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FUNCTIONAL STATE OF LIPITRANSPORT SYSTEM IN PATIENTS WITH ATHERSCLEROSIS WITH FATTY LOAD

Abstract. *Postprandial dyslipidemia is considered as one of the leading factors affecting the development and progression of atherosclerosis, due to the prolonged exposure of lipoproteins in the systemic circulation, the activation of their oxidative modification. However, until now latent atherogenic abnormalities in the lipid transport system have not been adequately studied. The aim of our study was to study the state of the lipid transport system and its functional activity under fat loading conditions in patients with atherosclerosis. 51 patients took part in the survey, 26 of them men and 25 women, the average age of 55.65 ± 2.43 years, who signed the information agreement. All patients were divided into groups on nosological characteristics. The technique of the standard disposable food fat load, proposed by J. Patsch, has been applied. In the course of the study, the fatty acid spectrum of the blood and lipoprotein lipase activity were evaluated. A pronounced decrease in the lipid transport system tolerance to fat loading was revealed, which manifested itself in a significant increase in the content of saturated and decreased ω-3 polyunsaturated fatty acids in plasma against the background of inadequate lipoprotein lipase activity in patients with atherosclerosis.*
Key words*: fatty acid spectrum of blood, lipoprotein lipase, fat load, atherosclerosis.*

Introduction. Numerous international and national programs for combating diseases of the cardiovascular system convincingly show that atherosclerosis is one of the most widespread diseases of our time, which has maintained a stable tendency to growth during the last decades [1, 8].

In the pathogenesis of atherosclerosis, the main role is played both by disorders of the lipid transport system in the body, and by the various types of nutritional loads that are an integral part of everyday human life [4, 6, 7]. It was found that the disorders in postprandial metabolism of plasma lipids leads to a prolonged exposure of lipoproteins in the systemic circulation, activation of their oxidative modification, which increases the risk of atherosclerotic vascular injury [2, 10].

The literature highlights the use of fat loading to study the metabolism of lipoproteins in humans, which allows us to characterize the changes in the lipid transport system and to search for markers of possible atherogenic changes that occur in humans after taking fatty foods [3, 5, 9]. At the same time, to the present time, little attention was paid to the stage of lipid assimilation by the tissue itself. At the same time, it is known that somatic cells, primarily muscle, use mainly fatty acids in metabolism. The key mechanism of their use in tissues is cleavage due to lipoprotein lipase, fixed on the vessel wall [11, 12].

The objective of our study was to study the functional activity of the lipid transport system under fat loading conditions in patients with atherosclerosis, taking into account the activity of lipoprotein lipase.

Materials and methods of research. 51 patients took part in the survey, 26 of them men and 25 women aged 45 to 62 years (mean age 55.65 ± 2.43 years). All patients were divided into groups: 17 patients were included in the group with diffuse cardiosclerosis at normal values of arterial pressure (AP), among them 9 men and 6 women (mean age 57.62 ± 1.52 years). The group of patients with diffuse cardiosclerosis in combination with essential hypertension (AP + EH) included 10 men and 9 women (mean age 56.23 ± 1.96 years). The comparison group consisted of patients with stable coronary artery disease without special signs of coronary

atherosclerosis - 15 men (7 men and 8 women, mean age 58.22 ± 1.27 years). Practically healthy people were examined as controls - 12 people (8 men and 7 women, average age 42.97 ± 1.18 years). The above groups were comparable in age and sex. Each patient gave information consent to participate in the study.

A single fat load was performed according to the method of J. R. Patsch (1983), which consisted of taking 20% cream with 50 grams of white bread (based on 65 g of emulsified fat per 1 m2 of the body surface) on an empty stomach for 5 minutes. Blood was taken on an empty stomach, 3 and 6 hours after eating.

The fatty acid blood profile was assessed by the content of palmitic, stearic, oleic, linoleic, arachidonic, α-linolenic, eicosapentaenoic (EPA) and docosahexaenoic (DHA) acids (gas chromatography method according to the F. Marangoni (2004) on Agilent MS chromatography mass spectrometer D 1100 (Hewlett Packard, USA).

Activity of blood plasma lipoprotein lipase was determined by titration according to the method of T.Olivecrona (1992) in the modification of V.N.Titov (2003) obtained from the median cubital vein 15 minutes after the administration of heparin from Biolec (Ukraine) at a dose of 50 IU / kg. The indicator of enzyme activity is the amount of released fatty acids from triglycerides for 1 hour (mmol/l h).

Results of the study and their discussion. The comparative characteristics of the fatty acid profile in different study groups revealed multidirectional changes. All the groups showed an increased level of saturated fatty acids (SFA) in fasting state and a reduced concentration of polyunsaturated (PUFA), with both ω-3 and ω-6 relative to the control group (Fig. 1). The values of ω-3 PUFA and ω-6 PUFA were approximately equal in the study groups.

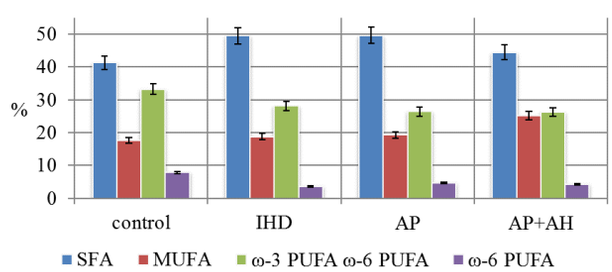

Fig. 1. The fasting level of fatty acids in the blood in patients of the study groups.

It should be noted that the level of monounsaturated fatty acids (MUFA) was elevated only in the group of patients with AT + EH (25.11 ± 2.27 vs. 17.66 ± 3.20%), in the remaining groups the concentration of the fatty acids was at the level of control values.

In the first postprandial phase, after loading (in 3 hours), more pronounced changes in the concentration of SFA in IHD groups (54.78 ± 2.17%) and AT + EH (54.35 ± 2.63%) were noted (Fig. 2). At the same time, the increase in total SFA concentration was due to an increase in the level of stearic acid by 16.83% and 74.16%, respectively. While in the AT group the changes were proportional.

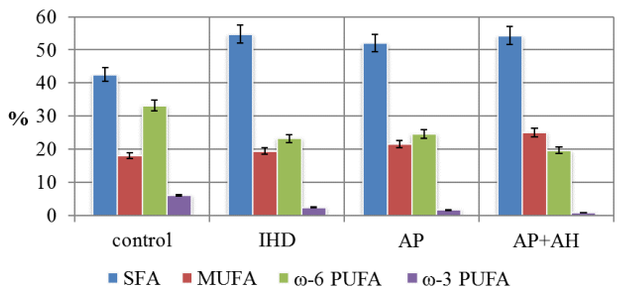

Fig. 2. The level of fatty acids in the blood of patients in the study groups 3 hours after the load.

In contrast to the indices of healthy volunteers in the study groups, the concentration of ω-6 PUFA decreased, and the level of MUFA increased. The change in the level of ω-6 PUFA in the IHD and AT + EH groups resulted from a drop in the concentration of linoleic acid (by 19.91% and 27.75%, respectively), while in the control group and AT - by arachidonic acid (By 6.32% and 41.17%, respectively). The dynamics of ω-3 PUFA in all groups was unidirectional with control values.

The second phase of postprandial fat loading was characterized by an elevated SFA level in all study groups, while in the control group there was a drop in the level equally due to palmitic and stearic acids (Fig. 3).

The level of the SFA in the groups of patients with IHD and AT was lower than the control values, while in the AT + EH group it slightly exceeded the control data. In the group of healthy volunteers, a decrease in ω-6 PUFA was noted primarily as a result of a decrease in the concentration of linoleic acid (more than 4.5 times), and the level of arachidonic acid at that time increased 2-fold. In the comparison group, the relative amount of ω-6 PUFA was at the

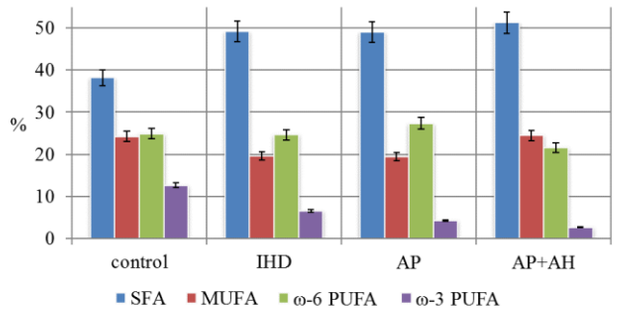

Fig.3. Dynamics of fatty acids after fat loading in the study groups.

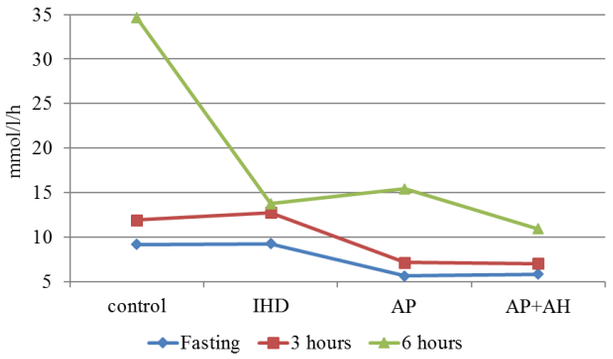

Fig. 4. Lipoprotein lipase activity in the study groups as a function of fat load time.

control level, but the change was due to a 2.5-fold increase in the concentration of arachidonic acid against a background of a 2-fold decrease in the level of linoleic acid. In the group of patients with AT, the content of ω-6 PUFA was higher both in control data and in comparison with other study groups. At the same time, the increase in concentration occurred as a result of an equal increase in the arachidonic titer and the fall of linoleic acid. Only in the AT + EH group there was a decrease in the level of ω-6 PUFA, the dynamics of changes was associated with an equivalent drop in linoleic acid against a background of increased arachidonic acid.

As to the ω-3 PUFA in all groups, a tendency to increase in concentration was observed. It was noted that the content of ω-3 PUFAs in the control group was higher than the initial data. In the IHD group, an increase in the concentration of ω-3 PUFA was due to α-linolenic acid, in patients with AT – EPA, and in the AT + EH group, insignificant growth was observed on the part of all acids. At the same time, the level of ω-3 PUFA in all study groups was lower than fasting data at the end of the test.

The studies showed an increase in the enzymatic activity of LPL throughout the study in all groups, without exception, relative to the baseline level (Figure 4). At the same time, the highest LPL activity was observed in the control group during the second phase of postprandial loading.

It should be noted that in patients with atherosclerosis, despite a low initial level of LPL, 6 hours after loading, the enzyme activity was maximal in comparison with other groups of patients, although 3 times lower than the control values.

At the same time, the level of fasting LPL in the IHD group was comparable to the control values, it exceeded slightly the activity in the middle of the test and the control indices, and the indices of the remaining groups, but by 6 hours after the load the level of LPL was lower than the data in the AT group.

Studies have shown that the detected changes in the activity of LPL in different phases of the fat load lead to a decrease in the effectiveness of lipolysis, which disrupts the mechanism of cholesterol transport and lipoprotein metabolism in general.

Conclusions. Thus, under the conditions of atherosclerotic disorders there was revealed a marked decrease in the tolerance of the lipid transport system to fat load, manifested in a significant disruption of the transport of fatty acids against the background of inadequate lipoprotein lipase activity. Alimentary fat loading led to a prolonged (more than 6 hours) increase in the content of SFA on the background of a decrease in ω-3 PUFA in plasma.

The main change of the fatty acid blood spectrum was a decrease in the content of unsaturated fatty acids. Since unsaturated fatty acids are the starting material for the formation of regulatory molecules, disturbances in the lipid transport system cause changes in regulatory mechanisms, which in turn aggravate lipid metabolism disorders, and thus stimulate atherogenesis.

Changes in the fractional composition of higher fatty acids in patients with AT + EH after fat loading, in our opinion, are associated with endothelial dysfunction of the vascular wall, which is significantly manifested against the background of alimentary fat load with intensive work of the lipid transport system. The dynamics of the fatty acid spectrum in the group of patients with ischemic heart disease testified of latent

disorders of the lipid transport system.

Prospects for the study. To study the state of the lipid transport system with carbohydrate load and to evaluate the correlation between changes in the lipid profile, fatty acids and lipoprotein lipase in the blood. This will allow in the future to receive new data on the pathogenesis of atherosclerosis.

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