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CHANGES OF LIPIDOGRAM AND MORPHOLOGICAL ASPECTS OF ENDOTHELIAL DYSFUNCTION AT PHYSICAL ACTIVITY OF VARYING INTENSITY

Abstract. *It was found out, that physical activities of high intensity are accompanied by development of severe endothelial dysfunction, which is manifested by atherogenic damage of the femoral artery. Use of physical activity of moderate intensity is characterized by anti-atherogenic changes in the blood serum of the animals and the normal structure of the femoral artery wall.*
Key words: *physical activities of various intensity, hypercholesterolemia, endothelial dysfunction, femoral artery.*

Introduction. Motor activity is an essential part of everyday life of each person and a base of active functioning of the body and its resistance to adverse actions. Accordingly, dynamic compliance between the needs of the body, which are caused by the load of physical activity, and admission of oxygen and various substrates to the organs of the musculoskeletal system needs to be achieved. This adaptation to physical activity (FA) is provided by optimal interaction of body systems [5]. Structural ensure of adaptation to FA is manifested at different hierarchical levels of its organization – from molecular to systemic. Although the adaptive capabilities of the organism are significant, they are limited, and beyond them there is the state of dysadaptation, which causes development of destructive reversible and irreversible pathological processes. In the process of adaptation to increased muscle activity cardiovascular system is one of the first to adapt to these conditions. At the same time, FA of varying intensity affects the structure and function both the heart with various vessels and blood system significantly [3,4]. The relevance of this problem is caused by both the practical use of physical activity of varying intensity and the need to understand the key mechanisms through which it affects the processes of atherogenesis [1].

Despite there is a large amount of studies devoted to vascular endothelial dysfunction, many questions are still unclear. In particular, the features of the development of endothelial dysfunction and the damage of other layers of femoral artery wall at a background of various physical activities are not studied.

Objective: to study changes of lipid spectrum of blood and degree of damages of femoral artery wall at physical activities of varying intensity.

Materials and methods. Study was performed with 30 white male outbred rats with the body weight of 180-240 g. Physical activities of high and moderate intensity (FAHI and FAMI) were simulated on 20 male rats by running in a treadmill at speeds of 36 and 24 m/min during 1 hour daily for 2 months according to the methodology. 10 animals were the control group. Experiments were carried out according to “General Ethical Principles of Animals Experiments”, ratified on the First National Congress of bioethics (Kyiv, 2001). Blood samples for experiments were taken fasting from the abdominal aorta under nembutal anesthesia.

For determination of total cholesterol (TCS), cholesterol of low density lipoproteins (LDL-C),

cholesterol of high density lipoproteins (HDL-C) in blood serum sets of firm "Olveks Diagnosticum" were used, and for determination of triglyceride (TG) and total lipids (TL) the sets of PLIVA-Lachema a.s. were used. Cholesterol of low density lipoproteins (LDL-C) was calculated by the Fridvald formula: LDL-C=TCS - HDL-C/2.2 [1], and the atherogenic factor (AF) was calculated by the formula of A.N. Klimov: AF = (TCS - HDL-C)/HDL-C [6].

Macroscopic evaluation of atherosclerotic changes of femoral artery carried out by the method of G.G. Avtandilov, and microscopic one was carried out on histological samples stained with hematoxylin-eosin and fuchsin. For statistical processing of the digital data modern computer program "STATISTICA 5.0" was used.

Results and discussion. Analysis of research works shows that different types of physical activities, in particular, of moderate or high intensity, both dynamic and static, influence the level of various lipid fractions in blood serum and the state of the endothelium of blood vessels significantly [1,2].

Studying the influence of physical activities of high and moderate intensity on the level of some lipid of blood system (Table) and on the structure of the femoral artery wall, it was noticed, that FAHI influence the mentioned parameters negatively, and FAMI influence positively. Thus, under the action of FAHI the level of TL increases on 26% ($p<0.001$), the level of TCS increases on 61% ($p<0.001$), the level of LDL-C increases on 52% ($p<0.001$), the content of triglycerides increases in 2.56 times ($p<0.001$), and the concentration of HDL-C increases on 141% ($p<0.001$). At the same time the atherogenic factor increases in 3.76 times ($p<0.001$) compared to the control group.

Due to some researches [2,5,6], the increased level of TG and TCS at FAHI is the compensatory reaction, which is aimed at power supply for skeletal muscles, working at the maximum tension. There is intensive mechanism of mobilization of fats from fat depots and their oxidation in skeletal muscle. This quickly leads to the formation of oxygen debt, development of the tension hypoxia and switching to anaerobic way of energy supply (anaerobic glycolysis) with development of metabolic acidosis due to accumulation of lactic and pyruvic acids. In such conditions fatty acids are not fully oxidized. At the metabolic acidosis the activity of lipoprotein lipase, which catalyzes hydrolysis of lipoproteins in the bloodstream, decreases significantly. The excess of fatty acids and lipoproteins in the circulating blood continues until the body returns to aerobic energy supply and capture of lipids in the liver is over.

Table

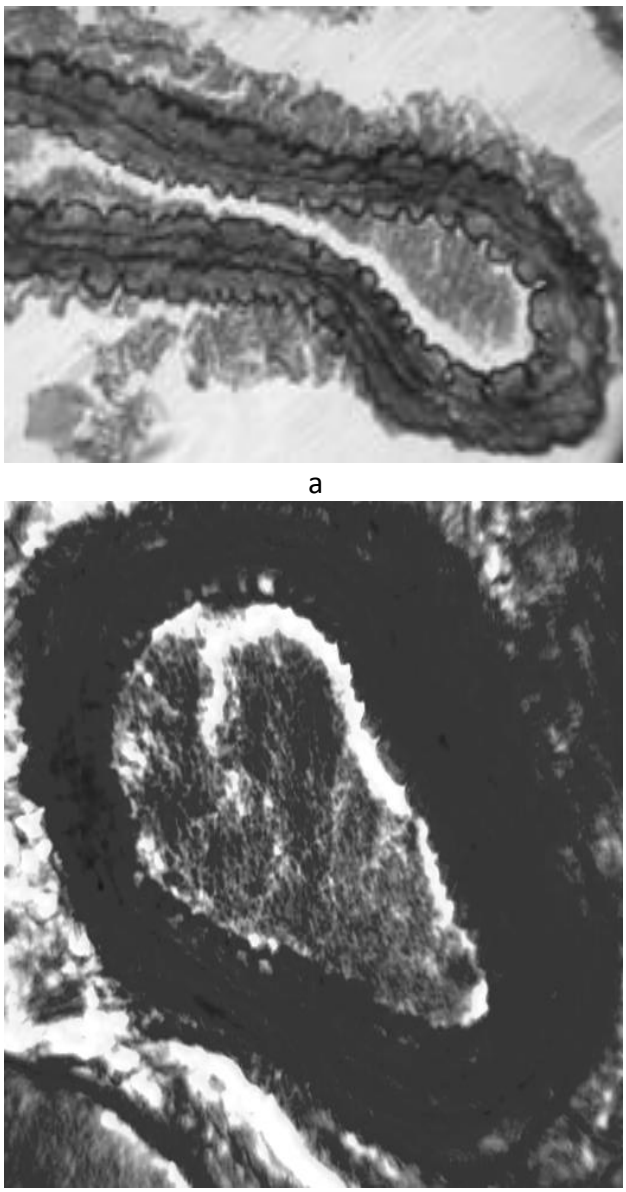
Content of lipids in the blood serum of various groups of the experimental animals (M±m)

Indexes	Control (n=10)	FAHI (n=10)	FAMI (n=10)
Total lipids, g/l	3,88± 0,13	4,90 ± 0,02*	3,75 ± 0,15
Total cholesterol, mmol/l	1,27 ±0,02	2,05 ±0,30*	1,20 ± 0,04
Triglycerides, mmol/l	1,21 ±0,03	3,10 ±0,01*	1,24 ± 0,04
LDL-cholesterol, mmol/l	1,14 ±0,01	1,73 ± 0,02*	0,80 ±0,01*
HDL-cholesterol, mmol/l	0,29 ±0,02	0,70 ± 0,08*	0,88 ±0,01*
Atherogenic factor	0,51 ±0,03	1,92 ±0,07*	0,36 ±0,05*

*Note: * - the changes are statistically significant (P <0.05) relatively to controls*

Increase in the content of atherogenic lipids in the blood serum causes damage of the inner vascular membrane, including the one of femoral artery, accompanied by development of endothelial dysfunction and significant violations of hemodynamics. The results of histological study show, that the main structural manifestations of damage of the intima are local destruction of the endothelial edema and separation of the inner elastic membrane, edema of the muscle membrane, local destruction of the external elastic membrane. These changes are well observed when comparing the damaged sample with the normal structure of femoral artery wall (Fig. 1a, b), which agrees to the literature data [4,6].

In contradistinction to FAHI, at FAMI there is a decrease in the concentration of TL in the



a

b

Fig. 1. Structure of the femoral artery wall of the control rat (a) ant its local damage at FAHI (b). Hematoxylin and eosin stain. Magnification: 8x10.

blood serum on 3,4%, of TCS - on 6%, LDL-C - on 30%, while the contents of TG and HDL-C increase on 2% and 203% accordingly. At the same time AF decreases in 1.42 times compared to the control. It is well known, that at FAMI red muscles with slow contraction type and dense capillary net, which fibers contain a lot of mitochondria, are mainly involved in the process of contraction. This provides a high level of aerobic oxidation in the muscles and reliable maintenance of homeostasis of the blood [3], which provides for optimal conditions for the transport processes. In this connection, moderate physical activities have antiatherogenic properties and provide normal structure of the walls of the blood vessels, which is confirmed by histological studies of femoral artery.

Thus, physical activity of moderate intensity have antiatherogenic character in the lipid spectrum of the blood serum. This is the result of enhancement of the blood flow through the capillaries of the muscles and activation of the endothelial lipoprotein lipase, which helps to eliminate atherogenic forms of lipids from the blood and to increase the content of lipoproteins with antiatherogenic properties in the blood [2,4,6]. Hence, physical activities of moderate intensity can be recommended to apply in order to correct the lipid changes of the blood system.

Conclusions. 1. Physical activities of high intensity are accompanied by the significant changes of lipid transport system of blood, which results in an increase in the content of TL, TCS, TG, LDL-C in blood serum, increase in the atherogenic factor and decrease in the concentration of HDL-C.

2. On the contrary physical activities of moderate intensity lead to an increase in the concentration of HDL-C and a decrease in the content of TL, TCS, TG, LDL-C and atherogenic factor.

3. Structural reorganization of the femoral artery wall at FAHI is characterized by the destruction and detachment of the endothelial layer, edema and stratification of the inner elastic membrane and muscle membrane, whereas there is no of these changes at FAMI.

Prospects for further research. It is planned to study the correlative relationships between the production of substances with multidirectional properties (NO and endothelin-1) by endothelium, and to study blood lipid spectrum at hypercholesterolemia and physical activity of varying intensity with its following confirmation by electron microscopy.

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