

Creatine, Arginine α -Ketoglutarate, Amino Acids, and Medium-Chain Triglycerides and Endurance and Performance

Jonathan. P. Little, Scott C. Forbes, Darren G. Candow,
Stephen M. Cornish, and Philip D. Chilibeck

Creatine (Cr) supplementation increases muscle mass, strength, and power. Arginine α -ketoglutarate (A-AKG) is a precursor for nitric oxide production and has the potential to improve blood flow and nutrient delivery (i.e., Cr) to muscles. This study compared a commercial dietary supplement of Cr, A-AKG, glutamine, taurine, branched-chain amino acids, and medium-chain triglycerides with Cr alone or placebo on exercise performance and body composition. Thirty-five men (~23 yr) were randomized to Cr + A-AKG ($0.1 \text{ g} \cdot \text{kg}^{-1} \cdot \text{d}^{-1}$ Cr + $0.075 \text{ g} \cdot \text{kg}^{-1} \cdot \text{d}^{-1}$ A-AKG, $n = 12$), Cr ($0.1 \text{ g} \cdot \text{kg}^{-1} \cdot \text{d}^{-1}$, $n = 11$), or placebo ($1 \text{ g} \cdot \text{kg}^{-1} \cdot \text{d}^{-1}$ sucrose, $n = 12$) for 10 d. Body composition, muscle endurance (bench press), and peak and average power (Wingate tests) were measured before and after supplementation. Bench-press repetitions over 3 sets increased with Cr + A-AKG ($30.9 \pm 6.6 \rightarrow 34.9 \pm 8.7$ reps; $p < .01$) and Cr ($27.6 \pm 5.9 \rightarrow 31.0 \pm 7.6$ reps; $p < .01$), with no change for placebo ($26.8 \pm 5.0 \rightarrow 27.1 \pm 6.3$ reps). Peak power significantly increased in Cr + A-AKG ($741 \pm 112 \rightarrow 794 \pm 92$ W; $p < .01$), with no changes in Cr ($722 \pm 138 \rightarrow 730 \pm 144$ W) and placebo ($696 \pm 63 \rightarrow 705 \pm 77$ W). There were no differences in average power between groups over time. Only the Cr-only group increased total body mass ($79.9 \pm 13.0 \rightarrow 81.1 \pm 13.8$ kg; $p < .01$), with no significant changes in lean-tissue or fat mass. These results suggest that Cr alone and in combination with A-AKG improves upper body muscle endurance, and Cr + A-AKG supplementation improves peak power output on repeated Wingate tests.

Keywords: exercise, power, ergogenic aids, athletic performance

Increasing dietary creatine (Cr) intake through supplementation improves muscle performance in a single bout (Dawson et al., 1995; Earnest, Snell, Rodriguez, Almada, & Mitchell, 1995; Volek et al., 1997) and repeated bouts of high-intensity exercise (Casey, Constantin-Teodosiu, Howell, Hultman, & Greenhaff, 1996; Dawson et al.; Greenhaff et al., 1993; Izquierdo, Ibanez, Gonzalez-Badillo, & Gorostiaga, 2002; Kilduff et al., 2002; Okudan & Gokbel, 2005). The primary

Little, Forbes, Cornish, and Chilibeck are with the College of Kinesiology, University of Saskatchewan, Saskatoon, SK, Canada. Candow is with the Faculty of Kinesiology and Health Studies, University of Regina, Regina, Saskatchewan, Canada S4S 0A2.

mechanism by which Cr supplementation improves muscle performance is thought to be an increase in skeletal-muscle total Cr and phosphocreatine (PCr) content, thus enhancing the ability to replenish adenosine triphosphate via the creatine kinase reaction (Greenhaff, Bodin, Soderlund, & Hultman, 1994). Other possible effects of increased total Cr and PCr content include accelerated resynthesis of PCr during the recovery periods from repeated high-intensity exercise (Greenhaff et al., 1994; Yquel, Arsac, Thiaudiere, Canioni, & Manier, 2002), increased hydrogen-ion-buffering capacity (Greenhaff et al., 1993; Yquel et al.), and increased net muscle protein synthesis leading to improved muscle mass (Ingwall, Weiner, Morales, Davis, & Stockdale, 1974).

L-arginine is another supplement that has been reported to improve exercise performance. The body of research on L-arginine and muscle performance is relatively small, but supplementing with L-arginine and compounds containing it has been shown to improve maximal strength (Campbell et al., 2006; Elam, Hardin, Sutton, & Hagen, 1989), Wingate peak power (Campbell et al.), repeated sprint performance (Buford & Koch, 2004), and fatigue resistance (Buford & Koch; Stevens, Godfrey, Kaminski, & Braith, 2000). Although the mechanism by which L-arginine supplementation enhances short-term exercise performance is not fully known, L-arginine is required for endogenous synthesis of nitric oxide (Soeters, Hallemeesch, Bruins, van Eijk, & Deutz, 2002), which functions to promote vasodilation and increase blood flow. Increased blood flow could improve exercise performance by facilitating nutrient delivery (i.e., creatine, glucose) or metabolic waste-product removal from exercising skeletal muscle. Studies in healthy older adults (Bode-Boger et al., 2003), patients with vascular disease (Kubota, Imaizumi, Oyama, Ando, & Takeshita, 1997), and normotensive rats (Ohta, Takagi, Sato, & Ignarro, 2007) have shown increased muscle blood flow after supplementing with L-arginine.

Combining Cr and L-arginine supplementation is intriguing for two main reasons. First, because both Cr and L-arginine supplementation appear to improve muscle performance yet work by different proposed mechanisms, their effects could be additive. Second, because L-arginine might enhance muscle blood flow, combining L-arginine with Cr could increase the delivery of Cr to skeletal muscle and increase the effectiveness of Cr supplementation. Coingesting Cr with nutrients that stimulate insulin secretion, such as carbohydrates (Green, Hultman, Macdonald, Sewell, & Greenhaff, 1996) or alpha-lipoic acid (Burke, Chilibeck, Parise, Tarnopolsky, & Candow, 2003), and performing low-intensity exercise after Cr ingestion to promote blood flow (Robinson, Sewell, Hultman, & Greenhaff, 1999) have been shown to enhance muscle Cr retention, demonstrating that skeletal-muscle Cr uptake can be manipulated. The primary purpose of this study was to determine the effects of a commercial dietary supplement containing Cr and L-arginine alphaketoglutarate (A-AKG; a modified salt of L-arginine) as the main ingredients on muscle performance in young male adults. Because both Cr (Kilduff et al., 2002) and A-AKG (Campbell et al., 2006) supplementation have been shown to increase fat-free mass, we also assessed changes in body composition. We hypothesized that Cr and A-AKG supplementation would increase exercise performance and muscle mass compared with Cr alone or placebo.

The commercial Cr + A-AKG supplement (Xpand nitric oxide reactor, Dymatize Enterprises Inc., TX) used in the current study also contained other ingredients (e.g., branched-chain amino acids, medium-chain triglycerides, L-glutamine). The available evidence and potential mechanisms supporting improved exercise performance after short-term supplementation with these compounds is limited. Therefore we assumed that the ingredients with ergogenic potential in the supplement were Cr and A-AKG.

Methods

Participants

Thirty-seven healthy physically active men (22.8 ± 2.8 year) volunteered for the study. They were participating in moderate physical activity ~2–3 times per week and were instructed not to change their diet or physical activity patterns before or during the study. All participants were required to fill out a Physical Activity Readiness Questionnaire (PAR-Q), which screens for health problems that might present a risk with performance of physical activity (Thomas, Reading, & Shephard, 1992). The study was approved by the University of Saskatchewan Biomedical Research Ethics Board for research in human participants. Participants were informed of the risks and purposes of the study before written consent was obtained. Participants had been free from other ergogenic aids for at least 12 weeks before initial testing to eliminate any effects from other supplementation.

Experimental Design

The study used a double-blind, repeated-measures design in which participants were randomized to one of three supplement groups: Cr + A-AKG, Cr, or placebo. Participants were required to visit the laboratory on two occasions before the start of the study, once to determine their bench-press 1-repetition maximum (1-RM) strength and again 3 days later for familiarization with the experimental protocol by performing three sets of bench-press repetitions to fatigue (separated by 1-min rest intervals) at an intensity corresponding to 70% 1-RM followed by three 30-s Wingate cycle tests (separated by 2-min rest intervals) at a load corresponding to 0.075 kp/kg body mass. There was a 10-min rest period between the bench-press endurance tests and Wingate cycle tests.

Approximately 3–7 days after the familiarization trial participants returned for presupplementation testing. Body composition was measured by air-displacement plethysmography (BodPod, Life Measurement Inc., Concord, CA) followed by the same exercise protocol as during the familiarization session, except that finger-prick blood lactate samples were taken (details below). Participants consumed the supplement for 10 consecutive days before returning to the laboratory for post-testing. The same testing protocol was repeated at this time. Participants were instructed to refrain from caffeine for 48 hr, physical activity for 24 hr, and food and drink for 3 hr before testing. The dependent variables measured before and after 10 days of supplementation were (a) body mass, fat mass, and lean tissue

mass; (b) bench-press muscle endurance; (c) peak and average power during three repeated Wingate tests; and (d) blood lactate concentration before, during, and after the repeated Wingate tests. Side effects were determined by verbally prompting participants on the posttesting day to indicate any side effects they had experienced during the study. Participants were also told to report any side effects during the study by contacting the investigators.

Supplementation

Participants were randomly assigned to one of three supplement groups: Cr + A-AMG ($0.1 \text{ g} \cdot \text{kg}^{-1} \cdot \text{day}^{-1}$ Cr + $0.075 \text{ g} \cdot \text{kg}^{-1} \cdot \text{day}^{-1}$ A-AMG, found in 0.35 g/kg Xpand nitric oxide reactor), Cr ($0.1 \text{ g} \cdot \text{kg}^{-1} \cdot \text{day}^{-1}$ Dymatize Enterprises Inc., TX), or placebo (PLA, $1 \text{ g} \cdot \text{kg}^{-1} \cdot \text{day}^{-1}$ sucrose-based fruit punch) for 10 days. The Xpand supplement was mixed with 0.65 g/kg sucrose-based fruit punch, and the Cr was mixed with 0.9 g/kg of the sucrose-based fruit punch to match the supplements for caloric content, color, and taste. The supplements were separated into 10 equal doses, and the participants were instructed to mix a single dose with ~1 L of water and consume half the serving 30 min before and the other half 30 min after a workout or, on nonworkout days, consume half the dose in the morning and half in the evening. Ingredients in the Xpand supplement are shown in Table 1.

Table 1 Ingredients in the Cr + A-AMG Supplement (Xpand Nitric Oxide Reactor, Dymatize Enterprises, TX)

Ingredient	Daily supplement amount (g/kg)
Tricreatine malate	0.1
Arginine alpha-ketoglutarate (A-AMG)	0.075
Betaine-anhydrous	0.05
Taurine	0.05
Glutamine-AMG, N-acetyl-L-glutamine	0.025
Vitamin B3	5×10^{-4}
Vitamin B6	225×10^{-6}
Folic Acid	22×10^{-7}
Vitamin B12	9×10^{-7}
Xpansion matrix: glycocyamine, glucuronolactone, L-citrulline, medium-chain triglycerides, caffeine, aqueous cinnamon extract, vinpocetine 99%, vincamine 99%, silicon dioxide	1.0
Recovery matrix: BCAA complex (L-leucine, L-isoleucine, L-valine), L-tyrosine, N-acetyl cysteine, L-phenylalanine, vanadyl sulfate	0.052

Note. Ingredients are taken from the product label, and amounts are for the daily supplemental dose given to participants expressed relative to body mass.

Muscle Strength and Endurance

The procedures for determining bench-press 1-RM were previously described (Candow, Burke, Smith-Palmer, & Burke, 2006). All bench-press testing was performed on a plate-loaded machine (Lever chest-press machine, Winnipeg, MB, Canada). Reproducibility of our 1-RM test, expressed as a coefficient of variation was 1.9% (Candow, Chilibeck, Burke, Davison, & Smith-Palmer, 2001). For bench-press muscle endurance, participants performed three sets of bench-press repetitions to volitional fatigue, separated by 1-min rest intervals, at an intensity corresponding to 70% 1-RM. Reproducibility of the bench-press endurance test was assessed previously in our laboratory by testing 15 participants 3 days apart. The coefficient of variation was 1.5% (Forbes, Candow, Little, Magnus, & Chilibeck, 2007).

Anaerobic Power

Peak and average power were assessed using repeated Wingate cycle-ergometer tests. Blood lactate concentration was measured at rest, immediately after each Wingate cycle test, and 2 min postexercise using an automated lactate analyzer (Accutrend Lactate, Roche Diagnostics, Mannheim, Germany) according to the manufacturer's instructions. Ten minutes after the bench-press endurance test, each participant was positioned on the Wingate cycle ergometer (Monark), and seat height, handlebar height and position, and toe straps were adjusted based on the settings determined during the familiarization trial. Participants were instructed to cycle at a slow cadence (~50–60 rpm) against light resistance for 5 min. Five seconds before data collection, participants were instructed to pedal at maximal rate to ensure optimal power and force production at the beginning of the test and to continue cycling at a maximal speed for the duration of the 30-s test at a load corresponding to 7.5% of their body mass (Bar-Or, 1987). Participants were verbally encouraged throughout the test. This procedure was repeated for three tests, separated by 2 min of active rest against zero resistance between tests. Reproducibility of peak and average power was determined previously in our laboratory by testing 10 participants 3 days apart. The coefficients of variation were 4.1% for peak power and 3.6% for average power (Forbes et al., 2007).

Dietary Intake and Physical Activity

Dietary intake (total calories, carbohydrates, protein, and fat) was determined by having participants complete 3-day food diaries (2 weekdays and 1 weekend day) at the start of the study. Food diaries were assessed by the USDA interactive eating index (www.mypyramidtracker.gov). Physical activity levels were determined at baseline by questionnaire (Godin & Shephard, 1985).

Statistical Analysis

A 3 (group; Cr + A-AKG vs. Cr vs. PLA) \times 3 (exercise sets) \times 2 (time; before vs. after the 10-day supplementation period) ANOVA with repeated measures on the last two factors was used to assess differences between conditions for

bench-press repetitions, as well as for peak power and average power during the Wingate tests. A 3 (group) \times 5 (blood lactate at five time points) \times 2 (time) ANOVA with repeated measures on the last two factors was used to assess changes in blood lactate concentration. Body-composition measures were analyzed with a 3 (group) \times 2 (time) ANOVA with repeated measures on the second factor. Tukey's post hoc tests were used to determine differences between means when significance was found. Differences between groups for dietary intake and physical activity levels were determined by a one-factor ANOVA. Statistical significance was set at $p \leq .05$. All results are expressed as $M \pm SD$. Statistical analyses were carried out using Statistica, version 7.0 (StatsSoft Inc., Tulsa, OK).

Results

Of the original 37 young men who volunteered, 35 participants (Cr + A-AKG $n = 12$; Cr $n = 11$; PLA $n = 12$) completed the study. Two withdrew because of time constraints. There were no side effects reported from supplementation. There were no differences between groups for average daily dietary intake (kcal: Cr + A-AKG $3,067 \pm 569$; Cr $3,269 \pm 699$; PLA $2,775 \pm 1026$; carbohydrates: Cr + A-AKG 351 ± 88 g; Cr 406 ± 74 g; PLA 332 ± 147 g; fat: Cr + A-AKG 105 ± 16 g; Cr 120 ± 38 g; PLA: 101 ± 35 g; protein: Cr + A-AKG 146 ± 44 g; Cr 139 ± 55 g; PLA 127 ± 45 g) or physical activity levels (physical activity scores in arbitrary units: Cr + A-AKG 86 ± 32 ; Cr 89 ± 32 ; PLA 64 ± 18).

As expected, there was a significant set main effect for bench-press endurance ($p < .001$); that is, performance dropped across sets. There was a significant Group \times Time interaction ($p < .05$, Figure 1), with total bench-press repetitions over three sets being significantly increased after supplementation in the Cr + A-AKG ($+4 \pm 3.7$ reps, or 12.4%) and Cr groups ($+3.4 \pm 3.2$ reps, or 11.9%; $p < .01$) but no change for placebo ($+0.3 \pm 2.4$ reps, or 0.3%).

There was a significant set main effect for Wingate peak and average power (both $p < .001$), with performance decreasing across sets as would be expected. For peak power, there was a significant Group \times Time interaction ($p < .05$, Figure 2). Peak power (average of the three Wingate tests) significantly increased after supplementation in the Cr + A-AKG group ($+54 \pm 82$ W, or +7.1%, $p < .05$), with no differences in the Cr (-11 ± 47 W, or -1.5%) and PLA groups (-9.4 ± 34.7 W, or -0.8%). There were no significant differences between supplement groups for Wingate average power (Group \times Time interaction, $p = .089$; Figure 3). Blood lactate concentration increased across sets during the Wingate test ($p < .01$), but there were no differences between groups (data not shown).

There were no significant differences between groups over time for lean-tissue mass or fat mass (Table 2). There was a significant Group \times Time interaction, however, for body mass ($p < .05$), with post hoc tests revealing an increase in body mass from pre- to postsupplementation in the Cr group only ($p < .01$, Table 2).

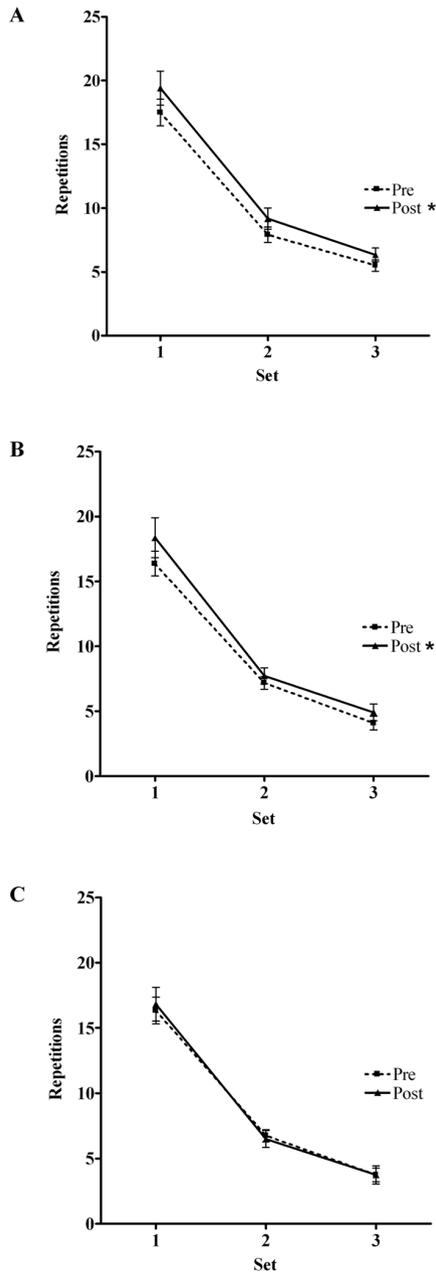


Figure 1 — Bench-press repetitions over three sets in the Cr + A-AKG (A), Cr (B), and placebo (C) groups before (pre) and after (post) 10 days of supplementation. Values are $M \pm SD$. *Significant increase in total number of bench-press repetitions from pre- to post-supplementation ($p < .01$).

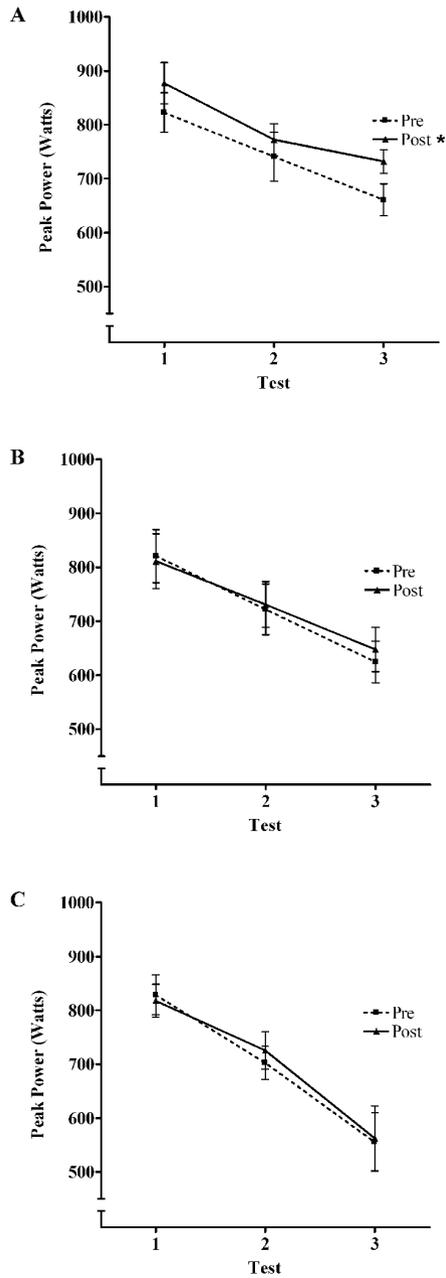


Figure 2 — Peak power output over three repeated Wingate cycling tests (separated by 2 min rest) in the Cr + A-AKG (A), Cr (B), and placebo (C) groups before (pre) and after (post) 10 days of supplementation. Values are $M \pm SD$. *Significant increase in peak power from pre- to postsupplementation ($p < .05$).

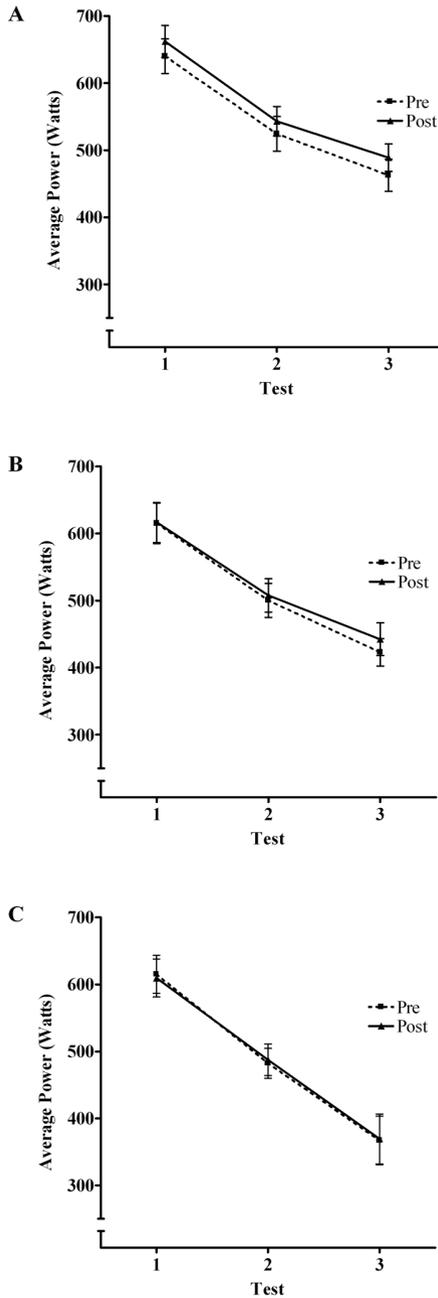


Figure 3 — Average power output over three repeated Wingate cycling tests (separated by 2 min rest) in the Cr + A-AKG (A), Cr (B), and placebo (C) groups before (pre) and after (post) 10 days of supplementation. Values are $M \pm SD$.

Table 2 Body-Composition Measures ($M \pm SD$) Before and After 10 Days of Supplementation

	Cr + A-AKG		Cr		Placebo	
	Pre	Post	Pre	Post	Pre	Post
Body mass (kg)	81.1 \pm 9.3	81.5 \pm 9.9	79.9 \pm 13.0	81.1 \pm 13.8*	78.9 \pm 11.3	78.8 \pm 13.7
Lean-tissue mass (kg)	68.4 \pm 4.4	69.5 \pm 4.6	66.6 \pm 7.6	67.1 \pm 8.2	65.1 \pm 6.2	64.8 \pm 5.8
Fat mass (kg)	12.5 \pm 6.1	12.0 \pm 6.6	13.2 \pm 6.4	14.1 \pm 6.4	13.8 \pm 8.7	13.9 \pm 9.0
% body fat	14.9 \pm 5.7	14.1 \pm 6.2	15.8 \pm 5.8	16.8 \pm 5.4	16.5 \pm 7.4	16.5 \pm 8.3

*Significant increase in body mass from pre- to postsupplementation.

Discussion

The current study demonstrates that short-term supplementation with Cr ($0.1 \text{ g} \cdot \text{kg}^{-1} \cdot \text{day}^{-1}$) and Cr + A-AKG ($0.1 + 0.075 \text{ g} \cdot \text{kg}^{-1} \cdot \text{day}^{-1}$) can improve high-intensity exercise performance. Ten days of both Cr and Cr + A-AKG supplementation increased the total number of repetitions that could be performed over three sets of repeated bench-press exercise. Only Cr + A-AKG supplementation, however, induced significant performance improvements in peak power during three repeated Wingate cycling tests. This provides preliminary evidence that combining Cr with A-AKG might be superior to Cr supplementation alone for power-type athletes.

Short-term Cr supplementation (5–10 days) has been shown to increase high-intensity exercise performance over placebo (for review see Bemben & Lamont, 2005). The mechanism behind the performance improvement is usually attributed to an increase in intramuscular PCr stores, leading to an increased capacity to replenish adenosine triphosphate through PCr hydrolysis. Although we did not measure intramuscular PCr, the increased muscle endurance on the repeated bench-press test was likely caused by an increase in PCr. PCr is an important energy substrate for repeated resistance-training exercise (Lambert & Flynn, 2002), so increased PCr availability after both Cr and Cr + A-AKG supplementation could have enhanced total work capacity. Previous research has reported an increase in the total number of bench-press repetitions performed at a similar load (~70% 1-RM) after short-duration Cr supplementation (Earnest et al., 1995; Volek et al., 1997). The lack of a significant difference between the Cr and Cr + A-AKG groups for bench-press performance provides evidence that the addition of A-AKG did not enhance skeletal-muscle Cr retention, although a direct measurement of muscle Cr uptake would be needed to confirm this. Alternatively, the high muscle tension and short duration of the bench-press exercise might have negated any potential vasodilatory impact from A-AKG supplementation.

The effects of Cr supplementation on Wingate cycle performance are mixed, with some studies showing a positive effect (Okudan & Gokbel, 2005) and others not observing the same benefits (Deutekom, Beltman, de Ruiter, de Koning, & de Haan, 2000; Green, McLester, Smith, & Mansfield, 2001). For example, Okudan and Gokbel reported that Cr supplementation (20 g/day for 6 days) in untrained men led to improvements in peak power and total work output during five repeated Wingate cycling tests. Our findings of no beneficial effect from Cr on peak or average power support the findings of Deutekom et al. and Green et al. (2001). Although it is difficult to compare results across studies, differences in participant training status, dose and duration of Cr supplementation, and testing methodology (i.e., number of repeated Wingate tests and duration of rest intervals) might have influenced the results.

Despite no effect from Cr supplementation alone on repeated Wingate cycle performance, we did find an increase in Wingate peak power after Cr + A-AKG supplementation. This might suggest that A-AKG itself, or in synergism with Cr, improves the ability to generate power on repeated Wingate tests. Our results support the work of Campbell et al. (2006), who found a significant increase in Wingate peak power in participants who supplemented with A-AKG (12 g/day)

during 8 weeks of resistance training. In addition, our results are the first to show that adding A-AKG to Cr supplementation enhances high-intensity exercise performance over Cr supplementation alone. L-arginine is required for endogenous synthesis of nitric oxide (Soeters et al., 2002), which functions to promote local vasodilation. Therefore, supplementing with A-AKG might enhance anaerobic-exercise performance by increasing localized blood flow (Ohta et al., 2007; Paddon-Jones, Borsheim, & Wolfe, 2004), enhancing muscle glucose uptake (McConnell, Huynh, Lee-Young, Canny, & Wadley, 2006), or increasing lactate or ammonia clearance (Schaefer et al., 2002). We did not find any differences between groups for blood lactate concentration during the repeated Wingate tests; however, the complex interplay between muscle lactate production and removal might make this single measure difficult to interpret. The potential reasons for which Cr + A-AKG supplementation was superior to Cr alone for improving Wingate peak power but not bench-press performance are not entirely clear. Perhaps the effects of L-arginine were more evident with the longer rest periods between Wingate tests (2 min) than between bench-press sets (1 min). This might have allowed for greater oxygen delivery and PCr resynthesis or enhanced removal of metabolic inhibitors (e.g., H⁺, K⁺) during the recovery periods between repeated Wingate tests. Further research is needed to determine the effects of A-AKG (and related L-arginine compounds) on muscle blood flow and metabolism during high-intensity exercise.

Similar to previous Cr supplementation studies (e.g., Deutekom et al., 2000; Kilduff et al., 2004), we observed a small increase (~1.2 kg) in body mass after supplementation in the Cr-only group. Ten days of supplementation is likely too short to observe a meaningful increase in dry muscle mass. Therefore, the increase in body mass after Cr supplementation is likely attributed to net body-water retention (Kilduff et al., 2004), because Cr can elevate intracellular osmolarity and increase cellular hydration status (Balsom, Soderlund, Sjodin, & Ekblom, 1995). For example, reduced 24-hr urine excretion has been reported after acute Cr supplementation (Hultman, Soderlund, Timmons, Cederblad, & Greenhaff, 1996), and Francaux and Poortmans (1999) observed a significant increase in net water retention after 42 days of Cr supplementation and strength training. Furthermore, we have previously observed an increase in total body-water content (extracellular and intracellular) from Cr supplementation in vegetarians (Burke et al., 2003). It is not clear why we did not see similar increases in body mass after supplementation in the Cr + A-AKG group. The improvements in bench-press and Wingate performance would seem to indicate that Cr supplementation was effective at increasing intramuscular PCr in the Cr + A-AKG group. From Table 2, it can be seen that, on average, the Cr + A-AKG group increased lean-tissue mass by ~1.1 kg yet decreased fat mass by ~0.5 kg. Therefore, any increase in body mass might have been masked in the Cr + A-AKG group by the decrease in fat mass.

It is important to note that the Xpand supplement containing Cr and A-AKG also contained other ingredients (see Table 1). For example, it contained small amounts of the branched-chain amino acids (BCAAs), medium-chain triglycerides (MCTs), taurine, glutamine, and L-citrulline. BCAA and MCT supplementation might be beneficial when consumed within the hours before or during endurance-type exercise (see reviews by Blomstrand, 2006 and Jeukendrup & Aldred, 2004,

respectively). Supplementation in the current study, however, occurred for 10 days, and the exercise performed was of short duration. Therefore, it is unlikely that BCAA or MCT ingestion would have an ergogenic affect. Chronic taurine administration has been shown to enhance exercise time to exhaustion in rats (e.g., Miyazaki et al., 2004), but we are unaware of any human studies that support these findings. Glutamine is an amino acid that has been shown to help prevent protein degradation in clinical patients undergoing muscle wasting (Stehle et al., 1989), but its efficacy for increasing muscle mass and exercise performance in healthy individuals undergoing resistance training has not been supported (Candow et al., 2001). L-citrulline is an amino acid that, once ingested, is converted to L-arginine by the kidneys and other tissues, leading to an increase in plasma L-arginine (Hickner et al., 2006). Therefore, any potential for L-citrulline to improve exercise performance is likely through an L-arginine pathway (e.g., NO synthesis).

In conclusion, this is the first study to examine the combined effects of Cr and an L-arginine-containing compound on exercise performance. Because of the similar performance-enhancing effects of Cr and L-arginine supplementation (i.e., increased muscle strength and power, increased fatigue resistance during repeated high-intensity exercise), we designed the current study in an attempt to determine whether an L-arginine compound combined with Cr was superior to Cr supplementation alone. Because there are many NO-enhancing products (containing L-arginine) on the market today, it seems prudent to evaluate their effectiveness. The current study adds to the growing body of literature that reports improved resistance-training exercise performance after supplementing with Cr. This was demonstrated by an ~12% improvement in the number of repetitions performed on three repeated sets of bench press at 70% 1-RM after supplementation with both Cr and Cr + A-AKG. Ten days of supplementing with Cr + A-AKG, but not Cr alone, improved peak power on three repeated Wingate cycling tests. These results suggest that combining Cr with A-AKG might confer a further exercise performance advantage compared with Cr alone. These results have immediate application for athletes and exercising individuals involved in power-type events. Further research is required to determine the mechanisms by which A-AKG and other L-arginine-containing compounds (alone and in combination with Cr) improve high-intensity-exercise performance. In addition, future training studies are needed to determine whether the extra performance improvements seen with Cr + A-AKG supplementation result in enhanced adaptations to a training program.

Acknowledgments

Nutritional supplements were donated by Peak Performance Inc., Ontario, Canada.

References

- Balsom, P.D., Soderlund, K., Sjodin, B., & Ekblom, B. (1995). Skeletal muscle metabolism during short duration high-intensity exercise: Influence of creatine supplementation. *Acta Physiologica Scandinavica*, *154*(3), 303–310.
- Bar-Or, O. (1987). The Wingate anaerobic test. An update on methodology, reliability and validity. *Sports Medicine (Auckland, N.Z.)*, *4*(6), 381–394.
- Bemben, M.G., & Lamont, H.S. (2005). Creatine supplementation and exercise performance: Recent findings. *Sports Medicine (Auckland, N.Z.)*, *35*(2), 107–125.

- Blomstrand, E. (2006). A role for branched-chain amino acids in reducing central fatigue. *The Journal of Nutrition*, 136(2), 544S–547S.
- Bode-Boger, S.M., Muke, J., Surdacki, A., Brabant, G., Boger, R.H., & Frolich, J.C. (2003). Oral L-arginine improves endothelial function in healthy individuals older than 70 years. *Vascular Medicine*, 8(2), 77–81.
- Buford, B.N., & Koch, A.J. (2004). Glycine-arginine-alpha-ketoisocaproic acid improves performance of repeated cycling sprints. *Medicine and Science in Sports and Exercise*, 36(4), 583–587.
- Burke, D.G., Chilibeck, P.D., Parise, G., Candow, D.G., Mahoney, D., & Tarnopolsky, M. (2003). Effect of creatine and weight training on muscle creatine and performance in vegetarians. *Medicine and Science in Sports and Exercise*, 35(11), 1946–1955.
- Burke, D.G., Chilibeck, P.D., Parise, G., Tarnopolsky, M.A., & Candow, D.G. (2003). Effect of alpha-lipoic acid combined with creatine monohydrate on human skeletal muscle creatine and phosphagen concentration. *International Journal of Sport Nutrition and Exercise Metabolism*, 13(3), 294–302.
- Campbell, B., Roberts, M., Kerksick, C., Wilborn, C., Marcello, B., Taylor, L., et al. (2006). Pharmacokinetics, safety, and effects on exercise performance of L-arginine alpha-ketoglutarate in trained adult men. *Nutrition (Burbank, Los Angeles County, Calif.)*, 22(9), 872–881.
- Candow, D.G., Burke, N.C., Smith-Palmer, T., & Burke, D.G. (2006). Effect of whey and soy protein supplementation combined with resistance training in young adults. *International Journal of Sport Nutrition and Exercise Metabolism*, 16(3), 233–244.
- Candow, D.G., Chilibeck, P.D., Burke, D.G., Davison, K.S., & Smith-Palmer, T. (2001). Effect of glutamine supplementation combined with resistance training in young adults. *European Journal of Applied Physiology*, 86(2), 142–149.
- Casey, A., Constantin-Teodosiu, D., Howell, S., Hultman, E., & Greenhaff, P.L. (1996). Creatine ingestion favorably affects performance and muscle metabolism during maximal exercise in humans. *The American Journal of Physiology*, 271(1 Pt 1), E31–E37.
- Dawson, B., Cutler, M., Moody, A., Lawrence, S., Goodman, C., & Randall, N. (1995). Effects of oral creatine loading on single and repeated maximal short sprints. *Australian Journal of Science and Medicine in Sport*, 27(3), 56–61.
- Deutekom, M., Beltman, J.G., de Ruiter, C.J., de Koning, J.J., & de Haan, A. (2000). No acute effects of short-term creatine supplementation on muscle properties and sprint performance. *European Journal of Applied Physiology*, 82(3), 223–229.
- Earnest, C.P., Snell, P.G., Rodriguez, R., Almada, A.L., & Mitchell, T.L. (1995). The effect of creatine monohydrate ingestion on anaerobic power indices, muscular strength and body composition. *Acta Physiologica Scandinavica*, 153(2), 207–209.
- Elam, R.P., Hardin, D.H., Sutton, R.A., & Hagen, L. (1989). Effects of arginine and ornithine on strength, lean body mass and urinary hydroxyproline in adult males. *Journal of Sports, Medicine, and Physical Fitness*, 29(1), 52–56.
- Forbes, S.C., Candow, D.G., Little, J.P., Magnus, C., & Chilibeck, P.D. (2007). Effect of Red Bull energy drink on repeated Wingate cycle performance and bench-press muscle endurance. *International Journal of Sport Nutrition and Exercise Metabolism*, 17(5), 433–444.
- Francaux, M., & Poortmans, J.R. (1999). Effects of training and creatine supplement on muscle strength and body mass. *European Journal of Applied Physiology and Occupational Physiology*, 80(2), 165–168.
- Godin, G., & Shephard, R.J. (1985). A simple method to assess exercise behavior in the community. *Canadian Journal of Applied Sport Sciences*, 10(3), 141–146.
- Green, A.L., Hultman, E., Macdonald, I.A., Sewell, D.A., & Greenhaff, P.L. (1996). Carbohydrate ingestion augments skeletal muscle creatine accumulation during creatine supplementation in humans. *The American Journal of Physiology*, 271(5 Pt 1), E821–E826.

- Green, J.M., McLester, J.R., Smith, J.E., & Mansfield, E.R. (2001). The effects of creatine supplementation on repeated upper- and lower-body Wingate performance. *Journal of Strength and Conditioning Research*, 15(1), 36–41.
- Greenhaff, P.L., Bodin, K., Soderlund, K., & Hultman, E. (1994). Effect of oral creatine supplementation on skeletal muscle phosphocreatine resynthesis. *The American Journal of Physiology*, 266(5 Pt 1), E725–E730.
- Greenhaff, P.L., Casey, A., Short, A.H., Harris, R., Soderlund, K., & Hultman, E. (1993). Influence of oral creatine supplementation of muscle torque during repeated bouts of maximal voluntary exercise in man. *Clinical Science*, 84(5), 565–571.
- Hickner, R.C., Tanner, C.J., Evans, C.A., Clark, P.D., Haddock, A., Fortune, C., et al. (2006). L-citrulline reduces time to exhaustion and insulin response to a graded exercise test. *Medicine and Science in Sports and Exercise*, 38(4), 660–666.
- Hultman, E., Soderlund, K., Timmons, J.A., Cederblad, G., & Greenhaff, P.L. (1996). Muscle creatine loading in men. *Journal of Applied Physiology*, 81(1), 232–237.
- Ingwall, J.S., Weiner, C.D., Morales, M.F., Davis, E., & Stockdale, F.E. (1974). Specificity of creatine in the control of muscle protein synthesis. *The Journal of Cell Biology*, 62(1), 145–151.
- Izquierdo, M., Ibanez, J., Gonzalez-Badillo, J.J., & Gorostiaga, E.M. (2002). Effects of creatine supplementation on muscle power, endurance, and sprint performance. *Medicine and Science in Sports and Exercise*, 34(2), 332–343.
- Jeukendrup, A.E., & Aldred, S. (2004). Fat supplementation, health, and endurance performance. *Nutrition (Burbank, Los Angeles County, Calif.)*, 20(7-8), 678–688.
- Kilduff, L.P., Georgiades, E., James, N., Minnion, R.H., Mitchell, M., Kingsmore, D., et al. (2004). The effects of creatine supplementation on cardiovascular, metabolic, and thermoregulatory responses during exercise in the heat in endurance-trained humans. *International Journal of Sport Nutrition and Exercise Metabolism*, 14(4), 443–460.
- Kilduff, L.P., Vidakovic, P., Cooney, G., Twycross-Lewis, R., Amuna, P., Parker, M., et al. (2002). Effects of creatine on isometric bench-press performance in resistance-trained humans. *Medicine and Science in Sports and Exercise*, 34(7), 1176–1183.
- Kubota, T., Imaizumi, T., Oyama, J., Ando, S., & Takeshita, A. (1997). L-arginine increases exercise-induced vasodilation of the forearm in patients with heart failure. *Japanese Circulation Journal*, 61(6), 471–480.
- Lambert, C.P., & Flynn, M.G. (2002). Fatigue during high-intensity intermittent exercise: Application to bodybuilding. *Sports Medicine (Auckland, N.Z.)*, 32(8), 511–522.
- McConnell, G.K., Huynh, N.N., Lee-Young, R.S., Canny, B.J., & Wadley, G.D. (2006). L-arginine infusion increases glucose clearance during prolonged exercise in humans. *American Journal of Physiology. Endocrinology and Metabolism*, 290(1), E60–E66.
- Miyazaki, T., Matsuzaki, Y., Ikegami, T., Miyakawa, S., Doy, M., Tanaka, N., et al. (2004). Optimal and effective oral dose of taurine to prolong exercise performance in rat. *Amino Acids*, 27(3–4), 291–298.
- Ohta, F., Takagi, T., Sato, H., & Ignarro, L.J. (2007). Low-dose L-arginine administration increases microperfusion of hindlimb muscle without affecting blood pressure in rats. *Proceedings of the National Academy of Sciences of the United States of America*, 104(4), 1407–1411.
- Okudan, N., & Gokbel, H. (2005). The effects of creatine supplementation on performance during the repeated bouts of supramaximal exercise. *Journal of Sports, Medicine, and Physical Fitness*, 45(4), 507–511.
- Paddon-Jones, D., Borsheim, E., & Wolfe, R.R. (2004). Potential ergogenic effects of arginine and creatine supplementation. *The Journal of Nutrition*, 134(10, Suppl.) 2888S–2894S discussion 2895S.
- Robinson, T.M., Sewell, D.A., Hultman, E., & Greenhaff, P.L. (1999). Role of submaximal exercise in promoting creatine and glycogen accumulation in human skeletal muscle. *Journal of Applied Physiology*, 87(2), 598–604.

- Schaefer, A., Piquard, F., Geny, B., Doutreleau, S., Lampert, E., Mettauer, B., et al. (2002). L-arginine reduces exercise-induced increase in plasma lactate and ammonia. *International Journal of Sports Medicine*, 23(6), 403–407.
- Soeters, P.B., Hallemeesch, M.M., Bruins, M.J., van Eijk, H.M., & Deutz, N.E. (2002). Quantitative in vivo assessment of arginine utilization and nitric oxide production in endotoxemia. *American Journal of Surgery*, 183(4), 480–488.
- Stehle, P., Zander, J., Mertes, N., Albers, S., Puchstein, C., Lawin, P., et al. (1989). Effect of parenteral glutamine peptide supplements on muscle glutamine loss and nitrogen balance after major surgery. *Lancet*, 1(8632), 231–233.
- Stevens, B.R., Godfrey, M.D., Kaminski, T.W., & Braith, R.W. (2000). High-intensity dynamic human muscle performance enhanced by a metabolic intervention. *Medicine and Science in Sports and Exercise*, 32(12), 2102–2108.
- Thomas, S., Reading, J., & Shephard, R.J. (1992). Revision of the Physical Activity Readiness Questionnaire (PAR-Q). *Canadian Journal of Sport Sciences*, 17(4), 338–345.
- Volek, J.S., Kraemer, W.J., Bush, J.A., Boetes, M., Incledon, T., Clark, K.L., et al. (1997). Creatine supplementation enhances muscular performance during high-intensity resistance exercise. *Journal of the American Dietetic Association*, 97(7), 765–770.
- Yquel, R.J., Arzac, L.M., Thiaudiere, E., Canioni, P., & Manier, G. (2002). Effect of creatine supplementation on phosphocreatine resynthesis, inorganic phosphate accumulation and pH during intermittent maximal exercise. *Journal of Sports Sciences*, 20(5), 427–437.