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Amino Acid Imbalance and Atherosclerosis

P.A. Karavay*[1], L.I. Nefyodov[2], N.L. Karavay[3]

[1]*Department of Cardiology of Grodno State Regional Hospital, Belarus*
[2]*Department of Biochemistry Yanka Kupala Grodno State University, Belarus*
[3]*Department of Hyperbaric Oxygenation of Grodno State Regional Hospital Belarus*

Abstract

A mini-review of literature data on the mechanisms of formation of the stock of free amino acids and their derivatives in atherosclerosis and methods for correcting metabolic imbalance.

Keywords: Amino acids, Derivatives, Atherosclerosis

Corresponding Author: **P.A. Karavay**
Department of Cardiology of Grodno State Regional Hospital, Belarus. Tel: +375296376982,
Email: pavel-261995@mail.ru

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Introduction

Atherosclerosis is characterized not only by disturbances in the metabolic flows of carbohydrate (inhibition of gluconeogenesis and activation of glycolysis), lipid (activation of lipolysis, ketosis), but also protein (protein- and hypoalbuminemia), hyperglobulinemia and negative nitrogen balance)[1-4]. The question of the information content of the established changes in the levels of individual amino acids in atherosclerosis and their significance in comparison with other clinical and biochemical criteria remains practically unclear. The unresolved problem of the choice of individual amino acids in the amino acids used for the directed correction of metabolic imbalance in atherosclerosis [5-7].

The importance of amino acids in the regulation of the functions of pathological conditions (vasoaterogenesis, arterial thrombosis) of the cardiovascular system has been convincingly established in a number of studies. Repeatedly described is a decrease in blood lipid levels under the action of glycine and its derivatives, the positive effect of cysteine and aspartate in patients with hyperlipidemia, the lipid-lowering effect of arginine in plasma. High concentrations of amino acids and their derivatives in platelets have been demonstrated, upon activation of which the agonist binds to a specific receptor, forming a complex through which an energy signal that activates phosphatase and mobilizes ionized calcium from the dense tubular system to the cytoplasm is transmitted A study of the amino acid sequences of glycoprotein receptor polypeptides that specifically bind hem coagulation substrates showed the possibility of inhibiting platelet aggregation, adhesion and blood clot formation using synthetic and natural (snake venom) polypeptides containing arginine, glycine, asparagine, valine, proline, phenylalanine and cysteine[1-10]. The protective effect of BCAA (valine, leucine, and isoleucine) in the myocardium is manifested in the maintenance of contractility, macroergs levels (ATP, creatinine phosphate), normalization of aortic and coronary blood flow, cardiac output and cardiac output. The BCAA activates the production of catabolites of the adenine system during post ischemic reperfusion[5], activates the utilization of introduced amino acids to high-energy substrates of Krebs cycle, and helps to restore the functional capabilities of smooth muscle structures[11].

The anti-atherogenic properties of the derivative of sulfur-containing amino acids Tau may be due to the fact that the synthesis of tauro-

cholates promotes lipid absorption, lipolysis, and absorption of fatty acids in the intestine. On the other hand, conjugation of taurine (Tau) with bile acids affects the elimination of cholesterol from the body and thereby controls cholesterogenesis. The anti-atherogenic effect of S-adenosylmethionine, evaluated by increasing the level of glutathione and improving macro- and microcirculation, was investigated against the background of the atherogenic effect of cholesterol[6]. S-adenosylmethionine is recommended as an additive in amino acid mixtures for parenteral nutrition. Currently, the best known commercial preparations of S-adenosylmethionine in Europe are Samyr, Samet and Gambrel. Summarizing the above, it should be noted that the use of amino acid preparations for atherosclerosis is rational and the strategy for their use should be based on the elimination of the amino acid imbalance present in this disease, and the correction of the free sulfur-containing amino acids stock, including the use of taurine, whose anti-atherogenic properties should be considered quite promising[1-8].

Recently, new evidence has been obtained of the participation of amino acids in the pathogenesis of atherosclerosis. Thus, data were obtained on changes in extracellular levels of neurotransmitter amino acids during atherosclerotic brain damage — an increase in the concentration of both excitatory (glutamate, aspartate) and inhibitory amino acids (GABA and taurine) compared with the control. Certain amino acids (leucine) stimulate protein synthesis and inhibit autophagy degradation of the protein regardless of changes in cell volume, since they stimulate motor and protein kinase, which is one of the components of signal transduction of insulin. In the case of low energy supply of cells, motor stimulation with amino acids is inhibited by activation of camp-dependent protein kinase. Amino acid-dependent signaling also promotes insulin production by β-cells. This stimulates the anabolic effect of amino acids[13].

The potential contribution of amino acids to maintaining the electrical conductivity of the heart and stability during ischemia is underestimated. Despite the obvious evidence that amino acids have a cardio protective effect in ischemia and other cardiac disorders, their role in the metabolism of the ischemic heart has not yet been fully elucidated. Studies on the determination of taurine and a number of amino acids predominant in the myocardium (glutamate, aspartate, glutamine and asparagine) in coronary insufficiency showed their differences in the content in the left and right ventricles in coronary insufficiency. A comparison of the levels of these amino acids in aortic stenosis and coronary heart disease in myocardial biopsy specimens showed higher concentrations of taurine in the left ventricle in both situations. With severe, progressive cardio sclerosis in the rabbit myocardium, the content of phenylalanine and tyrosine increased, which was also found in patients with coronary heart disease, and the degree of increase in the level of amino acids changed depending on the clinical forms of coronary atherosclerosis (angina pectoris of various functional classes, myocardial infarction)[1-15].

With regard to coronary heart disease, a special role is played by violations of the formation of methionine, leading to the accumulation in the blood and urine of its predecessor, homocysteine. Examination and treatment of patients with homocysteinuria revealed early and active development of atherosclerosis in young patients: hyperhomocysts (e) anemia is a significant risk factor for the development of atherosclerosis and coronary heart disease. Clinical studies have revealed a significant effect of methionine on the growth of smooth muscle cells, followed by vascular endothelial dysfunction and the development of arterial hypertension with a high risk of thrombosis. In addition to these factors, an increase in homocysteine levels stimulates the growth of smooth muscle cells in the vascular wall, exacerbating the narrowing of the bloodstream.

Lysine is involved in the formation of collagen, the strengthening of the vascular wall, in the formation of carnitine, promotes the utilization of fatty acids for the energy potential of cells and the preservation of the body's immune reactivity. Arginine, a semi-essential amino acid, serves as a precursor to nitric oxide, which affects platelet aggregation and adhesive ability, reducing the ability to thrombosis and reducing the vascular reactivity of atherosclerotic altered arteries and promotes the formation of collagen in the walls of blood vessels[15].

In the blood plasma of patients with endothelial disorders in atherosclerosis, the levels of citrate, GABA, glutamate and cysteine were significantly different in comparison with myocardial ischemia in the content of glutamate and phenylalanine. On this basis, a differential diagnosis of aortic damage with coronary heart disease is considered possible[4].

The human heart uses a large number of free amino acids) as regulators of both myocardial protein metabolism and energy metabolism. The dependence of the myocardium on the amino acid fund of the heart increases with heart failure due to the high activity of the anabolic in the myocardium and the lack of energy for cardiomyocytes. Anabolic reactions in the heart are dependent on the oxidation of fatty acids and glucose. Normally, the functional activity of the Krebs cycle is significantly dependent on the concentration of amino acids. Free amino acids are stimulators of mitochondrial energy under anaerobic conditions, and also contribute to the substrate supply of cycle. Essential to the availability of heart amino acids is that their absorption by the myocardium depends solely on their arterial levels. The content of BCAA amino acids in myocardial metabolism is the most significant activator of anabolism in the heart, the level of which is not dependent on insulin. A slight increase in arterial amino acids leads to a significant increase in myocardial uptake. Amino acids play a crucial role in the metabolism of proteins and heart energy. In heart failure, the arterial pool of free AA, which is the determining factor in the absorption of amino acids by the myocardium, has not been practically studied. So, in comparison with the control, arterial amino acid levels were reduced in patients with heart failure. This decrease was associated with the severity of chronic heart failure and left ventricular dysfunction, in particular the level of aspartic acid[12]. The development and progression of atherosclerosis, which ultimately leads to cardiovascular disease, is causally associated with hypercholesterolemia. Mechanically, the interaction between lipids and the immune system during the progression of atherosclerotic plaques contributes to the chronic inflammation observed in the artery wall during atherosclerosis. Localized inflammation and increased intercellular interaction can affect the polarization and proliferation of immune cells through changes in amino acid metabolism. In particular, the amino acids L-arginine (Arg), L-homoarginine (hArg) and L-tryptophane (Trp) have been extensively studied in the context of cardiovascular diseases, and their effect has been established as key regulators of vascular homeostasis, similar to the functions of immune cells. Cyclic effects between endothelial cells, congenital and adaptive immune cells occur with a change in the metabolism of Arg, hArg and Trp, which have a significant effect on the development of atherosclerosis. Thus, the metabolism and biological functions of Arg, L-homoarginine, and Trp allow them to be reasonably used for the treatment of atherosclerosis[7-22].

Thus, in the pathogenesis of atherosclerosis and its complications, a significant place is given to the processes of formation of amino acid imbalance in biological fluids and tissues. This implies the effective use of individual amino acids or their minicompositions as drugs for the prevention and treatment of atherosclerosis. From the standpoint of diagnostic significance, changes in the concentrations of a number of metabolically and functionally related amino acids or their derivatives

are substantiated.

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