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Biochemical and Heart Adaptations to Physical Training and Supplementation With Amino Acids

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Abstract. Dorofeyeva, E.E., and A.E. Dorofeyev. Biocehmical and heart adaptations to physical training and supplementation with amino acids. *J. Strength Cond. Res. 18(4)000–000. 2004.*—This study evaluated the role of amino acids supplementation on the heart's adaptation under extensive training conditions. Sixty active athletes (bicyclists and swimmers) were separated into 2 groups: 30 were given amino acid mixture (1 g per 10 kg of body weight) for a period of 1 month, and the other 30 were given placebo for the same duration (control group). In the same time period, 20 subjects of similar age not engaged in physical training or sports activities were used as the additional control group. Blood concentrations of alanine transaminase (ALT), asparagine transaminase, lactate dehydrogenase (LDH), gamma-glutamil transpeptidase, alkaline phosphatase (ALP), amylase, triglycerides, albumin, interleukin-6 (IL-6), and interleukin-10 (IL-10) were determined for all subjects before and after the intervention period. Concentrations of LDH and ALP were increased, but concentrations of ALT, albumin, and triglycerides were decreased in the blood of trained athletes compared with healthy subjects not engaged in sports activities. In the athletes, some increases in IL-6 levels were noted; however, they were significantly ($p < 0.05$) lower than in patients with myocardiodystrophy. The values of IL-10 in athletes were higher than concentrations of IL-10 in patients with myocardiodystrophy but still lower than the normal values. The inhibition of IL-10 in blood may play an important role in the induction of apoptosis in cells of the heart muscle. After amino acid supplementation, the athletes' values for albumin, triglycerides, IL-10, LDH, and ALP were significantly increased compared with the post-placebo control groups. Enzyme activities of other enzymes remained unchanged in all groups. Histological data from a secondary study of actual heart tissue showed that the amino acids supplementation may have inhibiting effects on myocardial apoptosis. The criteria of efficiency of the amino acids supplementation were defined by the albumin, IL-6, and IL-10 concentrations.

Key Words. cellular, myocardial tissue, protein, adaptation, apoptosis

Introduction

Intense physical training results in many important metabolic adaptations. During exercise, concentrations of glucose, free fatty acids, and amino acids in the blood of athletes are reduced, whereas lactate increases (5). Free amino acids are also an energy source (about 10%) for muscle function and are involved in many important regulatory functions. Amino acids are not only the substrates for catecholamines synthesis and other biologically active substances, but they are also inhibitors of liver dystrophy, myocardiac dystrophy, and possible inhibitors of apoptosis. The most efficient energy source for cardiomyocytes metabolism, in the condition of reduced level of carbohydrates, is fatty acids. Lipolysis of fat stores is stimulated by catecholamines. Catabolism of fatty acids in the heart muscle during physical exercise is most efficient when blood concentrations of oxygen and glucose are optimal. During extensive short-term exercise conditions, anaerobic type of oxidation is typical for all muscle and leads to accumulation of lactic acid and peroxide. The increase of these catabolites, together with extensive stress conditions, can activate the immune system by increasing secretion of cytokines, particularly interleukin-6 (IL-6) and interleukin-10 (IL-10) (4). Cytokines may stimulate apoptosis after myocardial hypertrophy, which can result in failure of adaptation and the formation of myocardiodystrophy. The increased concentrations of amino acids in the blood may also inhibit proteolysis of muscles and stimulate lipolysis (2). The purpose of this investigation was to examine the role of amino acids supplementation on the heart adaptations in highly trained athletes. A secondary purpose in another of our studies in this line of research was to further examine the different stages of apoptosis in cells of actual heart tissue to gain further understanding of cell function.

Methods

Experimental Approach to the Problem

The Ethics Committee at Donetsk Medical University approved the investigations that were part of this research. Subjects and their parents (when appropriate) volunteered and gave their informed consent after they were told of the risks of the investigation. Sixty trained athletes (bicyclists and swimmers, age 16–22 years) were randomized and then separated into 2 groups of 30. One group was given amino acid mixture (1 g per 10 kg of body weight) each day for a period of 1 month, whereas the remaining group was given placebo for the same duration (control group). At the same time period, 20 subjects (16–22 years) matched for age but not engaged in physical training or sports activities were used as the additional control group for normal activity (control-II).

The amino acid mixture consisted of L-Leucin, L-Isoleucin, L-Treonin, L-Fenilalanin, L-Metionin, L-Lisin, L-Valin, L-Cistin, L-Istidin, L-Tirosin, and L-Triptofan (Big One, Professional Dietetics, Via Ciro Menotti 1/A, Milan, Italy). The physical examinations and blood sampling were carried out twice a month at the beginning of study (presupplement period) and at the end of study (postsupplement and postplacebo period). Blood concentrations of alanine transaminase (ALT), asparagine transaminase

TABLE 1. The effect of amino acid on the blood level of biochemicals in athletes and nonactive persons (control II).†

Biochemical	Conditions				
	Preplacebo (n = 30)	Pre–amino acid (n = 30)	Post-placebo (n = 30)	Post-amino acid (n = 30)	Control II (n = 20)
Album (g·L^{-1})	37.6 ± 3.1	35.2 ± 2.8	29.9 ± 3.1	46.4 ± 4.2*,**	43.1 ± 0.04
Triglycerides (mmol·L^{-1})	0.78 ± 0.05	0.77 ± 0.08	0.57 ± 0.05	0.98 ± 0.07*,**	1.0 + 0.15
LDH (mkkat·L^{-1})	4.58 ± 0.63	4.59 ± 0.33	4.89 ± 0.52	3.31 ± 0.31*,**	3.27 ± 0.31
AST (mkkat·L^{-1})	0.34 ± 0.05	0.35 ± 0.07	0.36 ± 0.05	0.36 ± 0.06	0.48 ± 0.04
ALT (mkkat·L^{-1})	0.21 ± 0.06	0.22 ± 0.03	0.34 ± 0.04	0.24 ± 0.02	0.52 ± 0.05
ALP (mkkat·L^{-1})	4.53 ± 0.41	4.54 ± 0.36	4.72 ± 0.46	2.42 ± 0.21*,**	2.10 ± 0.22
AM (mkkat·L^{-1})	0.76 ± 0.06	0.74 ± 0.04	0.91 ± 0.10	0.78 ± 0.07	1.2 ± 0.12
GGT (mkkat·L^{-1})	0.24 ± 0.05	0.23 ± 0.04	0.42 ± 0.04	0.29 ± 0.03	0.60 ± 0.05
IL-6 (pg·ml^{-1})	18.7 ± 1.7	17.5 ± 1.5	25.4 ± 2.7	19.4 ± 1.7**	15.2 ± 1.2
IL-10 (pg·ml^{-1})	22.5 ± 2.2	21.6 ± 1.9	18.1 ± 2.1	30.1 ± 3.8*,**	34.7 ± 4.1

* Statistically significant ($p < 0.05$) difference between pre- and post-supplementation.
** Statistically significantly ($p < 0.05$) difference between post-placebo and post-supplementation.
† LDH = lactate dehydrogenase; AST = asparagine transaminase; ALT = alanine transaminase; ALP = alkaline phosphatase; AM = amylase; GGT = gamma-glutamil transpeptidase; IL = interleukin.

(AST), lactate dehydrogenase (LDH), gamma-glutamil transpeptidase (GGT), alkaline phosphatase (ALP), amylase (AM), triglycerides, albumin, IL-6, and IL-10 were determined. The electrocardiogram and echocardiograph measurements were also obtained.

We used postmortem samples in a second study that examined the apoptosis of the heart cells in 3 types of heart tissue: (a) tissue recovered from 9 patients who had myocardiodystrophy and died from ulcerative colitis, (b) tissue recovered from a deceased athlete who had been a study subject on amino acid supplement, and (c) tissue recovered from 2 athletes who had been subjects in the placebo group and had died in a car accident. Again, approval for this study and consent from the subjects' relatives were obtained and approved by the Ethics Committee at Donetsk Medical University.

Heart muscle was stained with hematoxylin and eosine. Apoptosis were determined by the initial stage of chromatin condensation and picnosis of nucleuses, by convertible stages and irreversible sage of cells fragmentation, and by formation of apoptotic body. IL-6 and IL-10 levels were studied by standard enzyme-linked immunosorbent-assay system methods.

Statistical Analyses

The data were presented as mean ± *SD*, and all comparisons were accomplished with alpha-corrected Student's *t*-tests. Significance was chosen at the $p \leq 0.05$ level.

RESULTS

Because of extensive levels of exercise training, the concentrations of LDH and ALP were increased, but concentrations of ALT, albumin, and triglycerides were decreased in the blood of active athletes compared with healthy subjects not engaged in sports activities or physical conditioning (see Table 1).

Concentrations of other enzymes, such as AST, AM, and GGT, in the athletes' blood remained at a similar level to the value observed in our healthy subjects (control-II). After supplementation, the athletes demonstrated significantly increased levels of albumin and triglycerides compared with the post-placebo and presupplementation time point. However, LDH and ALP blood values in the group of athletes who received supplements were significantly decreased compared with the post-placebo and presupplementation groups. The concentration changes in the above-listed compounds reflect their tendency for normalization under the amino acid supplementation. Blood concentrations of AST, ALT, and AM after the amino acid treatment period did not change in either of the athlete groups. Blood concentrations of measured enzymes in the postplacebo group were comparable with presupplementation and did not show any tendency for normalization.

The presupplementation group and patients with myocardiodystrophy and a background of ulcerative colitis showed increased concentrations of IL-6 (Table 1; 29.1 ± 2.8 pg·ml^{-1}) and decreased values of IL-10 (Table 1; 13.2 ± 2.1 pg·ml^{-1}) when compared with the control-II group. The inhibition of IL-10 in the blood may play an important role in induction of apoptosis in cells of heart muscle. The increased level of both cytokines after amino acid supplementation was remarkable, and IL-10 was practically normalized. The concentrations of IL-6 increased in athletes in the post-placebo condition from 18.6 ± 1.7 pg·ml^{-1} at presupplementation to 25.4 ± 2.7 pg·ml^{-1} at post-supplementation, but in post–amino acid supplementation group this increase was minimal (Table 1).

Postmortem histology of heart tissue from patients with myocardiodystrophy in the context of ulcerative colitis revealed nonuniform full-blooded tissue and an observed phenomenon of intramuscular and, around vascular sclerosis, dystrophy of cardiomyocytes and weak to moderate lymphocytic and plasmocytic cell infiltration. Hypertrophy of single fibers of heart muscle was also marked by places in a cell's structure infiltrate with a predominant number of macrophages. Apoptosis was found in 7 (77.8%) patients and was characterized by various stages in the process, beginning with condensation to fragmentation of chromatin and picnosis of nuclei with formation of apoptotic bodies. The athletes who were given the placebo showed changes in the heart tissue characterized by hypertrophy of some muscle fibers with weak or very weak cell infiltration and weak presence of apoptosis as picnosis of nuclei. However, fragmentation was sporadic or completely absent. Shahlamova and Gusinsca (3) suggest that condensation and picnosis of nuclei during hypertrophy of heart muscle indicates unfavorable prognostic and intensity of adaptation mechanisms. Histology of heart tissue of trained athletes on amino acid supplementation show hypertrophy of single fibers of heart muscle, weak cell infiltration, and primarily macrophages and lymphocytes. The apoptosis in heart muscle was absent.

Discussion

Processes regulating apoptosis in the heart muscle are not well known. Hypertrophy cardiomyocytes are capable of synthesizing IL-2, which is a hematocrit and attracts macrophages to the heart muscle. These cells produce cytokines particular of IL-6, which stimulate apoptosis. Heart cell apoptosis is converted at early stages by bcl-2 peptide (1). Increases in concentration of free amino acid improves metabolism of cardiomyocytes, which can promote normalization of synthesis in cells, including synthesis of bcl-2. This phenomenon is not observed on the background of myocardiodystrophy or significant loadings. The supplementation of amino acids resulted in the increase of IL-10 synthesis, which inhibits apoptosis.

Thus, the amino acid concentrations are one of the key moments in formation of organism adaptation to significant physical training. The increase of amino acid concentrations in the blood prevents apoptosis, stimulates lipolysis, and stimulates heart muscle to function in a more energetically favorable way for oxidation of substrates.

Practical Applications

Amino acids supplementation increased adaptations of athletes undergoing considerable amounts of extensive exercise training. Supplementation may be worthwhile for athletes during maximal training periods in a program. Amino acids are especially effective in bicycle athletes. The recommended dosage of amino acids can fluctuate from 1 g per 10 kg of body weight to higher. The criteria of efficiency of the amino acids supplementation are defined by the albumin, IL-6, and IL-10 concentrations.

References

1. Aruin, L.I., L.L. Cappuler, and V.A. Isakov. *Morphological Diagnostics of Stomach and Intestines Illnesses.* Moscow: Triada-Kh, 1998.
2. Dioguardi, F.S. Influence of the ingestion of branched chain amino acids on plasma concentrations of ammonia and free fatty acids. *J. Strength Cond. Res.* 11:242–245. 1997.
3. Shahlamova, V.A., and T.D. Gusinsca. Adaptation-structural changes of hypertrophy in the myocardia. *J. Modern Med.* 6:3–7. 1984.
4. Stehl, G., H. Sinn, A. Wunder, H.H. Schrenk, J.C. Stewart, G. Hartung, W. Maier-Borst, D.L. Heene. Plasma protein (albumin) catabolism by the tumor itself-implications for tumor metabolism and genesis of cachexia. *J. Oncol. Hematol.* 26:77–100. 1997.
5. Wilmore, J., and D.L. Costill. *Physiology of Sports and Lifting Activities.* Kiev: Olympic Sports, 1997.

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