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ORIGINAL RESEARCH

Oral Creatine Supplementation's Decrease of Blood Lactate During Exhaustive, Incremental Cycling

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Purpose: To determine the effects of creatine supplementation on blood lactate during incremental cycling exercise. ***Methods:*** Thirteen male subjects (*M* ± *SD* 23 ± 2 yr, 178.0 ± 8.1 cm, 86.3 ± 16.0 kg, 24% ± 9% body fat) performed a maximal, incremental cycling test to exhaustion before (Pre) and after (Post) 6 d of creatine supplementation (4 doses/d of 5 g creatine + 15 g glucose). Blood lactate was measured at the end of each exercise stage during the protocol, and the lactate threshold was determined as the stage before achieving 4 mmol/L. Lactate concentrations during the incremental test were analyzed using a 2 (condition) × 6 (exercise stage) repeated-measures ANOVA. Differences in power at lactate threshold, power at exhaustion, and total exercise time were determined by paired *t* tests and are presented as *M* ± *SD*. ***Results:*** Lactate concentrations were reduced during exercise after supplementation, demonstrating a significant condition effect ($p = .041$). There was a tendency for increased power at the lactate threshold (Pre 128 ± 45 W, Post 143 ± 26 W; $p = .11$). Total time to fatigue approached significant increases (Pre 22.6 ± 3.2 min, Post 23.3 ± 3.3 min; $p = .056$), as did maximal power output (Pre 212.5 ± 32.5 W, Post 220 ± 34.6 W; $p = .082$). ***Conclusions:*** Our findings demonstrate that creatine supplementation decreases lactate during incremental cycling exercise and tends to raise lactate threshold. Therefore, creatine supplementation could potentially benefit endurance athletes.

Keywords: endurance, lactate threshold, phosphocreatine

The creatine kinase reaction uses phosphocreatine (PCr) to rephosphorylate adenine diphosphate to produce ATP and creatine (Cr), helping to buffer cellular energy needs (Greenhaff, 1997). Because PCr stores are limited, this reaction only provides fuel for short, high-intensity bouts of exercise (6–10 s; Wyss & Kaddurah-Daouk, 2000). Traditional Cr loading through oral ingestion of Cr monohydrate at 20–30 g/day for 5–7 days has been shown to increase muscle stores of Cr and PCr and decrease recovery time of PCr resynthesis (Greenhaff, Bodin, Soderlund, & Hultman, 1994). The performance benefits due to such supplementation are most clearly seen with supramaximal exercise, especially repeated short bouts of high-intensity exercise (Birch, Noble, & Greenhaff, 1994; Bosco et al., 1997; Casey, Constantin Teodosiu, Howell, Hultman, & Greenhaff, 1996) .

Glycolytic metabolism provides fuel for more sustained, high-intensity exercise beyond the initial seconds fueled by PCr. Lactate, a byproduct of glycolysis, can be measured and used to determine energy-system balance. It has been shown that lactate concentration after five repeated 6-s cycling intervals with minimal rest were lower after Cr supplementation (Balsom, Soderlund, Sjodin, & Ekblom, 1995). While the lowering of acute lactate concentrations after short, intense, and repeated exercise bouts may be of benefit in power-speed activities, it is the lactate threshold, or point where lactate begins to accumulate in the blood during more prolonged incremental or steady-state exercise, that has been correlated with performance in endurance exercise (Joyner & Coyle, 2008). In this regard, total work and the lactate threshold were improved by PCr injected intravenously 24 hr and 30 min before incremental cycling exercise (50 W plus 25 W every 3 min to exhaustion; Vorobiev, Vetrova, Larina, Popova, & Grigoriev, 1996). However, it is unclear if the ingestion of Cr to increase PCr stores would have the same results as intravenous PCr injection in a similar, incremental cycling protocol.

Traditional oral Cr supplementation was shown to have no effect on lactate concentrations after repeated and intermittent sprint cycling over the course of more prolonged exercise bouts, despite improvements in the sprint performances (Engelhardt, Neumann, Berbalk, & Reuter, 1998; Hickner, Dyck, Sklar, Hatley, & Byrd, 2010; Vandebuerie, Vanden Eynde, Vandenberghe, & Hespel, 1998). Likewise, lactate concentrations after steady-state submaximal cycling exercise (continuous 20-min stages at 40%, 50%, and 60% maximal work rate) were not influenced by Cr supplementation (van Loon et al., 2003). However, without an incremental exercise protocol to exhaustion with shorter stages, it is difficult to determine the threshold point for lactate accumulation. There is evidence in favor of an improved lactate threshold for

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incremental rowing exercise after traditional Cr loading (Chwalbinska-Moneta, 2003), but not for incremental running exercise (Stroud et al., 1994). While less lactate accumulation has been established after intravenous PCr injection during incremental cycling (Vorobiev et al., 1996), it is unknown how the lactate threshold is affected by traditional Cr loading. Therefore, the purpose of the current study was to determine the effects of short-term Cr loading on the 4-mmol/L lactate threshold and blood lactate concentrations at each stage of incremental cycling exercise to exhaustion. We hypothesized that blood lactate levels would be lower after supplementation. We further hypothesized that supplementation would raise the lactate threshold.

Methods

Experimental Protocol

To determine the effect of oral Cr supplementation on lactate during an incremental cycling test to exhaustion, subjects performed an exercise-testing protocol (methods to follow) followed by a standard 6-day supplementation protocol of Cr (5 g) + glucose (15 g) ingested four times a day taken, at equal intervals during waking hours. This supplementation protocol has been shown to increase intramuscular PCr and free CR (Greenhaff et al., 1994). After the supplementation period, subjects returned to repeat the exercise-testing protocol.

Subjects

Recreationally active men between the ages of 20 and 30 years ($M \pm SD$ age 23 ± 2 years, height 178.0 ± 8.1 cm, weight 86.3 ± 16.0 kg, % body fat 24 ± 9) participating in structured exercise at least three times per week contacted the laboratory in response to flyers posted in the university community. Before inclusion, potential subjects were screened for possible contraindications to exercise and current supplementation. Those taking supplements within the previous 3 months, as well as trained cyclists and those performing cycling as a regular activity, were excluded from the study. This ensured no training effect over the course of supplementation. Verbal and written consent were obtained before familiarization and testing. All methods and procedures were approved by the Institutional Review Board for Research with Human Subjects of Texas A&M University.

Baseline Testing

One day before the initial exercise-testing session, subjects reported to the laboratory in the fasted state. Body fat was determined by dual-energy X-ray absorptiometry (Lunar Prodigy, GE). Before both testing sessions, blood was collected from the antecubital vein into a serum separator Vacutainer tube using standard, sterile phlebotomy procedures. Blood was allowed to clot at room temperature and then centrifuged for 20 min for serum separation. The serum sample was then couriered to another laboratory for determination of serum Cr.

Experimental Exercise Protocol

The day after blood sampling, subjects reported to the laboratory to perform an incremental cycling test to voluntary exhaustion. Before testing, subjects were instructed to refrain from any lower body exercise training outside of activities of daily living for at least 48 hr. In addition, they were asked to not participate in any cycling during the week preceding the second testing session, as this was not a training study. Testing was performed on an electronically braked cycle ergometer (Lode Excalibur, Lode, Groningen, Netherlands). Subjects were allowed to adjust the seat and handle bars for comfort, and the positions were recorded for future testing. The cycling test began on a "go" command. The preprogrammed protocol began at 30 W and increased by 30 W every 3 min until volitional fatigue. Cadence was set at 70 rpm. Fatigue was defined as the point at which subjects were no longer able to maintain a 70-rpm cadence for 10 s. An electronic metronome was set to help subjects maintain cadence. At the conclusion of exercise, subjects exited the ergometer and were immediately moved to a chair for 10 min of seated rest. Movement time from cycle to chair for additional collection approximated 30 s.

Blood Sampling and Lactate Measures

Before each experimental exercise protocol, subjects were seated quietly in a phlebotomy chair for 5 min before the insertion of a 22-gauge shielded intravenous catheter (Becton Dickinson, Sandy, UT). The catheter was inserted into a vein in the right arm and capped with an Interlink injection site cap (Baxter, Deerfield, IL) to allow for multiple blood draws. After insertion of the catheter, 2–3 ml of 0.9% sodium chloride (Braun, Scarborough, Ontario) was injected into the portal site. A 3-ml syringe (Bectin Dickinson, Franklin Lakes, NJ) was used to withdraw a waste sample, after which another sample was drawn with a new 3-ml syringe to obtain resting blood lactate (REST). Once the subject began exercise testing, 2–3 ml of 0.9% sodium chloride was injected to flush the portal during the last 30 s of each stage, after which a waste sample of approximately 3 ml was drawn followed immediately by another sample of approximately 2 ml, which was immediately analyzed for blood lactate concentration. This procedure was also followed immediately postexercise (IPE), as well as 5 (5MIN) and 10 (10MIN) min after exercise. All samples were analyzed for blood lactate using a portable Accutrend lactate analyzer (Sports Resource Group, Minneapolis, MN). Lactate threshold was defined as the exercise stage immediately preceding the stage where the lactate concentration exceeded 4 mmol/L.

Supplementation Protocol

Subjects were provided Cr + glucose in individual dosing packages of 5 g Cr + 15 g glucose. They were instructed

to take four individual doses four times per day evenly distributed throughout their waking hours for 6 consecutive days until they reported to the laboratory for the second exercise-testing session. This supplementation protocol has previously been shown to increase muscle Cr and PCr levels (Greenhaff et al., 1994). All subjects verbally reported taking supplements as instructed for the entirety of the study.

Statistical Analysis

All statistical analysis was performed using SPSS Version 16.0 (SPSS, Chicago, IL). A one-way ANOVA was used to determine differences between serum Cr before (Pre) and after (Post) supplementation. Statistical analysis of blood lactate during exercise was performed using a 2 (condition: presupplement, postsupplement) × 6 (stage: 30 W, 60 W, 90 W, 120 W, 150 W, 180 W) repeated-measures ANOVA. One hundred eighty watts was used as a cutoff, as only 50% ($n = 6$) of the subjects exceeded this power output. To determine differences between REST, 5MIN, and 10MIN, a one-way ANOVA repeated on condition was used. A paired Student's t test was used to determine differences in power output at the 4-mmol/L lactate threshold, maximal power, and time to fatigue pre- and postsupplementation. Maximal power was determined as the power output during the final stage of exercise for each subject. Time to fatigue was the total exercise time completed by each subject during the incremental protocol. Post hoc analysis was performed where necessary using Bonferroni correction.

Results

No significant differences were observed in resting serum Cr values ($p = .12$) or resting lactate levels ($p = .26$) pre- and postsupplementation. Results of lactate obtained during the exercise tests are presented in Figure 1. There was a significant exercise-stage effect ($p = .001$) across all points due to the increasing lactate with each increase in workload. A significant condition effect ($p = .041$) was observed with no interaction effect ($p = .498$) observed, demonstrating that lactate concentrations throughout the exercise bout were lower after supplementation. There was a tendency for increased power at the 4-mmol/L lactate threshold with supplementation (Pre 128 ± 45 W, Post 143 ± 26 W; $p = .11$). Individual changes in power at the lactate threshold are displayed in Figure 2. No significant differences between pre- and postsupplement conditions were determined in lactate obtained IPE, 5MIN, or 10MIN (Table 1). Total exercise time to fatigue approached significant increases after supplementation (Pre 22.6 ± 3.2 min, Post 23.3 ± 3.3 min; $p = .056$). The average increase in exercise time was 0.66 ± 1.1 min. Individual changes in exercise time are displayed in Figure 3. Maximal power output at time of fatigue also approached significance (Pre 212.5 ± 32.5 W, Post 220 ± 34.6 W; $p = .082$).

Discussion

The current data indicate a significant effect of short-term Cr loading to reduce lactate levels during incremental

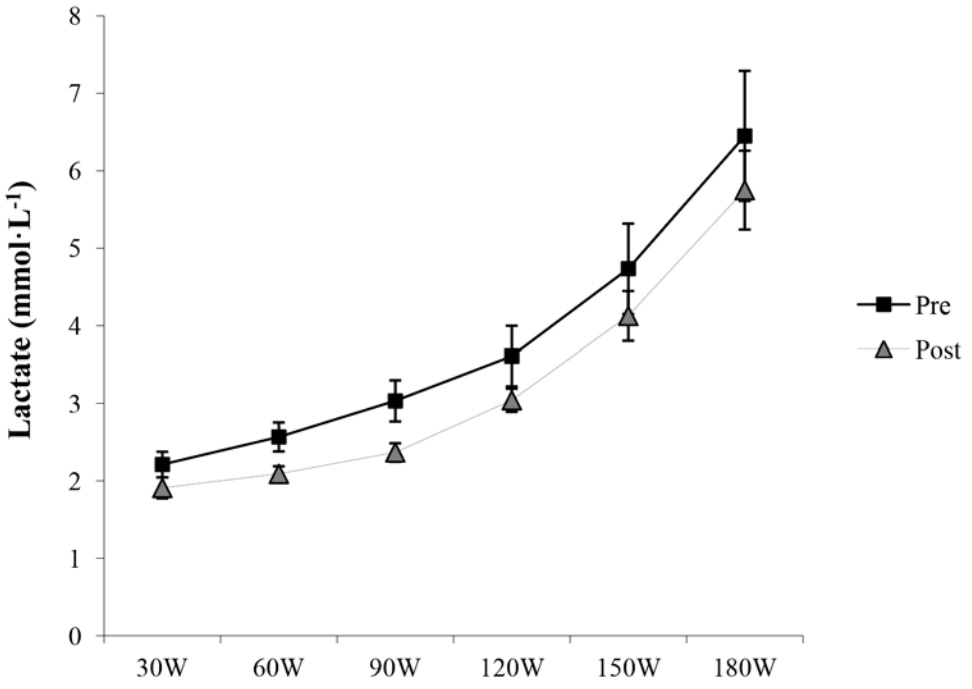

Figure 1 — Lactate levels during incremental cycling exercise before and after creatine supplementation. Significant effect ($p < .05$) for both exercise stage and condition. Values displayed as group mean for a given stage, and error bars represent *SEM*.

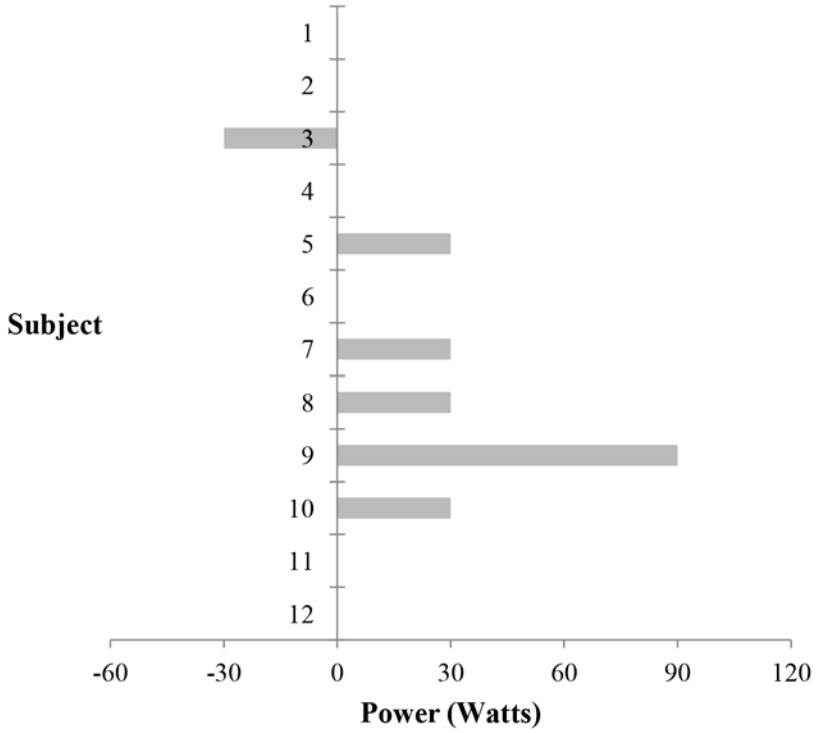

Figure 2 — Individual subject changes (Post – Pre) in cycling power output at 4-mmol/L lactate threshold with creatine supplementation. Group *M* ± *SD* before and after supplementation were as follows: Pre 128 ± 45 W, Post 143 ± 26 W; $p = .11$.

Table 1 Lactate Levels (mmol/L) Immediately (IPE) and 5 (5MIN) and 10 (10MIN) Minutes After Exercise, *M* ± *SD*

	Pre	Post	*p*
IPE	10.3 ± 2.3	11.1 ± 2.0	.261
5MIN	11.7 ± 2.1	12.0 ± 1.6	.586
10MIN	10.5 ± 2.1	11.2 ± 2.1	.313

cycling exercise to exhaustion. Our current findings also showed a 12% increase in power output with a trend toward significance ($p = .11$) at the 4-mmol/L lactate threshold after supplementation. Five of the 12 subjects showed improvement, and only 1 had a decrement in this performance measure (Figure 2). In addition, maximal exercise time increased by 40 s ($p = .056$) on average, a change that approached significance, with only 2 subjects failing to improve.

To our knowledge, no other investigators have studied the effects of Cr supplementation on lactate during incremental cycling exercise. Similar to our findings, using the same creatine-supplement-dosing strategy (20 g/day for 5–6 days) and a similar incremental protocol on a rowing ergometer, Chwalbinska-Moneta (2003) demonstrated reduced lactate measurements in trained rowers during exercise after supplementation. Both the placebo group and the supplemented group of rowers had decreased lactate measurements at stages later in the exhaustive exercise protocol, but only the Cr-supplemented group experienced reduced blood lactate at lower intensities, as well. Therefore, there was not a significant overall condition effect of reduced lactate throughout the test, as observed in our current findings with cycling exercise. The supplemented rowers did show an increase in their lactate threshold when plotted as a log function against the log of workload, while the placebo group did not (Chwalbinska-Moneta, 2003). Similarly, our current findings showed a tendency for increased power at the 4-mmol/L lactate threshold after supplementation.

The discrepancies between the previously discussed findings (Chwalbinska-Moneta, 2003) and our own may be due to differing modes of exercise and the subjects' training experience. Both the Cr-supplemented and control groups of rowers were involved in heavy training during the time of study. This is a confounding factor that resulted in the placebo group's experiencing decreased lactate levels during later stages of exercise similar to their Cr-supplemented counterparts (Chwalbinska-Moneta, 2003). It is well established that intense endurance training, such as performed by the rowers in the study by Chwalbinska-Moneta, induces adaptations that may result in lower blood lactate after training at the same exercise intensity as before training (Hurley et al., 1984). In their study, Chwalbinska-Moneta noted a significant decrease in heart rate and blood lactate concentrations at submaximal workloads, indicating that the intensity of training was sufficient to induce adaptations even if observations were made only 7 days apart.

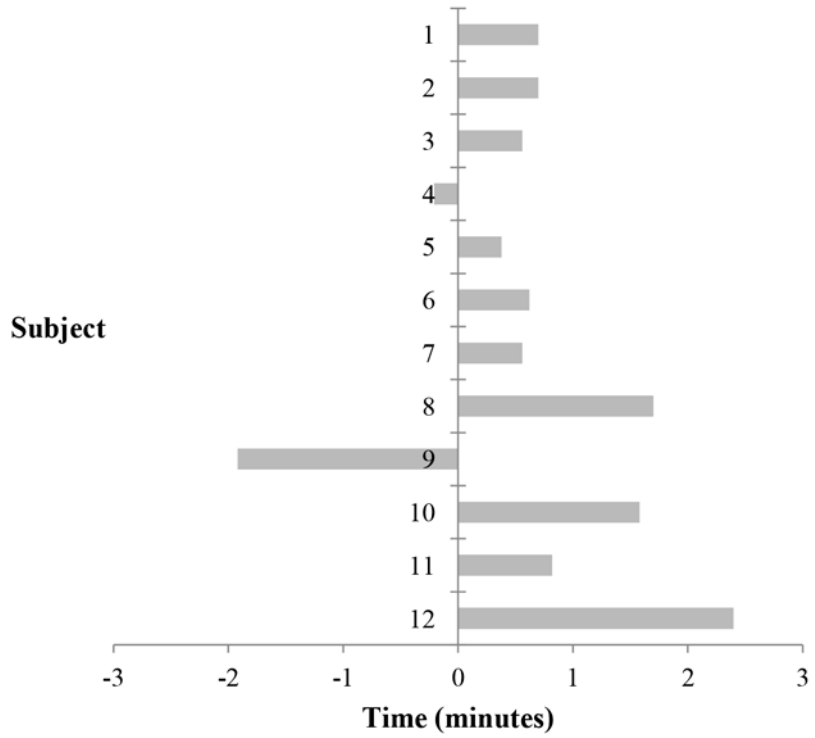

Figure 3 — Individual subject changes (Post – Pre) in maximal cycling time with creatine supplementation. Group $M \pm SD$ before and after supplementation were as follows: Pre 22.6 ± 3.2 min, Post 23.3 ± 3.3 min; $p = .056$.

Counter to our current results, Stroud et al. (1994) observed no changes in lactate at each stage or in lactate threshold using an incremental treadmill protocol in trained runners (6-min stages with increases of 5% VO_{2max}). While differing modes were used, the current protocol and that of Stroud et al. were similar, using the same Cr-supplement dosing strategy (20 g/day for 5–6 days) and having subjects repeat the protocol after supplementation. Because subjects in the current study were not endurance trained, they were more likely to have a higher proportion of fast-twitch (FT) fibers and reduced mitochondrial density than the runners in the study by Stroud et al. While measurements of fiber type were not made in either study, Gollnick, Armstrong, Saubert, Piehl, and Saltin (1972) demonstrated that slow-twitch (ST) fibers predominate in the muscles of endurance-trained men. In addition, oxidative capacity is greater in both ST and FT fiber types in endurance-trained men (Gollnick et al., 1972). Glycogen breakdown is much larger in FT than in ST fibers (Gollnick, Piehl, & Saltin, 1974). Given the probability of a higher proportion of FT fibers in the current study coupled with the increased total Cr as a result of oral supplementation, the rate of glycogenolysis would therefore be lower due to the greater reliance on PCr and less accumulation of adenine monophosphate. The reduced lactate then may be attributable to less reliance on anaerobic glycolysis and buffering of adenine diphosphate phosphorylation. This indirectly supports the conclusions made by Casey et al. (1996) in response to similar decreases in lactate after 6-s maximal-intensity bursts demonstrated by Balsom, Ekblom, Soderlund, Sjodin, and Hultman (1993)

There is no doubt that there are large interindividual differences in the change in total Cr in muscle as evidenced by the work of Harris, Viru, Greenhaff, and Hultman (1992) and Greenhaff et al. (1994). More important, Greenhaff et al. demonstrated that any measureable effect on PCr resynthesis as a result of Cr ingestion was only observed in individuals demonstrating more than a 20-mmol/kg increase in total Cr. This was also a concern of Stroud et al. (1994), given their results after Cr ingestion on both lactate and respiratory-gas exchange. In fact, this may have been the case, as using trained subjects, Nelson et al. (2000) demonstrated lower oxygen cost while performing a graded cycle-ergometer test to exhaustion identical to the one used in the current study. Based on their results, Nelson et al. speculated that the mechanism responsible for their finding was an increase in muscle PCr levels delaying the decrease in the ratio of ATP to adenine diphosphate needed to stimulate mitochondrial respiration. The results demonstrated by Nelson et al. and the current study suggest that the buffering of cellular energy needs by increasing the availability of PCr through Cr supplementation is a possible mechanism that might allow for decreased reliance on glycolysis and subsequent decreases in lactate production at each stage of incremental exercise observed in the current study.

It has also been proposed that Cr supplementation may enhance oxygen uptake during repeated intermittent low- and high-intensity (alternating 30% and 90% max for 3 min each) bouts of cycling exercise (Rico-Sanz & Marco, 2000). Rico-Sanz and Marco found an increase in oxygen consumption during the higher intensity aerobic-exercise segments with supplementation, but lactate concentrations were not lowered for the Cr-supplemented group or placebo. Since the high-intensity efforts were likely well above the subject's lactate threshold, it is not necessarily a good indicator of the effects of Cr on lactate accumulation during graded exercise. At the same time, others have found improved efficiency and lower levels of oxygen consumption during submaximal exercise after Cr supplementation (Murphy, Watsford, Coutts, & Richards, 2005; Nelson et al., 2000).The proposed mechanisms for improved O_2 utilization in relation to the PCr:Cr ratio have been described by Walsh et al. (2001), who did not find that oral Cr supplementation altered these mechanisms in vitro. Given that we did not measure oxygen consumption during our current study, we are unable to conclude whether altered oxygen uptake could explain any of the changes in lactate accumulation. Typically, increased oxygen consumption at a given physical workload would be considered a negative in terms of performance, as this would suggest a decrease in exercise efficiency. However, if maximal oxygen consumption was also increasing or the change in oxygen consumption was simply due to a shift in energy systems being used, perhaps it is not a performance decrement.

Given the results of the current study, it is likely that the mechanism of action in which Cr supplementation causes its effects may vary based not only on fiber type, or the composition of mixed fiber types, but on training status of the individual, as well. While Cr is likely the most studied supplement, with each study a new question arises as to how it may affect performance. Future research is needed to determine if these mechanisms differ and how they may best benefit the individual.

Conclusions

While many studies have analyzed the beneficial effects of Cr supplementation on sprint and power performance (Birch et al., 1994; Bosco et al., 1997; Casey et al., 1996), few have measured its effects on endurance (Balsom, Harridge, Soderlund, Sjodin, & Ekblom, 1993; Engelhardt et al., 1998; Finn et al., 2001). It has been suggested that the improvements in sprint speed and maximal power seen during repeated bouts of maximal anaerobic exercise may also carry over to intermittent sprint efforts spread throughout an endurance-exercise bout (Engelhardt et al., 1998). This is thought to be due to the greater provision and resynthesis of fuel by the PCr energy system. These findings may be of benefit to endurance athletes such as racing cyclists and draft-legal triathletes, who are required to perform multiple surges and accelerations throughout their primarily aerobic races. However, given that the lactate threshold is a key component of endurance-exercise performance (Joyner & Coyle, 2008), if Cr supplementation were to improve this marker, it could have application to all endurance athletes, not just those racing in more tactical-style events with surges and accelerations. Our findings suggest that Cr supplementation decreases lactate throughout incremental cycling exercise in recreationally active subjects, while the lactate threshold and maximal exercise time approached significant gains. More work needs to be done to determine if the observed trend of an increased lactate threshold during incremental exercise would translate into the ability to perform longer at steady-state exercise intensities near the lactate threshold. In addition, future studies measuring more physiological markers (particularly VO_2) and including a placebo group could help elucidate the potential benefits and mechanisms of Cr supplementation for endurance-exercise performance markers.

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