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L-arginine does not improve biochemical and hormonal response in trained runners after 4 weeks of supplementation

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ABSTRACT

It has been hypothesized that L-arginine improves exercise performance by increasing nitric oxide synthesis and levels of insulin and growth hormone (GH). Metabolic and hormonal responses to chronic L-arginine supplementation may clarify the mechanisms underlying its putative physiologic effects on physical performance. Therefore, the aim of this study was to investigate the effects that 4 weeks of supplementation with L-arginine would have on metabolic and hormonal parameters at rest and in response to exercise. Fifteen healthy runners were divided into treatment (ARG; 6 g L-arginine) and placebo (PLA; 6 g cornstarch) groups. On the first visit, blood samples were collected for baseline, and the supplement or placebo was provided. After 4 weeks of supplementation (second visit), blood samples were collected at the following intervals: at rest, immediately after the first 5-km time-trial running test (5km-TT), immediately after the second 5km-TT, and after 20 minutes of recovery (+20). In addition to exercise performance (total running time), plasma nitrate, nitrite, nitrate plus nitrite, cyclic guanosine monophosphate, lactate, ammonia and serum insulin, GH, insulin-like growth factor 1, and cortisol concentrations were evaluated. There were significant increases in plasma nitrite, cyclic guanosine monophosphate, lactate, ammonia and serum GH, and cortisol at the first 5km-TT, immediately after the second 5km-TT, and +20 in both ARG and PLA. Nitrate plus nitrite and nitrate increased only at +20. No significant change was observed in serum insulin and insulin-like growth factor 1 in any sample period. Total running time did not differ significantly between the 2 tests, in either ARG or PLA. Thus, according to our results, 4 weeks of L-arginine supplementation did not cause beneficial changes in metabolic and hormonal parameters, beyond those achieved with exercise alone.

Abbreviations: 5km-TT, 5-km time-trial running test; +20, after 20-minute recovery; ADMA, asymmetric dimethylarginine; ARG, L-arginine–supplemented group; cGMP, cyclic guanosine monophosphate; eNOS, endothelial nitric oxide synthase; GH, growth hormone; HPLC, high-performance liquid chromatography; IGF-1, insulin-like growth factor 1; IP-1, first 5km-TT; IP-2, after the second 5km-TT; NO, nitric oxide; NOx, nitrate plus nitrite; PLA, placebo group; POST, after 4 weeks; PRE, baseline measurements; TRT, total running time.

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1. Introduction

Supplements based on the amino acid L-arginine have been suggested to promote vasodilation, due to the alleged increase in nitric oxide (NO) production in exercising muscle [1]. Supposedly, this vasodilation increases blood perfusion and should; theoretically, increase the supply of nutrients to muscle cells during exercise, thereby improving exercise adaptations.

Evidence demonstrates that muscle blood volume is increased during the recovery period of sets of resistance exercise after acute L-arginine supplementation [2]; however, this increase was not accompanied by significant increases in NO production and strength performance. There are 2 possible reasons for the absence of significant changes in NO production: (1) acute L-arginine supplementation produces only local changes and is not enough to cause systemic changes in NO production and (2) L-arginine supplementation causes vasodilation via mechanisms other than NO. Data suggest that insulin causes vasodilation in skeletal muscle in humans. Giugliano et al [3] demonstrated that intravenous L-arginine infusion (1.0 g/min for 30 minutes) in healthy individuals increased blood flow and inhibited plaque aggregation. According to the authors, these effects may have been partially due to the increase in endogenous insulin that was triggered by L-arginine.

Besides its alleged effect on vasodilation, L-arginine has also been mentioned as a possible stimulus of growth hormone (GH) release [4-8]. This condition may increase rates of protein synthesis and, consequently, accelerate muscle recovery in physically active individuals. Collier et al [5] observed a significant increase in the plasma concentration of GH in individuals supplemented with 5 or 9 g of L-arginine. In 14 trained runners, Colombani et al [6] also observed a significant increase in the plasma concentration of GH after 14 days of arginine aspartate supplementation (15 g orally). However, when compared to the placebo group, Forbes and Bell [7] observed no significant difference in plasma concentrations of GH, insulin-like growth factor 1 (IGF-1), nitrate plus nitrite (NOx), or insulin 180 minutes after supplementing 14 physically active individuals with a single dose of L-arginine (0.075 g/kg or 0.15 g/kg of body mass). In addition, Forbes et al [8] also observed no significant difference in GH after subjects consumed 0.075 g/kg body mass of L-arginine or placebo before performing an acute bout of submaximal exercise (60 minutes at 80% of power output, achieved at ventilatory threshold). Based on these 4 studies, it appears that, in physically active participants, only chronically administered oral L-arginine may be required to stimulate GH production.

In addition to the conflicting results, only limited data are available from chronic studies investigating the metabolic and hormonal effects of L-arginine supplementation in response to exercise. Thirteen studies have combined chronic L-arginine supplementation and exercise [6,9-20]. Among these studies, only one [6] assessed the effects of the supplement on metabolic and hormonal parameters in response to running exercise.

In light of the limited scientific information demonstrating the benefits of chronic L-arginine on the metabolic and hormonal parameters associated with running exercise, the present study was carried out with the primary purpose of observing the effect of 4 weeks of L-arginine supplementation on the markers of NO production (nitrate, nitrite, and cyclic guanosine monophosphate [cGMP]); plasma concentrations of lactate, ammonia, insulin, GH, IGF-1, and cortisol at rest; and during high-intensity running exercise. A secondary aim was to evaluate whether any change in these metabolic and hormonal variables following L-arginine supplementation would improve running performance.

We hypothesized that the 4-week L-arginine supplementation would result in maintaining high plasma L-arginine concentrations and would, consequently, promote changes in the metabolic (increases in NO production and lactate and ammonia removal) and hormonal (increases in insulin, GH, and IGF-1 and decreases in cortisol) parameters in response to running exercise, thus resulting in improvements in exercise performance.

2. Methods and materials

2.1. *Participants*

Fifteen healthy experienced runners (11 males and 4 females), who had at least 1 year of running conditioning, were recruited to participate in this 4-week study. All participants were fully informed of the nature and purpose of the investigation and provided written consent to participate. The inclusion criteria were participants who could run 10 km in less than 45 minutes (4:30 min/km, males) or less than 50 minutes (5:00 min/km, females) in an official race competition. The criteria for exclusion from the study were any known cardiovascular, pulmonary or metabolic diseases (asthma, diabetes, hypertension, dyslipidemia, smoking, etc); lower limb injury; and/or the use of either nutritional ergogenics or anabolic steroids during the 6 months before the beginning of the study. All experimental procedures were performed in accordance with the ethical standards of the Declaration of Helsinki and approved by the institutional ethics committee.

2.2. *Experimental design*

The study was conducted in a randomized, double-blind, and placebo-controlled fashion, over a period of 4 weeks. The randomized method used was counterbalanced (ABBA), taking into consideration the running time of each participant in the official 10-km race. Briefly, the participant with the best time was placed in group A, the participant with the second best time was placed in group B, the participant with the third best time in group B, the participant with the fourth best time in group A, and so on. After randomization, groups A and B were classified into either the L-arginine–supplemented group (ARG) or the placebo group (PLA), via simple randomization by an individual outside the research group.

All participants reported to the training center on 2 occasions; the first visit was held at the beginning of the study, and the second was 4 weeks after L-arginine or placebo supplementation. On the first visit, after an overnight fast, blood samples were collected for baseline measurements (PRE). After blood sample donation, participants were administered the supplement and then dismissed until 4 weeks later (the second visit) when the second blood sample was taken (POST). On this second occasion, another blood sample was