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Impact estimation of long regular exercise on hemostasis and blood rheological features of patients with incipient hypertension



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ABSTRACT

Background: For practice, it is still very important to search ways of early correction of arterial hypertension displays with the help of non-medication. In this connection, it seems to be important to identify the impact of regular athletic exercise on early developing of arterial hypertension, hemostatic and rheological abnormalities in persons of young age.

Methods: We investigated 99 young patients with arterial hypertension of the 1st degree. The patients were divided into two comparable groups. The first experimental group consisted of 57 persons who regularly - one hour a day, six times a week, during a year - experienced athletic exercises. The second experimental group consisted of 42 persons and was composed of patients who had no wish to train physically and take medicines. Control group was composed of 43 healthy persons of the same age. In all the examined patients we fulfilled the investigation of basic indices of hemostasis, blood viscosity, erythrocytes' aggregation and deformability. The data were processed by Student's t-criterion.

Results: Patients of both experimental groups initially were noted to have hemostasis activation and negative changes of blood rheological features. In a year of regular athletic exercise patients of the first experimental group reached normalization of arterial pressure. They also had a decrease of platelets' aggregative ability (aggregation with ADP 2.13 ± 0.16 Un) and activity weakening of hemostasis plasma link (INR 1.12 ± 0.05 , APTT 29.8 ± 0.37 s) to control level. Avoidance of exercise in the second experimental group promoted further increase of functional activity of platelets and plasma hemostasis at simultaneous worsening of relevant blood rheological features.

Conclusion: At initial stages of arterial hypertension development in case of regular athletic exercise fulfilled by young patients it is quite possible to reach normalization of arterial pressure level, hemostasis activity, and hemorheology.

Keywords: arterial hypertension, hemostasis, platelets, erythrocytes, blood viscosity, exercises.

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INTRODUCTION

Arterial hypertension (AH) is met more and more often among the employable population of different world countries being an important reason for social deadadaptation, invalidation and mortality.^{1,2} Even at stable AH course lethality and frequency of sharp vascular thromboses development are left too big.^{3,4}

The basic aims of AH treatment are stable normalization of arterial pressure, improvement of patients' life quality, risk minimization of their different complications and rise of their ability to survive.^{5,6} At present we have well-worked medication which includes hypotension medicines of different pharmacological groups often having organoprotective action and positively influencing the activity of platelets and other components of

hemostasis system.^{7,8} As it turned out the ability to decrease platelets' functional activity belongs to calcium antagonists,^{9,10} APC (automatic phase control) inhibitors,^{11,12,13} blockers of angiotensin receptors,^{14,15,16} diuretics,^{17,18,19} and also statins^{20,21,22} applied for treatment of patients with AH and its combination with metabolic abnormalities.^{23,24} It becomes clear that application of these leads to weakens platelets' adhesion and aggregative ability, hemocoagulation activity and improves rheological blood features what allows to decrease the frequency of thromboses' development of any localization in case of patients with AH.^{25,26}

Great significance for practice has the search of ways to fulfill maximum early AH correction by non-medication able to block the development of

the given pathological process.^{27,28} The central place in their number is occupied by exercises having shown their ability at their regular fulfillment to decrease the level of arterial pressure, and in some cases to normalize it what sometimes allows to do without medicines for a long time.²⁹ In this connection, it seems to be important to clear up the impact of regular athletic exercises on early stages of AH development, hemostatic and rheological dysfunctions of young persons.

This study aimed to study the impact of long regular athletic exercises on indices of hemostasis system and blood rheology of young patients with arterial hypertension of the 1st degree existing not more than two years.

METHODS

The fulfillment of the study was approved by the ethic committee of South-West State University in t. Kursk (Russia) (record №4 from 17.04.2014) and Kursk Institute of Social Education (branch of Russian State Social University) (record №5 from 12.05.2014). In this study, we took 99 patients (42 women and 57 men) with primary AH of the first degree with low and middle cardiovascular risk, without signs of circulatory deficiency at the age of 28-32 years (on average 30.4 ± 0.6 years) with normal body mass. All the patients had a hereditary predisposition to AH (one parent or both had AH). In all the cases the examined patients had AH not more than two years. Patients with symptomatic AH were excluded. All the patients gave written informed volunteer agreement to take part in the study. As for associated diseases, 12 patients had chronic acalculous cholecystitis at the stage of persistent remission, and two patients had chronic gastritis at the stage of persistent remission. The patients didn't systematically receive hypotension therapy, only seldom at destabilizations of arterial pressure they took inhibitors of angiotensin-converting enzyme.

All the patients were divided into two experimental groups. Patients of the 1st group (57 patients) were prescribed regular aerobic exercises of middle intensity for one hour a day, six times a week during a year in the athletic section of Kursk Institute of Social Education (a branch of RSSU) (walking, jogging and broad jumps). The criteria for inclusion of the first group wished to cooperate with researchers and readiness to follow their recommendations strictly. In the second group, we included 42 patients who had no wish to take medicines and increase the level of their physical activity. Patients of both groups were given common recommendations about the necessity of changes in their way of life, including lowering of table salt

consumption, barring of overeating, avoidance of psychoemotional loads and were explained about the necessity of increased motion activity. The control group was composed of 43 healthy people (21 women and 22 men) of young age (the average age 30.1 ± 0.5 years). Patients of both groups were under dynamic control. Their full examination according to used in our work methods was made twice (before the beginning of the study and in a year). The control group was examined once. The examination included dynamic control of arterial pressure level.

All the examined patients were defined to have fibrinogen content in blood by modified Klaus' method, and also plasminogen activity by a kinetic method with the help of FP-901 device ("LabSystems", Finland) with chromogenic substrates of the firm "Dade Behring" (Germany).³⁰ With the help of reagents of the firm "Technology Standard" by the visual method, we defined the concentration of soluble fibrin-monomeric complexes (SFMC). Activated partial thromboplastin time (APTT) was investigated with coagulometer "HumaClot" of the firm "HUMAN GmbH" (Germany) with a set of reagents HemoStat aPTT-EL.³⁰ The measurement of international normalized relation (INR) was made by Quick's method.³⁰ Platelets' aggregative ability was examined at two-canals laser analyzer of platelets' aggregation "Biola" (Russia) by the turbidimetric method. As inductor we used $0,5 \text{mkM ADP}$.³¹ Registration of blood viscosity was fulfilled at the rotary viscometer AKR-2 (Russia). The following indices were defined: blood viscosity at shift speeds 200s^{-1} and 20s^{-1} with the consequent calculation of erythrocytes' aggregation index and erythrocytes' deformability index. Statistical processing of received results was made with the help of Student's t-criterion.

RESULTS

When the patients of both groups were taken into the investigation, they had a stable increase of arterial pressure corresponding to AH of the 1st degree. Patients from the first group on the background of regular exercise fulfillment were noticed to have normalization of arterial pressure level by the end of the investigation. At the same time patients from the second group having avoided exercise still had increased level of arterial pressure.

Examination of patients' hemostasis in both experimental groups at the beginning of investigation found no reliable differences in hemostasis defined indices' values (table).

At the beginning of investigation between both groups of patients, there were also found no reliable differences between indices of blood rheological

Table Changes in parameters of young patients with incipient arterial hypertension

Parameters	Patients with physical activity, n=57 M±m		Patients without physical exercise, n=42 M±m		Control, n=43 M±m
	initial state	after 1 year	initial state	after 1 year	
Arterial Pressure					
Systolic blood pressure, mmHg.	149.6 ± 2.37**	125.7 ± 1.73	148.7 ± 3.05**	149.2 ± 2.97**	120.3 ± 1.33
diastolic blood pressure, mmHg.	95.7 ± 0.98*	81.6 ± 0.75	96.3 ± 1.03*	97.1 ± 1.12*	82.1 ± 0.92
Indicators of Hemostasis					
INR	1.18 ± 0.10	1.12 ± 0.05	1.17 ± 0.09	1.22 ± 0.12	1.12 ± 0.07
APTT, sec	26.7 ± 0.45*	29.8 ± 0.37 ⁺	27.0 ± 0.50	25.2 ± 0.9*	29.3 ± 0.32
Fibrinogen, g/l	3.2 ± 0.22	2.6 ± 0.14 ⁺⁺	3.1 ± 0.32	3.8 ± 0.32 ⁺⁺	2.8 ± 0.11
SFMC, mg/decilitre	3.2 ± 0.16*	2.5 ± 0.18 ⁺⁺	3.1 ± 0.14*	3.2 ± 0.22 ⁺	2.6 ± 0.19
Plasminogen, %	85.2 ± 0.36	92.0 ± 0.48	84.9 ± 0.38	82.2 ± 0.57*	90.7 ± 0.45
Spontaneous platelets' aggregation, Units	1.26 ± 0.17*	1.15 ± 0.18 ⁺	1.25 ± 0.19*	1.42 ± 0.24 ^{***}	1.16 ± 0.14
Platelets' aggregation 0,5 mkM ADP, Units	2.48 ± 0.23*	2.13 ± 0.16 ⁺	2.52 ± 0.25*	2.92 ± 0.36 ^{***}	2.12 ± 0.17
Indices of Blood Rheology					
Index of erythrocytes' aggregation	1.29 ± 0.09	1.22 ± 0.06	1.28 ± 0.08	1.33±0.12	1.23 ± 0.06
index of erythrocytes' deformability	1.08 ± 0.10	1.13 ± 0.09	1.09 ± 0.07	1.06 ± 0.11	1.12 ± 0.07
Blood viscosity at 200 sec ⁻¹ , centipoise	4.41 ± 0.45	4.13 ± 0.30	4.39 ± 0.39	4.61 ± 0.49*	4.12 ± 0.34
Blood viscosity at 20 sec ⁻¹ , centipoise	6.48 ± 0.41	6.02 ± 0.32	6.52 ± 0.49	6.88 ± 0.57*	6.02 ± 0.39

Conventions: reliability of differences in groups of patients from control indices * - $p < 0,05$, ** - $p < 0,01$; reliability of indices' dynamics in groups of patients: + - $p < 0,05$, ++ - $p < 0,01$.

features. Blood viscosity at shift speed 200 s⁻¹ in the first group was 4.41 ± 0.45 centipoise and in the second group was 4.39 ± 0.39 centipoise. At shift speed 20 s⁻¹ values of blood viscosity were also comparable, being 6.48 ± 0.41 centipoise and 6.52 ± 0.49 centipoise, for the first group and second group, respectively. Initially, the index of erythrocytes' deformability and the index of erythrocytes' aggregation of patients in both groups didn't differ statistically from each other.

To the end of investigation period patients from the group regularly having exercise were noticed to have reliable lengthening of APTT, the tendency for an increase in plasminogen, tendency for decrease in INR and decrease in fibrinogen and SFMC concentration.

In the group of patients who avoided exercise till the end of the study, we managed to find a reduction of APTT duration, the increase in INR, a tendency to decrease in a plasminogen at increase of fibrinogen in blood and stability of SFMC.

Through 1 year of physical training in the first group of patients with spontaneous platelet aggregation decreased 9.6% driven on by 16.4%. Patients from the second group having refused from exercise had increase of spontaneous and ADP-induced platelets' aggregation. It exceeded initial values on 13.6% and 15.9%, respectively. At the same time, differences in platelets' aggregation in both groups to the end of the investigation were 23.5% ($p < 0.01$)

for spontaneous aggregation and 37.1% ($p < 0.01$) for stimulated one.

At repeated estimation of rheological blood features' relevant indices in a year we found the multidirectional tendency of blood viscosity in patients of both groups. Persons who regularly had exercise were noted to have the tendency to blood viscosity lowering at shift speeds 20s⁻¹ and 200s⁻¹ on 7.1% and 6.3%, respectively. In patients who refused from exercise given indices had the tendency to grow on 5.5% and 5.0%, respectively. In patients from the first group we also noticed the tendency to value decrease of erythrocytes' aggregation index on 5.7%, and in patients from the second group, we found the tendency to its growth on 3.9%. At the same time, erythrocytes' deformability index in the 1st group had the tendency to increase, and in the 2nd group had the tendency to decrease.

DISCUSSION

Continuation of advanced examination of different aspects of man's pathological physiology^{32,33} can provide a solid basis for further perfection of rehabilitation technologies.^{34,35} Summation of received by researchers knowledge will allow founding a firm basis for further health care development.^{36,37} In previous investigations with the help of different biological objects and human beings, hemostasis and hemorheology, react rather keenly on

environmental impacts^{38,39} including unfavorable environmental factors and development of different abnormalities in an organism^{40,41} and obvious pathology.^{42,43} It is also known that graduated exercise can make a many-sided favorable impact on a living being.^{44,45} It was noticed that on their background activity weakening of hemostasis system components and improvement of blood rheological parameters on the whole and rheological characteristics of erythrocytes are developing.^{29,46} With these very changes of hematologic indices we connect improvement of microcirculation processes and intensification of metabolic processes on the background of graduated exercise^{47,48} without any dependence on existing patients' heredity.⁴⁹⁻⁵²

As the result of fulfilled investigation on the background of patients' motion activity widening, we found normalization of arterial pressure level which was accompanied by a decrease of hemostasis activity and improvement in blood rheology. At the same time, in the case of absence of regular exercise estimation of hemostasis and blood rheology showed the reverse regularity which provided differences' evidence of relevant indices in both groups of patients with AH of the 1st degree to the end of the investigation.

Received results allow us to consider that regular athletic exercise weaken hemocoagulation process along both ways of its realization. It is evidently connected with activity lowering of most participating in it coagulation factors. In these patients' blood, we also noticed evident tendency to thromboplastin generation decrease and contact activation of XII factor weakening.⁴⁶ Regular exercise also led to fibrinogen and SFMC decrease in blood what pointed at inhibition of its polymerization which was blocked by activating in these conditions system of fibrinolysis. Renunciation of exercise made the opposite impact on the patients promoting the strengthening of all the hemocoagulation mechanisms and lowering of fibrinolysis activity.

Referring to literature data we can consider that widening of physical activity with the help of aerobic exercise stimulates antioxidant organism's protection.^{53,54} It promotes decrease of platelets' ability to both spontaneous and stimulated aggregation.^{55,56} We have some ground to consider that regular muscle activity rises the level of cyclic adenosine monophosphate in patients' platelets decreasing the formation of thromboxane A₂,⁵⁷ blocking the formation of thrombocyte aggregates in the lumen of the vascular bed.⁵⁸ Low level of physical activity in the second group of patients was accompanied by tendency to growth of platelets' aggregative ability, evidently as the result of lowering of cyclic adenosine monophosphate and

strengthening of thromboxane A₂ synthesis in them what inevitably led to quantity increase of platelets' dynamic aggregates in their blood.^{59,60}

Found in the second group of patients strengthening of erythrocytes' aggregation can mostly be provided by coming changes in their membranes' charge because of degradation on their surface of some glycoproteins under the influence of always strengthening in conditions of AH and low physical activity lipids' peroxidation.⁶¹ Intensification of oxygen active forms' generation in the given conditions provides the patients with oxidative alteration of membrane's structures at the simultaneous damage of globular plasma proteins possessing the ability to be connected as "bridges" between erythrocytes and realize their aggregation.⁶² At the same time, rise of lipids' peroxidation products in plasma and erythrocytes increases the threshold of their disaggregation because of stimulation of red corpuscles' cohesion in aggregates and speed rise of the given process on the background of oxidative lipids' damages of their membrane.⁶³

It should be supposed that the weakening of erythrocytes' aggregation found in the first group of patients is mostly provided by strengthening in conditions of increased physical activity of antioxidant organism's protectability and lowering the impact of catecholamines, the concentration of which lowers at regular muscle activity.⁶⁴ On this background there takes place decrease of α₁-receptors' activity, weakening of the system Ca²⁺-calmodulin and cascade of intracellular reactions of phosphatidylinositol.⁶⁵ At the same time there takes place lowering of α₂-adrenoreceptors' activity what leads to strengthening of adenylate cyclase in the course of physiological impacts from receptors to Gi-proteins what causes rise of cyclic adenosine monophosphate quantity in erythrocytes, blocks Ca²⁺ inflow into them providing not high erythrocytes' aggregation.⁶⁶

We can think that in patients having regular rational aerobic exercise erythrocytes are mostly able to deformation what is an important factor of supporting necessary perfusion in microcirculatory bed in them. It is possible that there is some rise of ATR content in their erythrocytes what positively influences the interaction of spectrin, actin and other integral proteins of erythrocyte membrane playing an important role in supporting of its features. Besides, in the first group of patients rise of erythrocytes' deformability should be connected with lowering of unbounded ions Ca²⁺ concentration in them what minimizes its interaction with membrane's proteins and makes it more deformable. At the same time in erythrocytes of patients from the second group there takes place apparent decrease of ATR content,

what negatively changes the interaction character of spectrin, actin and other integral proteins of erythrocyte membrane. Lowering of their erythrocytes' deformability should also be connected with the rise in them of the surplus of unbounded ions Ca^{2+} which interacting with membrane's proteins make it firmer and less deformable, positively influencing hemostasis processes.

Ability to aggregation and deformability of erythrocytes are closely connected with each other during hemocirculation. It is known that their aggregation mostly defines the value of solid blood viscosity at low shift speeds and erythrocytes' deformability at high ones.^{61,62} In this connection the very weakening of erythrocytes' aggregative ability of patients on the background of the rational widening of muscle activity promotes the improvement of blood fluidity at shift speed 20 s^{-1} , i.e. in capillaries and venules, and erythrocytes' deformability strengthening - in conditions of shift speed 200 s^{-1} , i.e. in arterial bed.

CONCLUSION

Regular physical activity of aerobic leads patients with AH of the 1st degree to stabilization of arterial pressure up to the normal level and decrease of plasma hemostasis and platelets' functional activity, weakening of erythrocytes' aggregative ability and improvement of blood fluidity at different shift speeds. Given changes in patients' organisms with initial displays of AH can positively influence microcirculation providing common health-improving effect. Purposeful avoidance of exercise by patients with AH of the 1st degree leads them to the preservation of steadily increased level of arterial pressure and to deepening of hemostatic and rheological abnormalities.

CONFLICT OF INTEREST

No conflict of interest to declare.

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