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Acute arginine supplementation fails to improve muscle endurance or affect blood pressure responses to resistance training.

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Acute Arginine Supplementation Fails to Improve Muscle Endurance Or Affect Blood Pressure Responses to Resistance Training

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Abstract

Greer, BK and Jones, BT. Acute arginine supplementation fails to improve muscle endurance or affect blood pressure responses to resistance training. *J Strength Cond Res* 25(7): 1789–1794, 2011–Dietary supplement companies claim that arginine supplements acutely enhance skeletal muscular endurance. The purpose of this study was to determine whether acute arginine α-ketoglutarate supplementation (AAKG) will affect local muscle endurance of the arm and shoulder girdle or the blood pressure (BP) response to anaerobic exercise. Twelve trained college-aged men (22.6 ± 3.8 years) performed 2 trials of exercise separated by at least 1 week. At 4 hours before, and 30 minutes before exercise, a serving of an AAKG supplement (3,700 mg arginine alpha-ketoglutarate per serving) or placebo was administered. Resting BP was assessed pre-exercise after 16 minutes of seated rest, and 5 and 10 minutes postexercise. Three sets each of chin-ups, reverse chin-ups, and push-ups were performed to exhaustion with 3 minutes of rest between each set. Data were analyzed using repeated-measures analysis of variance and paired *t*-tests. The AAKG supplementation did not improve muscle endurance or significantly affect the BP response to anaerobic work. Subjects performed fewer total chin-ups (23.75 ± 6.38 vs. 25.58 ± 7.18) and total trial repetitions (137.92 ± 28.18 vs. 141.08 ± 28.57) in the supplement trial ($p \leq 0.05$). Subjects executed fewer reverse chin-ups (5.83 ± 1.85 vs. 6.75 ± 2.09) during set 2 after receiving the supplement as compared to the placebo ($p < 0.05$). Because AAKG supplementation may hinder muscular endurance, the use of these supplements before resistance training should be questioned.

Key Words ergogenic aids, nitric oxide, anaerobic

Introduction

L-Arginine is a conditionally essential amino acid with a bioavailability of approximately 60% (21). The average arginine intake via an omnivorous Western diet is approximately 5 g·d^{-1} (29). The majority of endogenous arginine is made via L-ornithine and L-citrulline in the kidneys (8). but may not be sufficient after traumatic injuries (20). Arginine can be converted to nitric oxide (NO) via NO synthase resulting in acute vasodilation (20). This dilatory effect is partially mediated by endogenous insulin release (12), although this does not appear in the short term (<6 days) to be a rate-limiting step in NO synthesis (5). Although sales of arginine-containing supplements, sometimes marketed as "nitric oxide stimulators," have increased markedly in the past decade, there is scant evidence that they provide ergogenic benefits in healthy populations. Many companies' products claiming to stimulate NO release advertise increased muscular power, strength, and endurance as potential benefits.

One study reports that arginine and ornithine supplementation (1 g each per day) while resistance training (5 weeks; 3 sessions per week) significantly increases overall strength and lean body mass as compared to a placebo (9). Unfortunately, this study was a posttest–only design, and therefore, the groups' baseline strength and lean body mass may have differed. The majority of research regarding arginine supplements and performance has focused on aerobic training. Colombani et al. report that 14 days of arginine–aspartate did not affect indirect markers of muscle damage postmarathon and had no metabolic effects (7). Four weeks of arginine–aspartate supplementation had no effect on endurance performance or human growth hormone, cortisol, testosterone, and glucagon concentrations in trained athletes (1). However, Matsumoto et al. showed a decrease in proteolysis during endurance exercise with the ingestion of 2 g branched chain amino acids + 0.5 g arginine (19). Alternate studies have failed to find an ergogenic effect with arginine supple-mentation particularly in regards to a hypothesized exercise-induced or arginine-induced growth hormone release (1,10,18). To our knowledge, only 1 study has investigated the independent effects of arginine α-ketoglutarate (AAKG) (4). Campbell et al. report that 1RM bench press performance
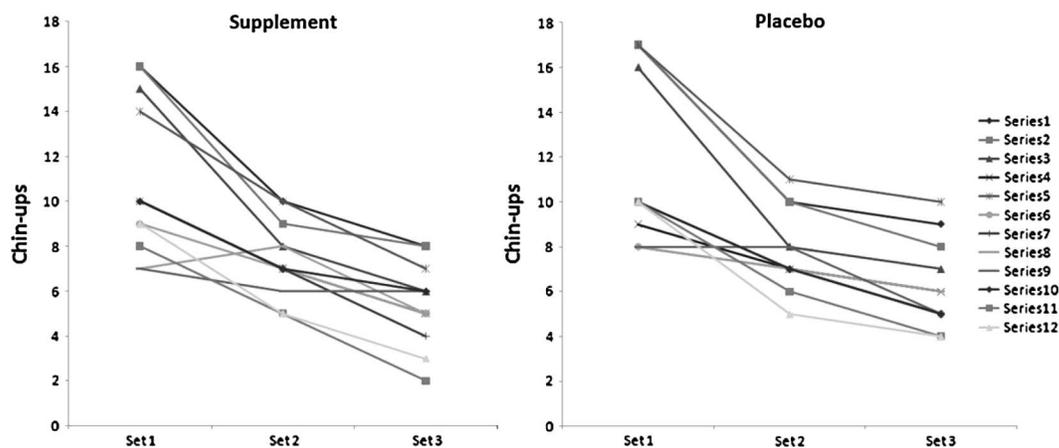
Figure 1. Chin-ups (individual subjects). Set 3 mean is significantly lower ($p < 0.01$) than set 1 for both trials. No differences between trials were found.

and Wingate peak power performance increased significantly with 8 weeks of AAKG supplementation (12 g daily), although isokinetic quadriceps muscle endurance was not affected.

This study was designed based on pilot data suggesting that AAKG supplementation may cause an acute decrease in local muscular endurance. The hemodynamic response to anaerobic exercise was also assessed as arginine supplementation decreases blood pressure (BP) in healthy subjects (25).

METHODS

Experimental Approach to the Problem

Upper body muscle endurance was assessed on 2 separate occasions in a double-blind, crossover design after consuming either 2 separate servings (3,700 mg per serving) of AAKG or a placebo 4 hours before, and 30 minutes before exercise. It was assumed that because most arginine supplements are marketed toward individuals engaged in resistance training, using resistance trained subjects would increase the applicability of the study.

Subjects

Twelve resistance trained college-aged men (22.6 ± 3.8 years; body fat $12.1 \pm 4.1\%$ as determined by 3-site skinfold analysis) volunteered to participate in this experiment. To qualify as "trained," the subject must have engaged in resistance training for the past 6 months (at least 2 sessions per week) and be able to perform 10 unassisted chin-ups with a 1-second pause between repetitions. Subjects who had taken any dietary
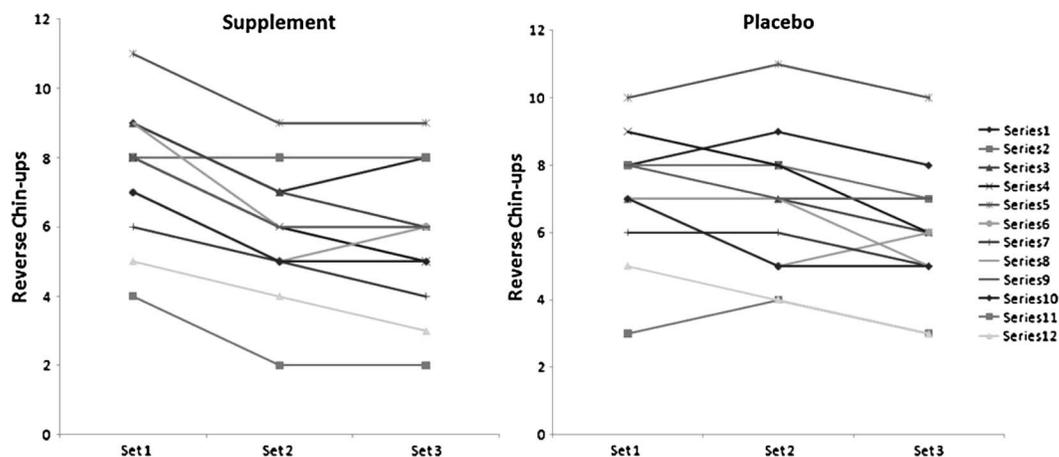

Figure 2. Reverse chin-ups (individual subjects). Set 2 mean was significantly higher in the Placebo trial than in the Supplement trial ($p < 0.01$). Set 2 mean for the Supplement trial and set 3 mean for both trials were significantly lower ($p < 0.01$) than set 1 for both trials.
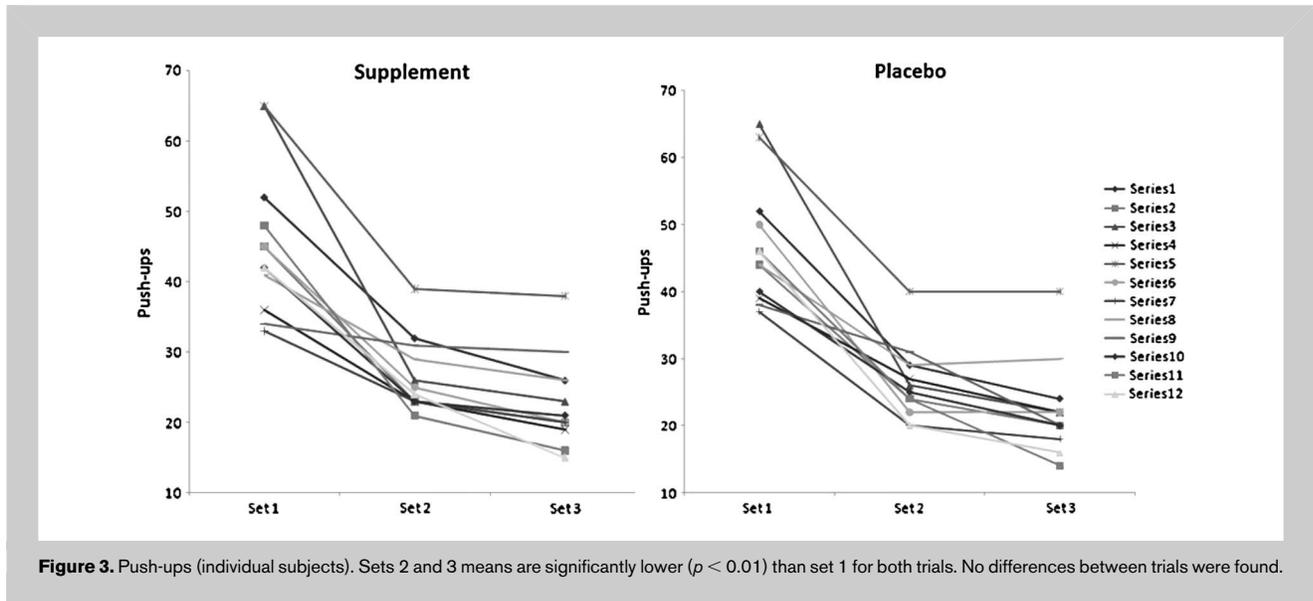
Figure 3. Push-ups (individual subjects). Sets 2 and 3 means are significantly lower ($p < 0.01$) than set 1 for both trials. No differences between trials were found.

supplement in the past 6 months were excluded, with the exception of vitamin, mineral, and protein supplements. If the protein supplement contained creatine or supplementary arginine not originating from the whole protein, the subject was excluded. Prehypertensive or hypertensive subjects were not excluded from the study as arginine supplementation can lower BP in both healthy and hypertensive individuals (13,25).

All subjects signed a consent form informing them of the aims, procedures and risks of the study. The consent form and study design were approved by the institutional review board at Sacred Heart University.

Figure 4. Mean ($\pm$ SD) total repetitions for exercise and complete trial. *Significantly different ($p \leq 0.05$) between trials.

Procedures
Subjects performed 2 trials of exercise separated by at least 1 week. Subjects were required not to perform upper body resistance training within 72 hours of each trial, and lower body training within 48 hours because musculature not connected to the arm and shoulder girdle still aids in stabilization during particular exercises. Seventy-two hours of rest was assumed to be an adequate recovery time from previous resistance work in trained subjects (6). Subjects did not consume food or caloric drinks for 4 hours before testing to control for postprandial effects on BP. Caffeine consumption on the day of testing was also prohibited because it has been shown to increase muscle endurance (11), and BP in nonhabituated users (22). Aerobic exercise was not permitted on the day of testing until the trial was over.

Three sets each of chin-ups (hands pronated), reverse chin-ups (hands supinated), and push-ups were performed to exhaustion with 3 minutes of rest between each set. Subjects waited on a "go" command at the initial hanging position with full elbow extension for each chin-up or reverse chin-up repetition. The repetition was counted if the subject's chin reached a parallel level with the bar. A tester held his arm in front of the subject to prevent excessive swinging of the body.
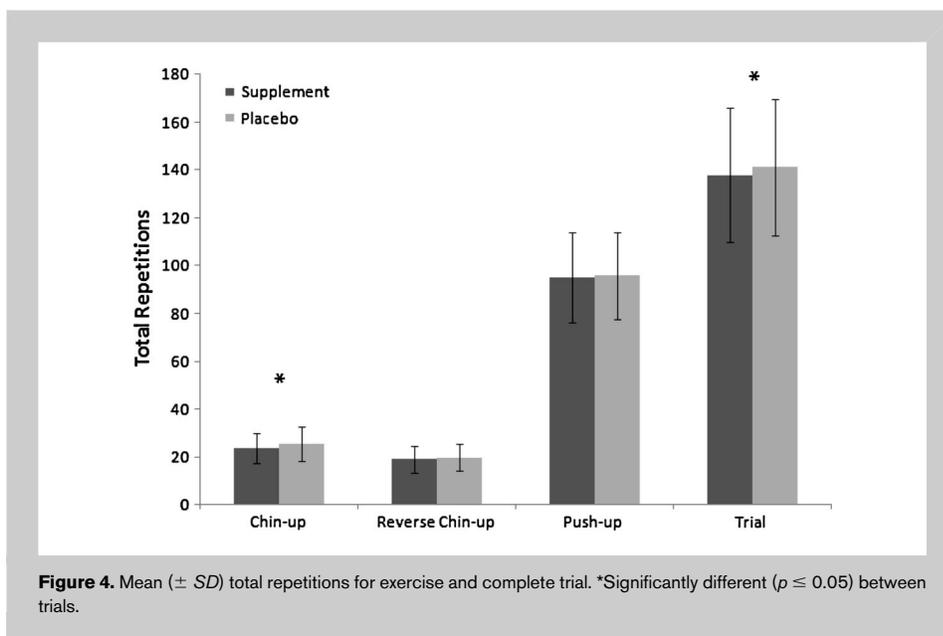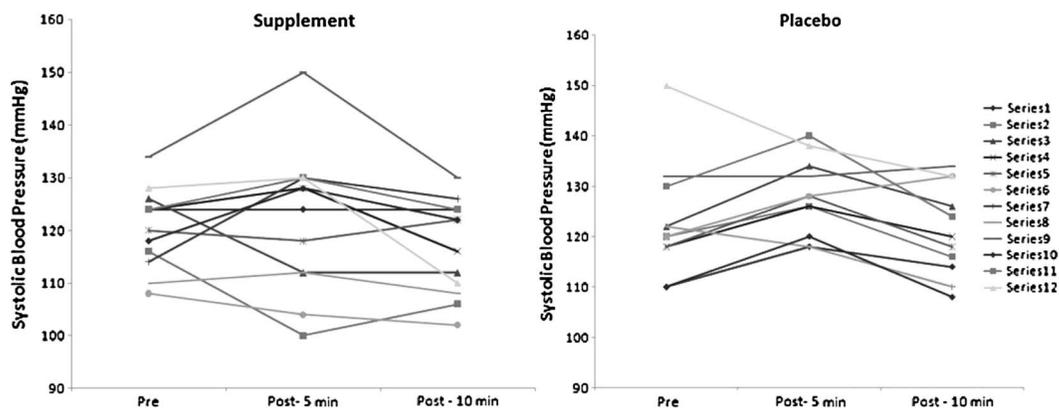
Figure 5. Systolic blood pressure (individual subjects). No significant differences between trials were found.

Markings on the apparatus ensured the subject maintained the same hand position during each trial and set. Push-up repetitions were counted if the subject's chest made contact with the tester's fist resting on the ground, and the elbows were fully extended after the concentric portion of the repetition. Subjects were instructed to do the push-ups as quickly as possible. The order of exercises was the same for all subjects. In regard to total repetitions this protocol had a significantly high test–retest reliability ($r = 0.98$, $p < 0.01$). When broken into its individual subcomponents, the reliability remains high ($r = 0.94$, $p < 0.01$).

Resting BP was manually assessed via auscultatory method at the brachial artery pre-exercise after 16 minutes of seated rest as suggested by Sala et al. (24), and 5 and 10 minutes postexercise.

Supplementation

At 4 hours before, and 30 minutes before exercise a serving of a commercially available AAKG supplement (Nitric Suspension™, German American Technologies™) or placebo (maltodextrin) was administered. The placebo was similar in color, size, and texture to the supplement. Each serving of the supplement contained 3,700 mg AAKG and 7 mg of piperine extract (Bioperine®). Many alternate widely used "nitric oxide stimulating" supplements could have been used, but their caffeine content could influence the results. Because of budgetary restraints, the ingredients of the supplement were not confirmed via an independent laboratory analysis, and therefore, quality control could be a confounding factor.

Statistical Analyses

The study followed a 2×3, trial $\times$ time, within-subjects design with repeated measures. Analyses of variance (ANOVAs) with repeated measures were used to analyze the variance of experimental treatments. Paired t-tests were
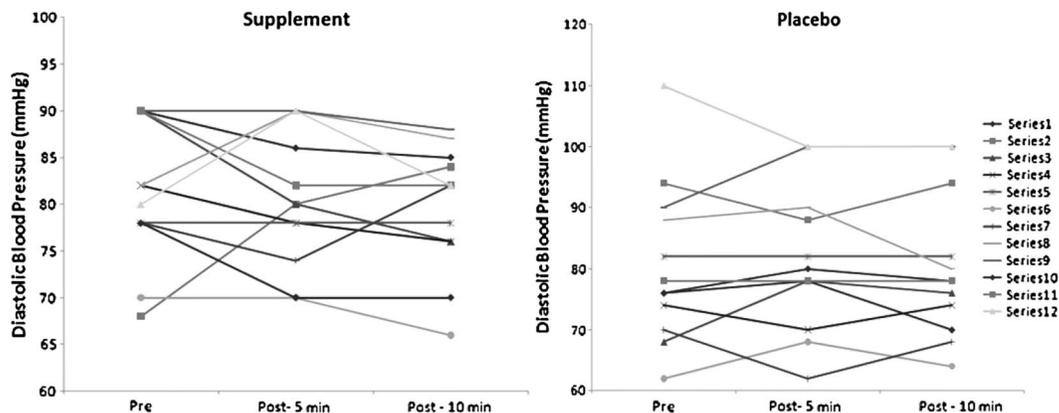

Figure 6. Diastolic blood pressure (individual subjects). No significant differences between trials were found.

used to determine significant differences for total trial repetitions and total repetitions per exercise (set 1 + set 2 + set 3). Acceptance for statistical significance was $p \leq 0.05$. Twelve subjects were chosen to achieve a power ≥ 0.80 based upon pilot data. The Tukey honestly significant difference (HSD) post hoc test was used to determine significant differences between means, and Mauchly's test of sphericity was used to confirm homogeneity of repeated-measures variability. Statistical calculations were performed using commercially available software (SPSS Inc., Chicago, IL, USA).

RESULTS

All 12 subjects who initially volunteered completed the testing procedures. Every volunteer had >2 years of resistance training experience, even though the qualification was only for 6 months. There were no order effects observed between the 2 trials ($p > 0.05$).

When examining individual sets, there was no trial × time interaction for the chin-up test (Figure 1); however, subjects performed fewer chin-ups during set 3 than during set 1 in both trials ($p < 0.01$).

In regard to reverse chin-ups, ANOVA with repeated measures revealed a significant main effect for trial and time ($p < 0.01$) and a trial × time interaction ($p < 0.01$; Figure 2). Subjects performed fewer reverse chin-ups in the Supplement trial than in the Placebo trial and performed fewer during set 3 than during set 1 in both trials. Subjects also executed fewer reverse chin-ups in the Supplement trial during set 2 than during set 1.

There were no trial × time interactions for push-up tests (Figure 3). Subjects performed fewer push-ups during sets 2 and 3 than during set 1 in both trials ($p < 0.01$).

When data were analyzed by exercise (repetition sum of individual sets), subject performed fewer chin-ups in the Supplement trial ($p < 0.05$) than in the Placebo trial (Figure 4). The total number of repetitions for the trial (repetition sum of all sets and exercises) was significantly lower in the Supplement trial ($p = 0.05$; Figure 4).

There were no significant main effects found with any BP measures (Figures 5 and 6).

DISCUSSION

An arginine-containing supplement had no positive ergogenic benefit in this study, and may acutely be counterproductive in developing muscular endurance. An NO-stimulated increase in blood flow to the working muscle may create a mechanical hindrance preventing a full range of motion during particular exercises (a reverse chin-up in this case). Nitric oxide has also been shown to decrease contractile force of mammalian skeletal muscle (27).

Arginine-induced NO production may directly stimulate protein synthesis via ERK 1/2 activation (28). Arginine supplementation may also be effective at indirectly stimulating protein synthesis when consumed with other amino acids. This results from enhanced amino acid delivery to skeletal muscle via arginine-induced NO production (20). If arginine supplementation proves useful in stimulating protein synthesis directly or indirectly, the results of this study indicate that it would be optimal to ingest the supplement postexercise in conjunction with other amino acids. Although Matsumoto et al. showed a decrease in skeletal muscle proteolysis with arginine supplementation during moderate-intensity aerobic exercise (19), the supplement also contained branched chain amino acids (BCAA), which decreases indirect indicators of muscle damage independently of arginine (14).

Almost all advertised benefits of arginine supplements rest on the assumption of NO stimulation. It should be noted that arginine-induced NO production is not a foregone conclusion, because production is not limited by arginine availability (5,17). Also, if vasodilation is produced via arginine feeding, it may be the result of insulin release as opposed to NO production (17), because insulin induces vasodilation (2).

No significant differences in BP were found between trials despite an over 5-mm drop in systolic BP 5 minutes postexercise in the supplement trial. Diets high in arginine via either oral supplementation or the inclusion of arginine-rich foods are reported to lower BP in healthy, human subjects (25). The BP response in this study may have been confounded by the presence of piperine extract in the supplement. Piperine is derived from the plant Piper nigrum or *Piper longum* L. (black pepper and long pepper, respectively) and may have thermogenic properties (26). However, there is no available evidence known to our laboratory that suggests piperine will affect BP at rest or postexercise.

Oral arginine doses of 10 g have been associated with gastrointestinal pain and diarrhea (23). Although none of the subjects in the present study (7.4 g·d^{-1}) reported gastrointestinal distress, 10 subjects voided between the first and second arginine feedings as compared to only 2 between the placebo feedings. In addition, Jackson identified several unfavorable metabolic effects that may result from single amino acid supplementation (16). The addition of a single amino acid, lysine, to a balanced amino acid solution exacerbated negative nitrogen balance over 10 days in patients under total parenteral nutrition (15). It should be noted, however, that this effect is specific to subjects already in a negative nitrogen balance.

Considering that acute arginine supplementation may contribute to decreased local muscular endurance and that prolonged arginine feeding (7 days) in high doses (appox 25 g·d^{-1}) can cause sodium and consequent water loss in the urine (3), its acute use before resistance training should be questioned and is in need of further study.

PRACTICAL APPLICATIONS

Although arginine-containing "nitric oxide stimulating" supplements are marketed to increase muscle endurance,

this study does not support this contention with acute ingestion. One study has demonstrated chronic AAKG supplementation efficacy in improving muscular strength but with no influence on body composition (4). As suggested by Paddon-Jones et al. (20), arginine ingestion may also be effective in indirectly stimulating protein synthesis when coupled with ingestion of essential amino acids. This contention and others that propose pathways involving direct stimulation of protein synthesis via arginine supplementation remain valid hypotheses (20), but industry instructions to ingest large doses of arginine before exercise may be unwarranted and potentially counterproductive in developing muscle endurance.

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