Effects of Amino Acids L-Arginine on Physical Performance

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Consumption of amino acids L-arginine (L-Arg) and L-citrulline (L-Cit) are purported to increase nitric oxide (NO) production and improve physical performance. However, standalone L-Arg supplementation seems ineffective in increasing NO synthesis or improve physical performance and perceptual feelings of exertion among recreationally active and trained athletes.

exercise performance | nitric oxide | L-arginine

1. Effects of L-Arginine on Nitric Oxide Production

Supplementation to increase L-Arg has drawn significant attention for its role in improving exercise performance through increasing NO synthesis [1]. Trained male cyclists ingested 0.075 g/kg L-Arg or a placebo 60 min before completing the submaximal cycling exercise protocol. Plasma metabolites were recorded in different time points including: 0 min (pre-supplementation), 60 min (start of exercise), 120 min (end of exercise/start of rest), and 180 min (end of rest period) [2]. Plasma L-Arg concentration increased from a resting concentration of 273 µM/L to about 679 µM/L at 60 min post-supplementation, and after that progressively decreased to eventually 377 µM/L at 180 min compared to 327 µM/L at 60 min and 265 µM/L at 180 min for the placebo. However, plasma L-Arg concentration was significantly increased for the supplement group compared to the placebo in all eight-time points from 60 min post-supplementation ($p < 0.05$). There were no significant differences in plasma nitrate/nitrite concentration in the supplement group compared to the placebo ($p > 0.05$). At time point 0, plasma nitrate/nitrite concentration was about 11.5 µM/L for the supplementation group and 15.1 µM/L for placebo; at time point 180, plasma nitrate/nitrite concentration was approximately 14.5 µM/L for supplementation group and 13.7 µM/L for placebo. Similarly, ingestion of 6 g/day L-Arg for three days significantly increased plasma L-Arg concentration from 60.1 ± 3.0 µM/L at baseline to 78.9 ± 6.5 µM/L 60 min post-supplementation ($p < 0.001$). Yet, there was no significant difference in plasma nitrate/nitrite concentrations for the supplement group (235.41 µM/L) compared to the placebo group (260.40 µM/L; $p > 0.05$) 60 min post-supplementation among elite judo male athletes [3]. In a study with 6 g L-Arg acute supplementation, Meirelles and Matsuura (2016) reported no significant changes in plasma nitrate concentration from pre-supplementation values to 60 min post-supplementation and exercise; the supplement group's plasma nitrate concentration slightly increased from 10.95 ± 4.09 to 11.99 ± 2.5 mM compared to the placebo group, which slightly decreased from 13.01 ± 1.18 to 11.83 ± 2.81 mM ($p > 0.05$) among resistance trained physical education students [4].

Vanhatalo et al. (2013) reported no significant changes in plasma nitrite concentrations from the supplement group compared to the placebo at the same time points, 0 to 90 min [5]. Plasma nitrite concentration of the supplement group changed from 204 ± 79 to 241 ± 114 nM ($p > 0.05$) compared to the placebo group, which changed from 223 ± 107 to 222 ± 105 nM ($p > 0.05$). Similarly, ingestion of 6 g L-Arg had no significant differences in plasma NO markers at all-time points for the supplementation group compared to the placebo in healthy male participants (0 min: 17.6 ± 3.9 vs. 14.6 ± 2.3 µM/L; 60 min: 16.8 ± 4.9 vs. 13.7 ± 2.7; 120 min: 15.1 ± 2.8 vs. 13.5 ± 3.5 µM/L; all at $p > 0.05$) [6]. Blum et al. (2000) reported no significant changes in plasma NO synthesis following daily oral administration of 6 g L-Arg or the placebo for one month in healthy adult women (L-Arg: 42.1 ± 24.5 vs. Pla: 39.1 ± 61.1 µM/L; $p > 0.05$) [7]. Based on these studies, a dose of 6 g L-Arg was ineffective in increasing NO. Viribay et al. (2020) suggested that a higher dose might be more efficacious [1]. However, Tang et al. (2011) reported that even 10 g L-Arg supplementation did not significantly change plasma nitrate and nitrite concentration among recreationally active male participants [8]. In support of this, Forbes and Bell (2011) reported that low and high acute doses of L-Arg supplementation had similar effects on plasma L-Arg levels, with neither significantly increasing blood markers of NO synthesis among active young males [9]. Alvares et al. (2012) reported that acute ingestion of L-Arg is insufficient to change systemic NO synthesis [6].

Chronic supplementation with 6 g/day for four weeks among trained runners was not sufficient to significantly increase NO synthesis for the supplement group compared to the placebo group (week 0: 1.9 ± 0.4; week 4: 2.6 ± 0.8 µM/L vs. week 0: 1.8 ± 0.5; week 4: 2.2 ± 0.6 µM/L; $p > 0.05$) [10].

Increasing and maintaining NO synthesis plays a major role in vasodilatory capacity and increases oxygen uptake in skeletal muscle [11]. The possible reason for the limited impact of L-Arg supplementation on NO synthesis may be related to L-Arg metabolism. The level of circulating plasma L-Arg is fundamental to increasing NO synthesis, and depleted plasma L-Arg may fail to upkeep NO synthesis. Augmenting NO production via oral consumption of L-Arg may be compromised. An estimated 60% of L-Arg is metabolized in the gastrointestinal tract, while a further estimated 15% is metabolized by the liver [12]. Alvares et al. (2012) suggested that there should be no need to supplement with L-Arg in healthy participants since sheer vascular stress is considered the main stimulus of endothelial NO synthesis during exercise [6]. Instead, L-Arg supplementation may benefit participants with atherosclerosis risk factors where endothelial dysfunction may impact NO synthesis [6]. Similarly, Chin-Dusting et al. (1996) reported that supplementation with L-Arg may not consistently improve endothelial function and muscle blood flow during exercise among patients [13]. Instead, favorable outcomes such as improvement in cardiac performance were reported in patients with moderate congestive heart failure [14].

2. The Effects of L-Arginine on Physical Performance and Perceptual Responses to Exercise

A limited beneficial effect was reported for wrestling elite athletes after ingesting a single dose of 1.5 g/10 kg body weight L-Arg capsule or placebo [15]. Time to exhaustion during an incremental test on a cycle ergometer was longer for the supplement group (1386.8 ± 69.5 s) compared to the placebo (1313 ± 90.8 s) ($p < 0.05$). There were no significant differences between the supplement and the placebo group for oxygen consumption (L-Arg: 52.47 ±

4.01 mL/kg/min vs. Pla: 52.07 ± 5.21 mL/kg/min), and heart rate (L-Arg: 181.09 ± 13.57 bpm vs. Pla: 185.89 ± 7.38 bpm) ($p > 0.05$). Pahlavani et al. (2017)reported that the ingestion of 2 g/kg body weight of L-Arg for 45 days significantly improved maximal oxygen consumption by 4.12 ± 6.07 mL/kg/min compared to the placebo (1.23 ± 3.36 mL/kg/min; $p < 0.05$) among male soccer players [16]. Interestingly, studies that reported significant improvements did not measure plasma concentrations of L-Arg, nitrate, or nitrite. Therefore, the mechanism that led to improvement in physical performance remains questionable in these studies.

Contrary to the reported effect of L-Arg supplementation in improving favorable aerobic capacity outcomes among healthy participants when combined with other components such as aspartate, BCAA, or other amino acids [17][18][19], ingestion of 0.075 g/kg L-Arg 60 min before submaximal cycling exercise had no significant improvement in cardio-respiratory parameters measured at the start and finish of the 60 min cycling protocol among aerobically trained cyclists compared to the placebo [2]. The volume of oxygen consumption had no significant changes in the supplement (start: 35.2 ± 6.5, end: 37.0 ± 6.1 mL/kg/min) or placebo groups, respectively (start: 34.9 ± 6.2, end: 36.5 ± 5.9 mL/kg/min); a non-significant result was also observed regarding heart rate in the supplementation group (start: 137 ± 12, end: 145 ± 14 bpm) and the placebo group (start: 137 ± 13, end: 144 ± 17 bpm) ($p > 0.05$). There were no significant differences between L-Arg and placebo conditions in the diastolic pressure at the start (79 ± 5 vs. 79 ± 8 mmHg) or finish (72 ± 11 vs. 72 ± 10 mmHg), and for systolic pressure at the start (125 ± 7 vs. 125 ± 7.5 mmHg) or finish (161 ± 13 vs. 159 ± 16 mmHg) (all at $p > 0.05$) of the cycling protocol. Another study reported no significant changes in steady-state pulmonary oxygen uptake during moderate-intensity exercise after 6 g L-Arg beverage consumption for the supplement group compared to the placebo group (2.422 ± 333 vs. 2.407 ± 318 m/kg/min; $p > 0.05$), and also no significant changes in the time to tolerate severe exercise (552 ± 150 vs. 551 ± 140 s; $p > 0.05$) [5]. Moreover, chronic L-Arg intake did not improve performance in trained endurance athletes [20]. Similarly, consumption of 5 g L-Arg or 5.5 g dextrin twice a day for a total of 13 days yielded no significant differences in mean power output, with a mean difference of 0.5 W during cycling performance ($p > 0.05$) [21].

Standalone L-Arg supplementation seems ineffective in improving strength among well-trained athletes or recreationally healthy participants [22]. For instance, growth hormone responses over time were blunted for the supplement group (288.4 ± 368.7 min/ng/mL) compared to a placebo (487.9 ± 487.0 min/ng/mL; $p < 0.05$), and there was no difference in RPE between the groups (14 ± 2 vs. 15 ± 2; $p > 0.05$) in resistance-trained athletes who consumed 0.075 g/kg of L-Arg or placebo 60 min prior to performing resistance exercise protocol [23]. Meirelles and Matsuura (2016) did not find significant differences in bench press and isokinetic knee extension performance after administration of 6 g L-Arg or placebo among resistance-trained physical education students [4]. Another study reported a substantial decline in post-exercise elbow extension ($p = 0.014$) and flexion peak torque ($p < 0.001$) after ingestion of 3 g L-Arg among physically active male and female participants [24]. The ineffectiveness of L-Arg may be related to its ability to blunt growth hormone response following exercise [25]. Resistance exercise alone is a potent stimulator of growth hormone release [26]. While L-Arg has been shown to increase growth hormone-releasing hormone, it does suppress endogenous growth hormone-inhibiting hormone and increases insulin-like growth factor 1 [27][28]. However, oral administration of L-Arg does not augment exercise-induced growth hormone increase [29]. Furthermore, growth hormone response to specific amino acid consumption is reportedly reduced in well-trained athletes [30]. A study by Alvares et al. (2014) suggested that only chronic L-Arg supplementation could stimulate growth hormone production in physically active participants [10]. Consistent with this suggestion, chronic L-Arg supplementation of about 1.5 to 2 g/day improved aerobic and anaerobic performance [1]. A study by Campell et al. (2006) reported that a chronic supplementation protocol might be effective for enhancing maximum bench press in strength-trained male participants [31]. However, a number of studies that reported the effectiveness of chronic L-Arg consumption had other active ingredients in the supplement, such as aspartate, ornithine, and alpha-ketoglutarate [18][20][28][32]. A study Hurst and Sinclair (2014) claimed that all the current literature that reported significant improvement with L-Arg supplementation had combined it with other compounds [33]. Furthermore, other authors reported no benefit of acute or chronic supplementation protocol of L-Arg 6 g/day for muscle strength, endurance, or the maximum number of repetitions [34].

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