistically significant differences were found between the observation groups in terms of blood rheology parameters (Table 2). The value of blood viscosity when determined under conditions of a shear rate of 200 s^{-1} exceeded the control in the first group by 6.8%, in the second group - by 4.0%. Under conditions of a shear rate of 20 s^{-1} , the values of blood viscosity in both observation groups were also comparable, exceeding the control level by 7.9% and 8.6%, respectively. Initially, the value of the erythrocyte deformability index and the value of the erythrocyte aggregation index in young men in both groups did not statistically differ from each other, tending to a physiologically unfavorable change compared to the control.

When re-examination in both groups of young men, it was possible to establish the presence of a multidirectional trend in the values of blood viscosity. In young men who regularly experienced muscle loads, a tendency was found to reduce blood viscosity at a shear rate of 20 s^{-1} by 7.8% and at a shear rate of 200 s^{-1} by 6.5%. In young men who refused to perform regular physical activity, the values of these indicators tended to increase by 5.7% and 5.9%, respectively. In the young men who made up the first group, a tendency to a decrease in the value of the erythrocyte aggregation index by 5.7% was found, and in the representatives of the second group, a tendency to an increase in this indicator by 4.6% was noted. The value of the erythrocyte deformability index in the first group of the observed underwent an upward trend, and in the second group showed a downward trend.

Table 1. Dynamics of the blood pressure level in the examined

Parameters taken for evaluation	Young men at risk of hypertension during physical activity, n=31, M±m		Young men at risk of hypertension in standard conditions, n=29, M±m		Control, n=34, M±m
	Exodus	After 1 year of observation	Exodus	After 1 year of observation	
Systolic blood pressure, mm Hg	138.2±2.26**	122.3±1.92 ⁺	136.1±2.90**	142.4±2.86**	118.6±1.24
Diastolic blood pressure, mm Hg	88.6±0.76*	80.3±0.68 ⁺	88.2±1.12*	93.6±1.16*	81.4±0.95

Legend: the significance of differences in the observation and control groups * - $p < 0.05$, ** - $p < 0.01$; the significance of changes in indicators in the observation groups: ⁺ - $p < 0.05$.

During the first examination, the young men of both observation groups showed similar disturbances in the homeostasis system (Table 3). In both groups, the outcome showed a significant comparable reduction in the duration of activated partial thromboplastin time, a similar tendency to a decrease in the level of plasminogen, a comparable tendency to an increase in the value of the international normalized ratio, a similar increase in blood concentrations of fibrinogen and soluble fibrin-monomer complexes, compared with the control level.

Severity of spontaneous platelet aggregation by 11.4%, stimulated aggregation - by 15.0% was found. In the second group of young men at risk of developing hypertension, the initial spontaneous and induced by the addition of ADP to plasma - platelet aggregation exceeded the control level by 10.5% and 17.8%, respectively.

At the end of the study, in the group of young men who regularly experience running loads, a statistically significant increase in the indicator of activated partial thromboplastin time was found, a tendency to an increase in the level of plasminogen in their blood was noted, a tendency to a decrease in the value of the international normalized ratio was revealed in them, a decrease

in their blood concentrations fibrinogen and soluble fibrin-monomer complexes. In the group of young men at risk of developing hypertension who avoided regular physical training, by the end of the study, a tendency to a decrease in the duration of activated partial thromboplastin time, a tendency to an increase in the international normalized ratio, a tendency to a decrease in the concentration of plasminogen in the blood with an increase in the level of fibrinogen in the plasma and a tendency to increase it contains soluble fibrin-monomeric complexes.

After 1 year of regular physical training in the first group of young men at risk of hypertension, a decrease in the activity of spontaneously occurring platelet aggregation by 11.4% and a decrease in the severity of ADP-stimulated platelet aggregation by 15.6% were noted. In the second observation group, which refused to perform regular physical activity, spontaneous and ADP-induced platelet aggregation exceeded the outcome level by 14.3% and 18.7%, respectively. Differences in platelet aggregation by the end of the study between the observation groups reached 26.3% for spontaneous platelet aggregation ($p < 0.01$), for the stimulated process - 40.6% ($p < 0.01$).

Table 2. Dynamics of blood rheology indices in the examined

Parameters taken for evaluation	Young men at risk of hypertension during physical activity, n=31, M±m		Young men at risk of hypertension in standard conditions, n=29, M±m		Control, n=34, M±m
	Exodus	After 1 year of observation	Exodus	After 1 year of observation	
The value of the erythrocyte aggregation index	1.30±0.08	1.23±0.07	1.31±0.05	1.37±0.10	1.24±0.08
The value of the erythrocyte deformability index	1.09±0.07	1.13±0.06	1.10±0.03	1.05±0.12	1.13±0.05
The value of blood viscosity at 200s ⁻¹ , sPoise	4.39±0.42	4.12±0.34	4.40±0.36	4.65±0.47*	4.11±0.28
The value of blood viscosity at 20 s ⁻¹ , sPoise	6.49±0.33	6.02±0.28	6.53±0.49	6.92±0.52*	6.01±0.35

Legend: the significance of differences in the observation and control groups * - $p < 0.05$, ** - $p < 0.01$.

DISCUSSION

Continuing a detailed study of many aspects of human physiology can create a reliable basis for continuing developments to improve technologies for comprehensive health improvement^{5,18}. A balanced analysis of the results achieved in the course of research can help increase the possibilities of modern healthcare¹⁹. In previous studies on animals and humans, it was found that the hemostatic system and the rheological properties of blood can strongly respond to various effects on the body²⁰. This is especially pronounced under the influence of an unfavorable nature and in the case of the formation of an obvious pathology¹⁰.

It is recognized that regular physical activity can have a very positive effect on the body of mammals and humans^{21,22}. Under these

conditions, the activity of various components of the hemostasis system is very physiologically beneficial, and the rheological properties of blood as a whole and the rheological parameters of its erythrocytes are optimized⁶. With changes in these blood parameters, modern researchers link the improvement of the microcirculation process and the stimulation of metabolism against the background of dosed feasible physical exertion^{10,23}.

The results of the study allow us to consider that regular jogging at a free pace physiologically favorably weakens hemocoagulation. Apparently, this is due to a decrease in the concentration of many coagulation factors in the blood. Probably, in the blood of young men who started running, there was a weakening of thromboplastin synthesis and contact activation of factor XII was inhibited^{24,25}. Systematic jogging led to a decrease in the

Table 3. Dynamics of hemostasis indices in the examined

Parameters taken for evaluation	Young men at risk of hypertension during physical activity, n=31, M±m		Young men at risk of hypertension in standard conditions, n=29, M±m		Control, n=34, M±m
	Exodus	After 1 year of observation	Exodus	After 1 year of observation	
The magnitude of the international normalized ratio	1.17±0.12	1.10±0.07	1.18±0.07	1.23±0.10	1.11±0.11
The value of the activated partial thromboplastin time, s	26.2±0.42*	29.4±0.35+	26.8±0.48*	25.0±0.32*	29.7±0.27
Fibrinogen concentration, g/l	3.3±0.17**	2.3±0.19++	3.2±0.23**	3.9±0.18***+	2.5±0.10
The amount of soluble fibrin-monomer complexes, mg/dl	3.3±0.14**	2.4±0.17++	3.2±0.10**	3.4±0.20**	2.4±0.17
Plasminogen concentration, %	85.0±0.31	92.2±0.44	84.8±0.35	81.8±0.48*	90.6±0.33
The activity of spontaneous platelet aggregation, units	1.27±0.15*	1.14±0.20+	1.26±0.16*	1.44±0.27***+	1.14±0.12
The activity of platelet aggregation stimulated by 0.5 μM ADP, units	2.45±0.26*	2.12±0.19+	2.51±0.22*	2.98±0.30***+	2.13±0.16

Legend: the significance of differences in the observation and control groups * - $p < 0.05$, ** - $p < 0.01$; the significance of changes in indicators in the observation groups: + - $p < 0.05$, ++ - $p < 0.01$.

amount of fibrinogen and soluble fibrin-monomer complexes in the blood, which indicated a slowdown in the process of fibrin polymerization. This process was inhibited by the fibrinolysis system activated during exercise²⁶. Refusal of regular physical training led to the opposite effect, contributing to the activation of hemocoagulation and the weakening of fibrinolysis.

An increase in aerobic physical activity enhances the antioxidant capacity of the body²⁷. This contributes to the inhibition of platelet aggregation in the blood. Obviously, regular physical activity increases the amount of cyclic adenosine monophosphate in the cytoplasm of platelets, weakens the synthesis of thromboxane A₂. This slows down the formation of platelet aggregates in the vascular bed. Low muscle activity in individuals of the second group was accompanied by the formation of a tendency to increase platelet activity. In many ways, this is due to a decrease in the level of cyclic adenosine monophosphate in their platelets and an increase in the synthesis of thromboxane A₂ in them. This contributed to an increase in the number of aggregates of different sizes from activated platelets in the blood of young men of the second group^{28,29}.

The increase in the severity of erythrocyte aggregation found in the representatives of the second group of subjects was largely provided by developing changes in the magnitude of the charge of their membranes. Apparently, they were based on the destruction of some of the existing glycoproteins on their surface under the action of lipid peroxidation. It is known that it is activated already at the very beginning of the development of AH, especially in conditions of low physical activity³⁰. The excess of free radicals formed in this case led to damage to the structures of the membrane and various plasma proteins in the examined patients. This led to the intensification of the appearance of "bridges" between individual erythrocytes, causing their aggregation. An increase in the level of lipid peroxidation products in the liquid part of the blood and in erythrocytes inevitably increases the threshold for their disaggregation due to increased binding of red blood cells in aggregates and damage to erythrocyte membranes³¹.

Obviously, the weakening of erythrocyte aggregation revealed against the background

of an increase in muscle activity in the first observation group is determined by an increase in the antioxidant defense system of the whole organism and a decrease in the influence of catecholamines, the level of which almost always decreases under conditions of activation of muscle activity³². Under these conditions, the number of α -receptors on erythrocytes decreases, the Ca²⁺-calmodulin system and reactions involving phosphatidylinositol are inhibited in them³³. In addition, the resulting decrease in the activity of α -adrenergic receptors contributes to the activation of adenylate cyclase. This leads to an increase in the level of cyclic adenosine monophosphate in erythrocytes, inhibits the entry of Ca²⁺ into them, creating conditions for weakening their aggregation³⁴.

CONCLUSION

Despite the existing limitations of the study, which consists in examining adolescent males who have a high predisposition to arterial hypertension due to the presence of arterial hypertension in both their parents and who do not have various metabolic disorders, clear conclusions can be drawn. Systematic physical training in the form of regular jogging contributes to the normalization of blood pressure levels in young men at risk of developing hypertension. Against this background, they have a decrease in the functional activity of platelets, hemocoagulation, the aggregation properties of erythrocytes decrease, and the liquid properties of the blood are optimized. Positive changes in the body that develop in young men at risk of developing hypertension during regular runs create conditions for optimizing microcirculation, which creates conditions for the general improvement of their body.

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Conflict of Interest

No conflict of interest is declared.

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