

Research letter

The condition of lipid metabolism, hemostasis and general homocysteine level as a manifestation of endothelial dysfunction at progressing course of atherosclerosis obliterans of the lower extremities

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Abstract: The problems related to studying predictors of atherosclerosis obliterans (ASO) of the lower extremities are quite relevant due to high disability and lethality rate of patients belonging to this group. This study aimed to evaluate the values of lipid profile, general homocysteine and hemostasis in relation to the clinical course of ASO.

Material and Methods — 55 patients with ASO of the lower extremities were divided into two groups: 30 patients with no progressive clinical course, 25 patients with progressive clinical course. The group division was based on the anamnesis (duration of the disease, decrease of painless walking distance during the year, the length of effect lasting from conservative treatment). Data presented as median with lower and upper quartiles – Me (LQ, UQ).

Results — As a result of research, there was a registration of moderate hyperhomocysteinemia – 23.6 (20.1, 26.4) mkmol/l, as well as high values of triglycerides – 2.10 (1.72, 2.51) mmol/l and low-density lipoproteins – 4.48 (3.95, 6.44) mmol/l, against low values of high-density lipoproteins – 1.14 (0.72, 1.40) mmol/l in lipid profile. Development of hypercoagulability and susceptibility to thrombosis in patients is manifestation of endothelial dysfunction, which plays a key role in progression of ASO of the lower extremities.

Keywords: atherosclerosis obliterans, progressive course, hemostasis, lipid profile, homocysteine

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Introduction

Atherosclerosis obliterans (ASO) of the lower extremities has been one of the frequent manifestations of generalized atherosclerosis. It's revealed in 2-3% of the population and forms 20% of all the patients with cardiovascular diseases. The severity of progressive course of ASO of arteries of lower extremities is due to gangrene, which forms during 3 to 5 years. It develops in 10-40% of the patients after they experience the first symptoms and eventually leads to an amputation of an extremity [1, 2].

The factors leading to progressive clinical course of ASO of the lower extremities are hypercholesterolemia, hypertension, smoking, diabetes, obesity, inactive lifestyle, old age [3-8]. It is known that in 1% of cases, the patients older than 55 years of age, during the first 5 years after the diagnosis is made, have critical ischemia of lower extremities and 20% have the episodes of acute ischemic conditions [9].

Dyslipidemia, endothelial dysfunction and changes of hemostasis system also take part in pathogenesis of atherosclerosis development and progressing [10]. According to one of the theories of development of atherosclerosis, the damage of endothelium lies in the base of pathological process, which is defined as an impairment of endothelial function. One of the first

manifestations of endothelial dysfunction is increase of endothelium adhesive qualities for thrombocytes and monocytes, the increase of permeability of the endothelium and the development of hypercoagulability [11, 12]. It's proved that the changes of hemostasis system are taking part in disease development and its progressing [13, 14].

The main functions of endothelium are regulation of vascular walls tonus, thrombocytes adhesion, and growth of smooth muscle cells in arterial wall. In other words, the dysfunction of endothelium characterizes the imbalance between vasodilatation and vasoconstriction factors, anticoagulant and procoagulant factors and also between vascular growth factors and its inhibitors [15-17].

Hyperhomocysteinemia is a predictor of blood clots development caused by atherosclerotic lesion of vessels [18]. The study of factors which influence the clinical course of ASO of the lower extremities is an actual task of the research.

Aim of study: to assess the values of lipid profile indicators, general homocysteine and hemostasis values in patients with ASO of the lower extremities depending on the clinical course.

Table 1. Values of lipid exchange and general homocysteine depending on clinical course of ASO of the lower extremities

Parameters	1 st group	2 nd group
TC, mmol/l	6.35 (6.20, 7.10)	5.40 (4.90, 5.80)*
LDL, mmol/l	3.02 (2.78, 3.30)	4.48 (3.95, 6.44)*
HDL, mmol/l	1.86 (1.43, 2.34)	1.14 (0.72, 1.40)
Tg, mmol/l	1.52 (1.03, 2.17)	2.10 (1.72, 2.51)
AI	2.36 (1.82, 2.94)	4.56 (3.92, 5.58)*
GH, mkmol/l	12.3 (10.2, 14.1)	23.6 (20.1, 26.4)*

* – statistically significant (P<0.05) difference between 1st and 2nd groups. TC, total cholesterol; LDL, low-density lipoproteins cholesterol; HDL, high-density lipoproteins cholesterol; Tg, triglycerides; AI, atherogenic index; GH, general homocysteine.

Table 2. Values of coagulatory component of hemostasis system depending on clinical course of ASO of the lower extremities

Parameters	1 st group	2 nd group
APTT, sec	35.7 (32.6, 36.4)	34.1 (31.9, 35.1)
PT, sec	13.5 (12.3, 14.7)	13.3 (11.9, 15.2)
TT, sec	14.5 (13.1, 15.4)	12.4 (11.6, 12.8)*
INR	1.01 (0.94, 1.17)	0.95 (0.86, 1.14)
Fibrinogen, g/l	3.6* (3.4, 4.1)	4.8 (4.5, 5.8)*

* – statistically significant (P<0.05) difference between 1st and 2nd groups. APTT, activated partial thromboplastin time; PT, prothrombin time; TT, thrombin time; INR, international normalized ratio.

Material and Methods

Design of this study was approved by Ethics Committee of Krasnoyarsk State Medical University n.a. V.F. Voyno-Yasenyetsky (Krasnoyarsk, Russia).

55 patients (46 men and 9 women) with ASO of the lower extremities arteries have undergone medical treatment at the Road Hospital at Krasnoyarsk station of Russian Railways from 2010 to 2013. The average age of patients was 68.4 years, where average ages for women and men were 73.8 and 67.8 years respectively. All patients had IIA-IIIB degree of ischemia according to classification of Leriche-Fontaine's and multilevel lesion of lower extremities arteries [19].

Patients were divided into two groups: the 1st group contained 30 patients with no progressive clinical course of ASO; the 2nd group had 25 patients with progressive clinical course of ASO. The division was based on the anamnesis (duration of the disease, decrease of painless walking distance during the year, length of conservative treatment's effect).

During examination, there have been used physical, laboratory and instrumental methods. As for instrumental method, Doppler echography of lower extremities arteries was made in all patients, and computed tomography (CT) angiography was made by special requirements. General laboratory methods were made for all patients. Total cholesterol (TC), high-density lipoproteins cholesterol (HDL), low-density lipoproteins cholesterol (LDL), triglycerides (TG) and atherogenic index (AI) were chosen as the indicators of condition of lipid metabolism. There have been made researches of hemostasis system such as: activated partial thromboplastin time (APTT), prothrombin time (PT), thrombin time (TT), international normalized ratio (INR) and fibrinogen. Determination of general homocysteine was made by hardphase chemiluminescent enzyme-linked immunosorbent analysis with the device "Arhitect i2000" (Abbott Laboratories, USA), which is a modular system with chemiluminescent technology "Chemiflex".

The obtained results were processed by statistical software package SPSS 17.0. Data presented as median with lower and upper quartiles – Me (LQ, UQ). We used Mann-Whitney U test for pairwise comparisons of studying groups of patients. If P<0.05, differences between groups were recognized as statistically significant.

Results

Comparative analysis of lipid profile, homocysteine and hemostasis values of patients with progressive clinical course (the 1st group) and with no progressive clinical course (the 2nd group) of ASO of the lower extremities was made in our study.

When derived results of research lipid profile values of patients with ASO of the lower extremities were analyzed, increase of total cholesterol was revealed in the 1st group of patients, and significant decrease of this index was revealed in the 2nd group (Table 1). LDL has significantly risen in the 2nd group of patients. Significant increase of triglycerides was revealed at the 2nd group (Table 1). Apparently, in case of progressive clinical course of ASO (2nd group), the activation of neuroendocrine system stimulates lipolysis, that leads to an increase in blood and cell membranes the levels of triglycerides, fatty acids and cholesterol (Table 1).

The concentration of general homocysteine in blood naturally and significantly rises in patients with progressive clinical course of ASO (2nd group) (Table 1).

The study of coagulation process of hemostasis system in patients with progressive and non-progressive clinical course of ASO showed the presence of changes, which are typical for activation of hemostasis system with development of hypercoagulation. There is significant shortening of APTT, TT and increase of fibrinogen level in patients with progressive clinical course (Table 2).

Discussion

Lipid profile of the 1st group of patients with ASO of the lower extremities maybe defined as antiatherogenic due to higher levels of TC and HDL. More atherogenic structure of lipid profile was revealed in the 2nd group of patients, as there are significantly higher levels of triglycerides and LDL against the lower levels of HDL. The most studied and significant risk factor of progression of pathological process is the so-called atherogenic lipid triad: large number of LDL, hypertriglyceridemia, and low concentrations of HDL cholesterol [20]. Moderate hyperhomocysteinemia was revealed in patients with progressive clinical course of ASO. It is in accordance with the literature that endothelial dysfunction may lead to pro-atherogenic effects associated with hyperhomocysteinemia [21-23].

The indicators of coagulation link of hemostasis show the tendency of development of thromboses. The manifestation of hypercoagulability in patients with ASO of the lower extremities might be rated as one of the signs of endothelial dysfunction [24].

The obtained data about the role of lipid metabolism disorder and manifestations of hypercoagulability at progressive clinical course of ASO of the lower extremities cohere with multiple findings in this field. A distinctive feature of this study is the assessment of level of general homocysteine as a marker of endothelial dysfunction at ASO of the lower extremities.

Conclusion

The progressive clinical course of ASO of the lower extremities is characterized by impairment of functional condition of endothelium, which is manifested in hypercoagulability, moderate homocysteinemia, as well as in high values of LDL against lowering concentration of HDL.

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Conflict of interest: none declared.

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