Influence of Anti-anginal therapy on essential amino acids in the blood plasma content of the blood of patients with stable angina

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Abstract
The study includes 55 patients with SA on exertion (functional class II – III) between the ages of 59 to 75 years (mean age of patients was 68, 2 ± 4.2 years). As the object of studies is serum amino acids. So the method of ion-exchange liquid-column chromatography is used. In the blood plasma were determined the following essential amino acids arginine, valine, histidine, isoleucine, leucine, lysine, methionine, tryptophan, fenilalanin. The study was carried out before and after the treatment (after 15-17 days). All patients received conventional antianginal therapy (beta-blocker (Bisoprolol - 5 mg), antiplatelet agents (Acetylsalicylic acid - 75 mg), a statin (Atorvastatin 10 mg), an ACE inhibitor (Enalapril 10 mg). Under the influence of antianginal therapy, it showed a significant decrease in the following essential amino acids: arginine, valine, histidine, isoleucine, leucine, lysine, threonine in the blood serum. Such amino acid changes of blood serum after treatment may indicate that, under the action of antianginal therapy, the metabolism of essential amino acids is enhanced and the synthesis of bioactive substances, improves antiplatelet blood system, the Krebs cycle, the immune system, the exchange of higher fatty acids.

Keywords: Stable angina, amino acids, Anti-anginal therapy.

1. Introduction
Amino Acid (AA) are key nutrients required for cell growth and functioning of vital activity. They serve as "building blocks" not only for the synthesis of proteins, but also many other components of the body and is a source of nitrogen and carbon [9]. At present, it is already known about the cardioprotective properties of AA in patients with different cardiovascular disease [1, 2, 3, 4, 8]. However, it is still not known the mechanisms of AA influence on processes of energy metabolism, as well as other possible routes of influences, which provide the best adaptation of the heart to hypoxia. Recent studies have shown that the human body suffering from coronary heart disease (CHD), is trying to adapt to new work conditions by biochemical transformations, one of which is – to increase the intake of AA in the metabolism of cardiomyocytes. AA are metabolized in the myocardium even in normal conditions [10], but, in fact, myocardial infarction leads to significant changes in biochemical reactions, which result in enhanced use of AA as metabolites [12]. AA metabolic disorders requires further study. Despite significant advances in the treatment of coronary artery disease, the effect of drug therapy on the amino acid composition of the serum of patients with different clinical forms of ischemic heart disease was not studied enough.

1.1 Objective: To study the effect of anti-anginal therapy on essential AA in the plasma content of patients with stable angina (SA).

2. Material and methods
The study involved 55 patients with stable angina on exertion (functional class II – III) between the ages of 59 to 75 years (mean age of patients was 68, 2 ± 4.2 years). The diagnosis of SA was set by the Ministry of Health of Ukraine from 03.07.2006 under protocol № 436 "On approval of the protocols of medical care in the specialty" Cardiology ". The survey did not include patients with heart failure II B and stage III, atrial fibrillation, concomitant diseases in the stage of декompensation, cancer, diseases of the musculoskeletal system. As an object of study, AA of blood serum was used. The method of ion-exchange liquid-column chromatography was used. In the blood plasma was determined the following essential AA: arginine, valine, histidine, isoleucine, leucine, lysine, methionine, tryptophan,
phenylalanine. Essential AA, if to compare with non-essential AA, it cannot be synthesized in the organism but must be acquired from food. The study was performed before and after the treatment (after 15-17 days). All patients received conventional antianginal therapy (beta-blocker (Bisoprolol - 5 mg), Antiplatelet agents (acetylsalicylic acid - 75 mg), Statins (Atorvastatin -10 mg), ACE inhibitor (Enalapril -10 mg).

The results have been processed on a PC using the software package Microsoft Office. Statistical analysis of the data was done using Microsoft Excel 2010. The significance of differences between the average performance of different groups provided by determining the Student -test or Pearson.

3. Results and discussion

Patients SA after treatment compared to the results before treatment, a significant decrease in the content of some AA in the blood serum was observed (Table 1).

Table 1: Essential AA in the serum of patients with SA before and after treatment. Mark / mol / 100 ml (M ± m)

<table>
<thead>
<tr>
<th>AminoAcids</th>
<th>Before Treatment (I)</th>
<th>After Treatment (II)</th>
<th>PI-II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arginine</td>
<td>6,494±0,05</td>
<td>1,190±0,06</td>
<td>P&lt;0,05</td>
</tr>
<tr>
<td>Valine</td>
<td>14,585±0,04</td>
<td>10,000±0,06</td>
<td>P&lt;0,01</td>
</tr>
<tr>
<td>Histidine</td>
<td>8,659±0,06</td>
<td>4,605±0,07</td>
<td>P&lt;0,01</td>
</tr>
<tr>
<td>Isoleucine</td>
<td>4,644±0,04</td>
<td>2,381±0,06</td>
<td>P&lt;0,05</td>
</tr>
<tr>
<td>Leucine</td>
<td>9,06±0,08</td>
<td>6,250±0,08</td>
<td>P&lt;0,05</td>
</tr>
<tr>
<td>Lysine</td>
<td>21,512±0,09</td>
<td>14,286±0,06</td>
<td>P&lt;0,01</td>
</tr>
<tr>
<td>Methionine</td>
<td>2,607±0,03</td>
<td>1,636±0,05</td>
<td>P&lt;0,05</td>
</tr>
<tr>
<td>Threonine</td>
<td>9,635±0,05</td>
<td>5,970±0,08</td>
<td>P&lt;0,01</td>
</tr>
<tr>
<td>Phenylalanine</td>
<td>6,796±0,05</td>
<td>5,714±0,04</td>
<td>P&lt;0,05</td>
</tr>
</tbody>
</table>

In patients with SA after treatment showed a significant decrease in the content of arginine to 5,304 mol / 100 ml (p <0,05). Arginine is a nitric oxide precursor, which affects platelet aggregation, reducing the ability to reduce artery vascular reactivity and promotes the formation of collagen in the vessel wall. Decrease in arginine may indicate increased synthesis of nitric oxide.

In patients with SA under the influence of antianginal therapy, a significant decrease in the content of lysine - to 7,226 mol / 100 ml (p <0,01) in the serum. Lysine forms a connection between transaminase and pyridoxal phosphate, as it has in its composition two amino groups: one affects the peptide bond to proteins enzymes, the second keeps reserves in the integrity of pyridoxal phosphate. Lysine takes part in the formation of collagen, strengthening the vascular wall, in the formation of carnitine that leads utilization of fatty acids for energy potential of cells and immune-reactivity [5]. In patients with SA after treatment showed a significant reduction of valine at 4,585 mol / 100 ml (p <0,01), isoleucine - 2,263nmol / 100ml (p <0,05) and leucine - 2,81nmol / 100ml, (g <0,05). Valine, leucine and isoleucine are essential AA with branched chain – Branched chain aminoacids (BSAAs) [7].

In the first step of catabolism, the same ferment catalyzes the process of transamination of all three AA to form the corresponding branched α-keto acids which are further subjected to oxidative - decarboxylation, whereby as a result we get acetyl-CoA and succinyl-CoA. BSAAs are characterized by positive effect on the heart, as seen in both animals and humans [11]. It was found that BSAAs contribute in the mitochondrial biogenesis of the myocardium and other muscles, preventing oxidative stress and increasing physical endurance, thus extending the life (in experiments on rats) [13]. Thus, reducing the levels of valine, isoleucine and leucine may be indirect evidence of increasing synthesis of acyl-CoA and succinyl-CoA - compounds that enter the Krebs cycle.

Patients with SA, under the influence of antianginal therapy also showed a significant decrease in histidine - 4,054nmkol / 100ml (p <0,01). Histidine has vasodilating effect, normalizes blood lipid composition, and is one of the most important regulators of blood clotting. Glycoprotein rich in histidine is a competitive inhibitor of plasminogen. High plasma levels of inhibitor of the activator of plasminogen 1 and the glycoprotein, which is rich in histidine leads to increased susceptibility to other thrombus. Among all other amino acid histidine is found in the largest amount in protein C. Protein C functions as a natural anticoagulant (blood factors inhibit 5a and 8a, and thus not allowing to form a blood clot); also involved in the process of fibrinolysis - the splitting of the thrombus (inhibitor of plasminogen is blocked, so that plasminogen is activated and cleaves already formed thrombus) [1]. From histidine is produced histamine, which, among other actions helps to reduce blood pressure, vasodilation. Decreasing histidine content in patients with SA after treatment may indirectly indicate improved functions of glycoprotein and Protein-C, which are important regulators of blood clotting, and thus reducing the risk of thrombosis.

In patients under the influence of SA antianginal therapy showed a significant decrease in threonine - to 3,665nmkol / 100ml (p <0,05). Threonine improved cardiovascular system and liver. It is also involved in the synthesis of glycine and serine, which strengthens linkage and all the muscles, including the myocardium [5]. Along with methionine, it participates in the decomposition of fats and fatty acids [6]. Reduction of threonine in patients with SA after antianginal therapy on one hand may indicate a decrease in the level of energy, and on the other strengthening its use in the synthesis of glycine and serine.

4. Findings

1. Under the influence of antianginal therapy in patients with SA, there is a significant decrease in the content of most essential amino acids, which may indicate a strengthening of amino acid metabolism in conditions of myocardial ischemia.

2. Reduced level of arginine could indicate increased synthesis of nitric oxide, Reduced level of lysine could indicate increased synthesis of carnitine and increased utilization of fatty acids, Reduced level of BAAs (valine, leucine and isoleucine) could indicate increased synthesis of acetyl-CoA and succinyl-CoA, the compounds which enter into the Krebs cycle, Reduced level of Histidine could indicate an improvement in the function of glycoproteins and Protein-C, which are important regulators of blood clotting. Reduced level of threonine could indicate increase in its own usage in the synthesis of glycine and serine.

5. References


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