Journal of Strength and Conditioning Research, 2001, 15(2), 178–184

The Effects of Creatine Supplementation on Exercise-Induced Muscle Damage

ERIC S. RAWSON, BRIDGET GUNN, AND PRISCILLA M. CLARKSON

Department of Exercise Science, University of Massachusetts-Amherst, Amherst, Massachusetts 01003.

ABSTRACT

This investigation evaluated the effects of oral creatine (Cr) supplementation on markers of exercise-induced muscle damage following high-force eccentric exercise in subjects randomly administered Cr or placebo (P) in a double-blind fashion. When injected, exogenous phosphocreatine has been shown to stabilize the muscle membrane in cardiac tissue and enhance recovery of strength and power following injury. Twenty-three men aged 18–36 years ingested either 20 g of Cr or P for 5 days. Criterion measures were maximal isometric force of the elbow flexors (MIF), range of motion (ROM) about the elbow, mid and distal arm circumference (CIR; to assess swelling), soreness with movement and palpation (SOR), and blood levels of creatine kinase (CK) and lactate dehydrogenase (LDH). Following the supplementation period, subjects performed 50 maximal eccentric contractions of the elbow flexors. Criterion measures were assessed pre-exercise, immediately postexercise, and for 5 days after exercise. Both groups experienced a significant loss of MIF and ROM (time effect, $p < 0.05$). There was a significant increase in CIR of the mid and distal biceps, SOR with movement and palpation, CK, and LDH (time effect, $p < 0.05$), indicating that there was significant muscle damage. However, there were no significant differences in any of the criterion measures between groups (group $\times$ time interaction term, $p > 0.05$). The pattern of change over the 6 days, in response to the eccentric exercise, was nearly identical between groups. These data suggest that 5 days of Cr supplementation does not reduce indirect markers of muscle damage or enhance recovery from high-force eccentric exercise.

Key Words: eccentric exercise, ergogenic aid, phosphocreatine, creatine monohydrate

Reference Data: Rawson, E.S., B. Gunn, and P.M. Clarkson. The effects of creatine supplementation on exercise-induced muscle damage. *J. Strength Cond. Res. 15(2):178–184. 2001.*

Introduction

Studies examining the effects of creatine (Cr) supplementation have demonstrated under a variety of different testing conditions improved performance in short-term, high-intensity exercise (1, 8, 11, 15, 25, 33, 34), although this has not been shown in all studies (2, 7, 18, 23, 30). Increased Cr and phosphocreatine (PCr) levels resulting from supplementation may enhance performance by improving PCr and ATP resynthesis (10); increasing body mass (1, 8, 10, 15, 34); directly increasing protein synthesis (14); allowing athletes to train at higher intensity levels (8, 16, 33); or decreasing muscle relaxation time (32).

PCr has another important function in muscle cells besides its role in energy production. Because of its amphipathic nature, PCr is able to bind to the polar phospholipid heads of the muscle membrane (27). By binding to the phospholipid heads, PCr can stabilize the membrane phospholipid bilayer, decreasing membrane fluidity and turning the membrane into a more ordered state (27). Because of this property, Cr supplementation and subsequent increased muscle PCr levels may exert a protective effect on skeletal muscle membranes during strenuous eccentric exercise.

High-force eccentric exercise alters sarcolemmal and sarcoplasmic reticulum (SR) membrane function (17, 36). There is evidence that the membranes are damaged by the mechanical event of the eccentric contraction and by an increase in lipid peroxidation from free radicals generated by macrophages that enter to repair the muscle (31). Macrophages also release noxious chemicals that cause soreness. Altered SR function results in an increase in intracellular calcium that can activate degradative pathways (3). Damage or degradation of muscle contractile proteins contributes to the loss in muscle function after eccentric exercise (13). Increased intracellular PCr could stabilize the membranes and subsequently prevent or reduce the cascade of events leading to degradation, loss in muscle function, and inflammation.

The increase in muscle proteins in the blood such as creatine kinase (CK) and lactate dehydrogenase (LDH), which result from unaccustomed eccentric exercise, have been well documented (5, 6, 19–21, 35). In a preliminary investigation, Port et al. (22) assessed the effects of Cr supplementation on blood levels of LDH in rats swimming to exhaustion. In the group that did

not receive Cr, postexercise LDH followed the time course that had been previously shown to follow unaccustomed exercise (22). However, less LDH was detected in the rats receiving Cr, despite the fact that they exercised longer. Although swimming is not typically associated with exercise-induced muscle damage, the authors suggested that these results could be due to the effects of Cr on muscle membrane integrity (22). In cardiac tissue, PCr supplementation has also been shown to decrease the loss of muscle proteins, indicating less cytoplasmic leakage and potentially less muscle damage (27). In fact, because of its membrane stabilization effects, PCr is used as a cardioprotective agent during heart surgery (27). In a review chapter, Clark (4) cited unpublished results from a study where PCr was injected into athletes during intense training and produced a ''striking reduction'' in delayed-onset muscle stiffness despite an increased training volume. It was postulated that this was a result of less muscle damage occurring during training, but muscle stiffness and soreness decrease during training as the muscles adapt to the exercise stress. Few details are available regarding the study cited by Clark (4), as the data were cited as unpublished observations and only briefly described in a review chapter.

Satolli and Marchesi (28) examined the effects of injectable PCr supplementation on patients with muscle atrophy and weakness of the thigh due to knee osteoarticular lesions. All subjects (n = 69) exhibited decreased muscle strength and power in their affected extremity as a result of surgery, distortions treated with a plaster cast, meniscectomy, or fractures (28). During the rehabilitation program, subjects treated with PCr showed an increase in torque values that was faster and greater for all movements than that in the control group, indicating a more rapid recovery of muscle strength (28). Perhaps the most impressive finding of this study was that there were no changes in the healthy extremity resulting from PCr supplementation, suggesting that PCr had a localized effect on the injured area. However, no mechanism of action was suggested. These additional benefits that have been shown clinically with PCr supplementation may have important implications for athletes undergoing intense training.

Because PCr has membrane stabilization effects, has been shown to reduce the loss of intracellular enzymes following intense exercise, and enhances recovery of strength and power following surgery and injury, we hypothesized that oral Cr supplementation would have similar effects following exercise-induced muscle damage. With this in mind, the purpose of this investigation was to compare the responses of subjects ingesting Cr with those ingesting a placebo (P) based on the following measures: the level of muscle proteins in the blood, maximal isometric force (MIF), range of motion (ROM), arm circumference (CIR), and muscle soreness (SOR). By measuring these established, indirect markers of exercise-induced muscle damage following a bout of high-force eccentric exercise, we examined if Cr supplementation offers protective effects on skeletal muscle under extreme exercise conditions.

Table 1. Subject characteristics. Values are means ± *SE.*

	Creatine group	Placebo group
Age (y)	20.0 ± 0.4	21.1 ± 1.6
Height (cm)	176.1 ± 1.5	179.2 ± 1.5

Methods

Experimental Design

This study was conducted in the Exercise Biochemistry Laboratory at the University of Massachusetts. On day 1, baseline measurements of MIF, ROM, CIR, SOR, and body mass (BM) were assessed. A blood sample was also taken during this visit. On day 2, MIF, ROM, CIR, SOR, and BM were reassessed to establish reliability of baseline measures. Beginning on day 3, subjects ingested either Cr or P for 5 days. Following Cr supplementation on day 8, subjects performed a standardized exercise protocol of the elbow flexors. A reassessment of MIF, ROM, CIR, and SOR was conducted prior to and immediately following the exercise session. Assessments of MIF, ROM, CIR, SOR, BM, and a blood draw were taken once per day on each of the following 5 days.

Subjects

Male subjects were recruited from the local Amherst area. The subject pool consisted of 23, non–weight-trained men, with 12 in the Cr group and 11 in the P group. Subjects were instructed to maintain a similar activity level and diet for the duration of the study. All subjects signed an informed consent document consistent with the University of Massachusetts policy for the protection of human subjects. Descriptive characteristics of the subjects are presented in Table 1.

Supplementation

Subjects were matched for MIF and then randomly assigned to a control group or placebo group and supplemented in double-blind fashion. Subjects received containers of either chewable Cr monohydrate tablets (Createam; NutraSense Company, Shawnee Mission, KS) or an equivalent volume of a similar-tasting and look-alike dextrose P. Subjects in the experimental group ingested 5 g of Cr and 7 g of dextrose 4 times per day for 5 days (20 $g \cdot d^{-1}$ for 5 days). This supplementation protocol has been previously shown to be effective in elevating muscle Cr and PCr levels (12). Subjects in the control group ingested 25 g of dextrose

4 times per day for 5 days. Subjects in both groups ingested 1 serving of Gatorade following ingestion of the supplement at 4 equal intervals throughout the day.

Muscle Function, Circumference, and Soreness Tests

MIF of the elbow flexors was assessed using a modified preacher bench (standard weightlifting equipment) attached to a strain gauge and interfaced with a computer (Jackson Evaluation System; Lafayette Instrument Co., Lafayette, IN). Subjects were seated on the bench with the elbow of the dominant arm fixed at 90°. Three maximal isometric contractions, with 1-minute rest between trials, were recorded and averaged as the criterion score. It is believed that this is the best measure of eccentric, exercise-induced muscle damage in human studies (35). ROM of the elbow joint angle was evaluated by measuring the flexed (FANG) and relaxed (RANG) arm angle using a goniometer. FANG was measured when the subject attempted to fully flex the elbow to touch the shoulder, whereas the elbow remained at their side. RANG was measured when the subject relaxed the arm, allowing it to hang by their side. CIR was measured to evaluate swelling using an anthropometric spring tape measure, at the distal and middle portion of the subject's upper arm, when the arm hung loosely by his side. Perception of SOR was assessed using a visual analog scale of a 100-mm continuous line, where 0 mm represents 'no pain' and 100 mm represents 'very painful.' SOR was evaluated upon movement (curling a 0.9-kg hand weight) and palpation.

Blood Samples

Blood samples were taken prior to the exercise bout and every 24 hours for 5 days thereafter. Venous blood samples were taken from the antecubital vein and serum CK and LDH were measured enzymatically using CK and LDH kits (Sigma Chemical Company, St. Louis, MO). Blood samples were stored frozen at −70° C until analyzed.

Exercise Protocol

Following 5 days of Cr supplementation, subjects underwent a high-force eccentric exercise protocol of the forearm flexors on a modified preacher bench. The exercise test consisted of 2 sets of 25 maximal eccentric contractions, with each repetition lasting 5 seconds, followed by a 15-second rest between each repetition and a 5-minute rest between the 2 sets. The primary investigator provided resistance manually by pulling downward on a lever arm attached to the preacher bench machine. Subjects resisted the downward force by pulling upward maximally on each repetition; thus each subject produced his maximal voluntary force on each repetition. This exercise protocol was previously used in our laboratory to induce muscle damage, and can result in a 10-fold increase in muscle serum protein activity, a 50% reduction in muscle strength, a 30% decrease in ROM, and severe soreness (5).

Statistical Analyses

All data were analyzed using Statistica for Windows, version 5.0 (StatSoft Inc., Tulsa, OK). To compare changes in MIF, RANG, FANG, CIR, SOR, CK, and LDH from pre- to postexercise, a 2-way, repeated-measures analysis of variance (ANOVA) was used. A significant interaction term of group by time would indicate a difference in the pattern of response between groups over time. Main-effect analyses and Tukey's post hoc tests were used to locate differences when ANOVA revealed a significant interaction. Intraclass correlation and an ANOVA were used to determine reliability and consistency of baseline measures over the 2 test days. There were no significant differences in any of the baseline measures between days, and the reliability for MIF, FANG, RANG, distal and mid CIR, and BM were $R = 0.96$, 0.95, 0.91, 0.99, 0.98, and 0.99, respectively. Thus the reliability was judged to be high. All data are presented as mean ± *SE*, and significance was set a priori at $p \leq 0.05$.

Results

MIF, FANG, RANG, and CIR were assessed presupplementation and following 5 days of supplementation. There was no significant effect of time, no significant effect of group, and no significant group by time interaction term in the analysis of MIF, FANG, RANG, and CIR (time effect, $p > 0.05$), indicating that there was no effect of the Cr supplementation on these measures. Also, there was no difference in force loss due to the exercise test between the groups. There was a significant main effect of time in the analysis of MIF, FANG, RANG, CIR, SOR, CK, and LDH (time effect, $p < 0.05$), indicating that all measures changed following eccentric exercise. However, there was no significant effect of group and no significant group by time interaction term in any of the criterion measures. Figure 1 presents the MIF data. Both groups experienced approximately a 50% reduction in MIF immediately postexercise, which did not return to baseline levels by the end of the measurement period. FANG significantly increased (Cr, +13°; P, +11°), and RANG significantly decreased (Cr, −10°; P, −11°) following exercise (see Figures 2 and 3, respectively). Both ROM measurements were significantly different from baseline levels immediately postexercise and at all time points during the measurement period.

Both distal and mid CIR of the biceps significantly increased (distal Cr, +1 cm; distal P, +0.9 cm; mid Cr, +1.6 cm; mid P, +1.7 cm) following eccentric exercise (see Figures 4 and 5). These values were significantly increased from baseline levels immediately postexercise and at all time points through the end of the measurement period. SOR with movement was signifi-

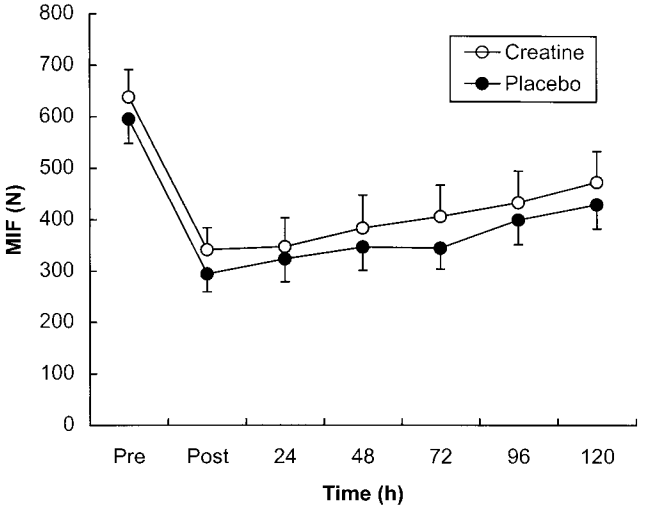

Figure 1. Maximal isometric force of the elbow flexors (MIF) following 50 maximal eccentric contractions of the elbow flexors. Subjects ingested either creatine (20 g·d^{-1} for 5 days) or placebo prior to the exercise test. Pre and Post represent measurements taken immediately before and after exercise. Subsequent measurements were taken every 24 hours.

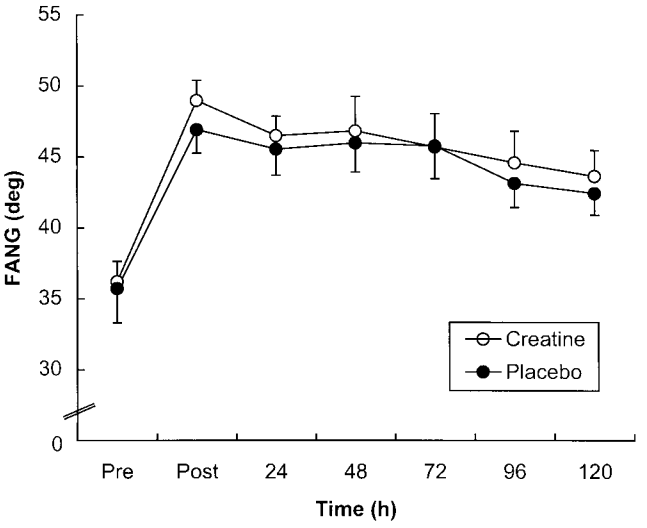

Figure 2. Flexed arm angle of the elbow flexors (FANG) following 50 maximal eccentric contractions of the elbow flexors. See Figure 1 legend for details.

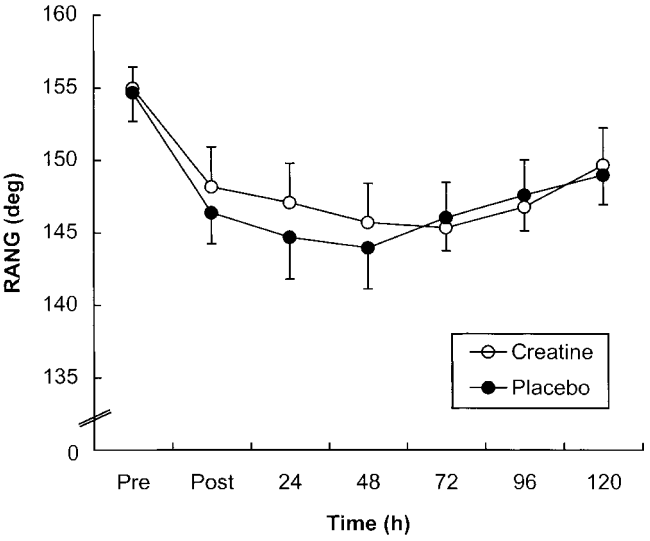

Figure 3. Relaxed arm angle of the elbow flexors (RANG) following 50 maximal eccentric contractions of the elbow flexors. See Figure 1 legend for details.

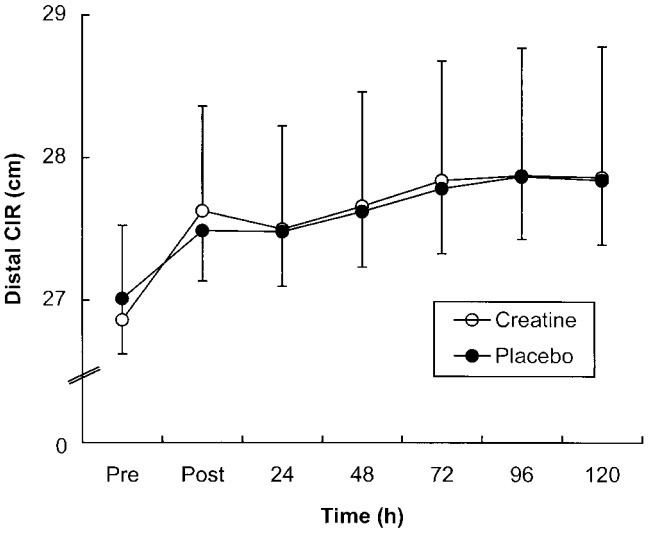

Figure 4. Distal circumference of the elbow flexors (CIR) following 50 maximal eccentric contractions of the elbow flexors. See Figure 1 legend for details.

cantly increased immediately postexercise and at all time points thereafter (peak SOR with movement: Cr, 47 mm; P, 52 mm). SOR with palpation was significantly increased at 24, 48, 72, and 96 hours after the exercise test (peak SOR with palpation: Cr, 46 mm; P, 49 mm).

Figure 6 presents the CK data. Serum CK was significantly increased at 48, 72, 96, and 120 hours following exercise. LDH was significantly increased at 48, 72, and 96 hours following the exercise test (see Figure 7). There was no significant group $\times$ time interaction ($p > 0.05$), no significant effect of group ($p > 0.05$), and no significant effect of time ($p > 0.05$) in BM, indicating that there was no change in body mass from pre- to postsupplementation (see Table 2).

Discussion

The purpose of this investigation was to compare following eccentric exercise the responses of subjects who ingested Cr with those ingesting a placebo to determine if Cr supplementation offers protective effects on skeletal muscle under extreme exercise conditions. High-force eccentric exercise alters sarcolemmal and SR membrane function (17, 36), leading to a cascade of events ultimately resulting in muscle degeneration, loss of function (13), and muscle soreness (31). Exog-

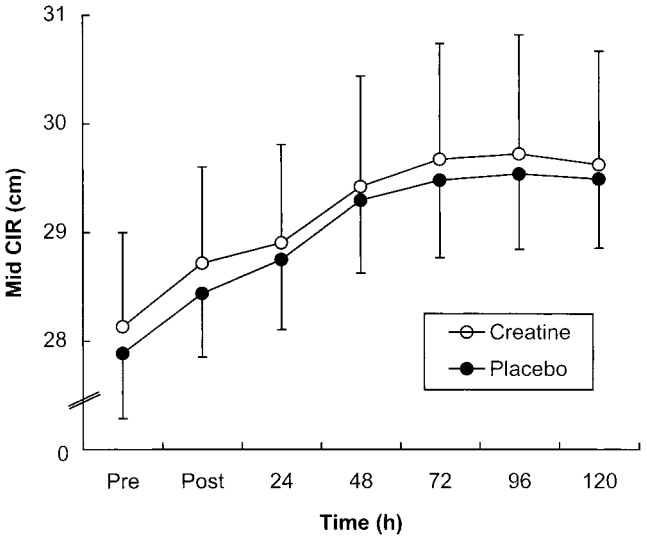

Figure 5. Mid circumference of the elbow flexors (CIR) following 50 maximal eccentric contractions of the elbow flexors. See Figure 1 legend for details.

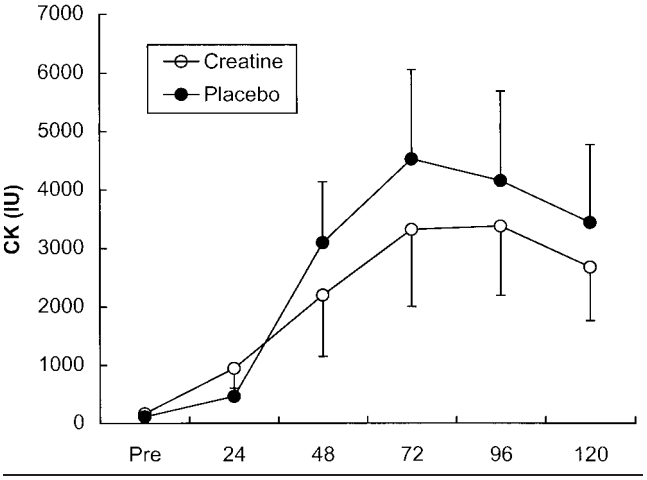

Figure 6. Serum creatine kinase (CK) following 50 maximal eccentric contractions of the elbow flexors. Subjects ingested either creatine (20 g·d^{-1} for 5 days) or placebo prior to the exercise test. Measurements were taken prior to exercise and every 24 hours thereafter.

enous PCr has been used as a treatment for acute myocardial infarction in order to reduce infarct size (26, 27). In cardiac tissue, PCr arranges membrane phospholipids in a more ordered fashion, decreasing fluidity and thus stabilizing the membrane. Saks (27) stated that because charged phospholipids are located on both sides of the muscle membrane, both exogenous and endogenous PCr may be equally important for sarcolemmal stability. Thus, Cr supplementation and subsequent increased muscle PCr levels may have similar protective effects on skeletal muscle membranes.

Despite the theoretical basis to hypothesize that Cr would reduce damage and enhance recovery, the results of the present study showed that, in response to eccentric exercise, the Cr-supplemented and the P

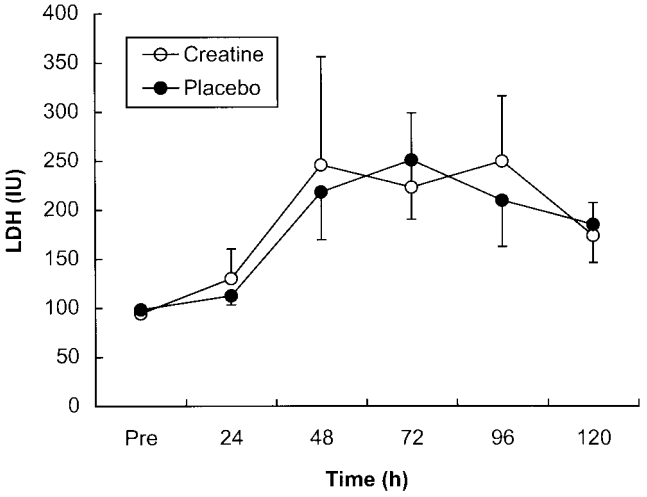

Figure 7. Serum lactate dehydrogenase (LDH) following 50 maximal eccentric contractions of the elbow flexors. See Figure 6 legend for details.

Table 2. Body mass before and after 5 days of supplementation with creatine (20 g·d^{-1}) or placebo. There was no significant difference in body mass ($p > 0.05$). Values are means ± *SE*.

	Creatine group	Placebo group
Body mass (kg)		
Before	76.6 ± 4.5	80.7 ± 2.0
After	77.0 ± 4.5	80.3 ± 1.8

group experienced a similar loss of MIF (Cr, 46%; P, 48%) and ROM (Cr, 23°; P, 22°), a similar increase in CIR of the distal (Cr, 1 cm; P, 0.9 cm) and mid (Cr, 1.6 cm; P, 1.7 cm) biceps, a similar development of SOR with movement (Cr, 47 mm; P, 52 mm) and palpation (Cr, 46 mm; P, 49 mm), and a similar increase in CK (Cr, 3,215 IU; P, 4,417 IU) and LDH (Cr, 156 IU; P, 153 IU; $p < 0.05$). Over the 6 days, the pattern of change in all criterion measures in response to the eccentric exercise was nearly identical between groups. In fact, it was remarkable how similarly the groups responded to the exercise test.

Previously, Satolli and Marchesi (28) have shown that 30 days of injectable PCr administration produced a faster and greater recovery of strength and power in patients with muscle atrophy and weakness of the thigh. However, this study has been criticized because subjects were not supplemented in double-blind, placebo-controlled fashion. Furthermore, the 'striking reduction' in delayed-onset muscle stiffness reported by Clark (4), where PCr was injected into athletes during intense training, is not supported by the current study where we found no difference in SOR at any time between subjects receiving Cr or P. Unfortunately, little detail is available regarding the study noted by Clark,

as the data were cited as unpublished observations and only briefly described in a review chapter (4).

The pattern of change in CK and LDH in the current study was similar to that following high-force eccentric exercise reported by Nosaka and Clarkson (19). However, we found no differences between groups in the activity of these proteins in the blood. These data are in contrast to Port et al. (22), who reported that rats who were not administered Cr had a characteristic and proportional rise in blood CK and LDH, but rats who were administered Cr did not show this pattern. The authors suggested that Cr administration positively affected cellular integrity, either by improving energetics or directly acting on lipid structures within the cell. These differences in the pattern of change of CK and LDH may be the result of the exercise protocol used by Port et al. (22), a swimming time to exhaustion test, which has a significantly smaller eccentric component than that of the current study. The mechanical stress imposed on the muscle fibers by the high-force eccentric exercise test used in the current study likely caused more muscle damage than the swimming test of Port et al. (22). It is possible that the strain placed on the muscles in the current study was too great for any membrane stabilization effects of the Cr supplement to produce a reduction in CK and LDH. Lieber and Fridén (17) have suggested that the initial events of exercise-induced muscle damage are related to disorganization of the sarcomere followed by a cascade of events that includes the altering of the sarcolemmal and SR membranes. Also, Robinson et al. (24) showed that exogenous PCr could cause a several-fold decrease in CK release in cardiac muscle under conditions of ischemia, which is also in contrast to data from the current study. Although ischemia can occur during exercise, the mechanical event of the high-force eccentric contractions is an additional stress that also was not imposed on the muscle membrane during this study.

In the current study, Cr supplementation had no effects on any of the markers of muscle damage, including MIF, ROM, CIR, SOR, CK, and LDH, which indicates that Cr supplementation had no membrane stabilization effects. It is possible that the exercise test was too severe for Cr to produce any measurable reduction in these markers of muscle damage. The high-force eccentric exercise test used in the current study produces profound changes in muscle function and the activity of muscle proteins in the blood. Any membrane-stabilizing effects of the Cr were likely no match for the strain placed on the sarcolemma by the high-force eccentric exercise.

In summary, subjects who performed 50 maximal eccentric contractions following ingestion of Cr (20 $g \cdot d^{-1}$) or P for 5 days displayed the characteristic response to high-force eccentric exercise, including decreased MIF and ROM and increased CIR, SOR, CK, and LDH. However, there were no significant differences in any of the criterion measures or in the patterns of change over the measurement period between the 2 groups. Thus, supplementation of 20 $g \cdot d^{-1}$ of Cr for 5 days does not decrease muscle damage or enhance recovery from high-force eccentric exercise.

Practical Applications

It has been suggested that soreness and accompanying muscle damage from overexertion exercise may negatively impact exercise performance by decreasing economy, impairing glycogen repletion, altering biomechanical execution, and decreasing strength (29). Furthermore, these changes may put an athlete at risk for injury (9). A nutritional supplement that may reduce the extent of, or enhance recovery from, exercise-induced muscle damage would benefit athletes during intense training phases and during recovery from injury; however, data from the current study support no such benefits. Subjects in both groups responded in a similar manner to the exercise test and displayed a similar time course of recovery on all muscle function, circumference, and soreness measurements (see Figures 1–5). Further, there were no differences between groups in the activity of muscle proteins in the blood.

Data from the current study can be applied to athletes undergoing intense resistance training with an eccentric component. Supplementation of 20 $g \cdot d^{-1}$ of Cr for 5 days does not decrease muscle damage or enhance recovery from high-force eccentric exercise, so Cr should not be considered as a recuperative aid from this type of exercise stress. Conversely, anecdotal reports of muscle strains and tears in athletes using Cr supplements are not supported by this study, as the Cr group did not experience more damage or a slower recovery compared with the P group. However, it should be stressed that the current study investigated the effects of acute Cr supplementation, and that there are few data available on the effects of longer-term Cr supplementation on muscle function. Athletes undergoing intense exercises, such as resistance training with an exaggerated eccentric component or plyometrics, should be aware that the effects of long-term Cr supplementation and the interactions between Cr and other purported ergogenic aids or physiological conditions, such as dehydration, have not been investigated.

References

1. Balsom, P.D., K. Söderlund, B. Sjödin, and B. Ekblom. Skeletal muscle metabolism during short duration high-intensity exercise: Influence of creatine supplementation. *Acta Physiol. Scand.* 154:303–310. 1995.
2. Barnett, C., M. Hinds, and D.G. Jenkins. Effects of oral creatine supplementation on multiple sprint cycle performance. *Aust. J. Sci. Med. Sport* 28:35–39. 1996.
3. Belcastro, A.N., L.D. Shewchuk, and D.A. Raj. Exercise-in-

duced muscle injury: A calpain hypothesis. *Mol. Cell. Biochem.* 179:135–145. 1998.
4. Clark, J.F. Uses of creatine phosphate and creatine supplementation for the athlete. In: *Creatine and Creatine Phosphate: Scientific and Clinical Perspectives.* M.A. Conway and J.F. Clark, eds. San Diego: Academic Press, 1996. pp. 217–226.
5. Clarkson, P.M., K. Nosaka, and B. Braun. Muscle function after exercise-induced muscle damage and rapid adaptation. *Med. Sci. Sports Exerc.* 24:512–520. 1992.
6. Clarkson, P.M., and I. Tremblay. Exercise-induced muscle damage, repair, and adaptation in humans. *J. Appl. Physiol.* 65: 1–6. 1988.
7. Cooke, W.H., P.W. Grandjean, and W.S. Barnes. Effect of oral creatine supplementation on power output and fatigue during bicycle ergometry. *J. Appl. Physiol.* 78:670–673. 1995.
8. Earnest, C.P., P.G. Snell, R. Rodriguez, A.L. Almada, and T.L. Mitchell. The effect of creatine monohydrate ingestion on anaerobic power indices, muscular strength and body composition. *Acta Physiol. Scand.* 153:207–209. 1995.
9. Ebbeling, C.B., and P.M. Clarkson. Exercise-induced muscle damage and adaptation. *Sports Med.* 7:207–234. 1989.
10. Greenhaff, P.L., K. Bodin, K. Söderlund, and E. Hultman. Effect of oral creatine supplementation on skeletal muscle phosphocreatine resynthesis. *Am. J. Physiol.* 266:E725–730. 1994.
11. Greenhaff, P.L., A. Casey, A.H. Short, R. Harris, K. Söderlund, and E. Hultman. Influence of oral creatine supplementation of muscle torque during repeated bouts of maximal voluntary exercise in men. *Clin. Sci.* 84:565–571. 1993.
12. Harris, R.C., K. Söderlund, and E. Hultman. Elevation of creatine in resting and exercised muscle of normal subjects by creatine supplementation. *Clin. Sci.* 83:367–374. 1992.
13. Ingalls, C.P., G.L. Warren, and R.B. Armstrong. Dissociation of force production from MHC and actin contents in muscle injured by eccentric contractions. *J. Muscle Res. Cell. Motility* 19:215–224. 1998.
14. Ingwall, J.S. Creatine and the control of muscle-specific protein synthesis in cardiac and skeletal muscle. *Circ. Res.* 38:I115–123. 1976.
15. Jacobs, I., S. Bleue, and J. Goodman. Creatine ingestion increases anaerobic capacity and maximum accumulated oxygen deficit. *Can. J. Appl. Physiol.* 22:231–243. 1997.
16. Kreider, R.B., M. Ferreira, M. Wilson, P. Grindstaff, S. Plisk, J. Reinardy, E. Cantler, and A.L. Almada. Effects of creatine supplementation on body composition, strength, and sprint performance. *Med. Sci. Sports Exerc.* 30:73–82. 1998.
17. Lieber, R.L., L. Thornell, and J. Fridén. Muscle cytoskeletal disruption occurs within the first 15 min of cyclic eccentric contractions. *J. Appl. Physiol.* 80:278–284. 1996.
18. Mujika, I., J.C. Chatard, L. Lacoste, F. Barale, and A. Geyssant. Creatine supplementation does not improve sprint performance in competitive swimmers. *Med. Sci. Sports Exerc.* 28: 1435–1441. 1996.
19. Nosaka, K., and P.M. Clarkson. Variability in serum creatine kinase response after eccentric exercise of the elbow flexors. *Int. J. Sports Med.* 17:120–127. 1996.
20. Nosaka, K., P.M. Clarkson, and F.S. Apple. Time course of serum protein changes after strenuous exercise of the forearm flexors. *J. Lab. Clin. Med.* 119:183–188. 1992.
21. Nosaka, K., P.M. Clarkson, M.E. McGuiggin, and J.M. Byrne. Time course of muscle adaptation after high-force eccentric exercise. *Eur. J. Appl. Physiol.* 63:70–76. 1991.
22. Port, K., S. Timpmann, L. Medijainen, and V. Ööpik. Influence of creatine administration on the postexercise CK and LDH enzyme activities. *Clin. Sci. Suppl.* 87:117. 1994.
23. Redondo, D.R., E.A. Dowling, B.L. Graham, A.L. Almada, and M.H. Williams. The effect of oral creatine monohydrate supplementation on running velocity. *Int. J. Sport Nutr.* 6:213–221. 1996.
24. Robinson, L.A., M.V. Braimbridge, and D.J. Hearse. Creatine phosphate: An additive myocardial protective and antiarrhythmic agent in cardioplegia. *J. Thorac. Cardiovasc. Surg.* 87:190–200. 1984.
25. Rossiter, H.B., E.R. Cannell, and P.M. Jakeman. The effect of oral creatine supplementation on the 1000-m performance of competitive rowers. *J. Sports Sci.* 14:175–179. 1996.
26. Saks, V.A., V. Stepanov, I.V. Jaliashvili, E.A. Konorev, S.A. Kryzkanovsky, E. Strumia, and J.F.S.D. Clark. Molecular and cellular mechanisms of action for the cardioprotective and therapeutic role of creatine phosphate. In: *Creatine and Creatine Phosphate: Scientific and Clinical Perspectives.* M.A. Conway and J.F. Clark, eds. San Diego: Academic Press, 1996. pp. 91–114.
27. Saks, V.A., and E. Strumia. Phosphocreatine: molecular and cellular aspects of the mechanism of cardioprotective action. *Curr. Ther. Res.* 53:565–598. 1993.
28. Satolli, F., and G. Marchesi. Creatine phosphate in the rehabilitation of patients with muscle hyponotrophy of the lower extremity. *Curr. Ther. Res.* 46:67–73. 1989.
29. Smith, L.L. Causes of delayed onset muscle soreness and the impact on athletic performance: A review. *J. Appl. Sport Sci. Res.* 6:135–141. 1992.
30. Terrillion, K.A., F.W. Kolkhorst, F.A. Dolgener, and S.J. Joslyn. The effect of creatine supplementation on two 700-m maximal running bouts. *Int. J. Sport Nutr.* 7:138–143. 1997.
31. Tidball, J.G. Inflammatory cell response to acute muscle injury. *Med. Sci. Sports Exerc.* 27:1022–1032. 1995.
32. van Leemputte, M., K. Vandenberghe, and P. Hespel. Shortening of muscle relaxation time after creatine loading. *J. Appl. Physiol.* 86:840–844. 1999.
33. Vandenberghe, K., M. Goris, P. Van Hecke, M. Van Leemputte, L. Vangerven, and P. Hespel. Long-term creatine intake is beneficial to muscle performance during resistance training. *J. Appl. Physiol.* 83:2055–2063. 1997.
34. Volek, J.S., W.J. Kraemer, J.A. Bush, M. Boetes, T. Incledon, K.L. Clark, and J.M. Lynch. Creatine supplementation enhances muscular performance during high- intensity resistance exercise. *J. Am. Diet Assoc.* 97:765–770. 1997.
35. Warren, G.L., D.A. Lowe, and R.B. Armstrong. Measurement tools used in the study of eccentric contraction-induced injury. *Sports Med.* 27:43–59. 1999.
36. Yasuda, T., K. Sakamoto, K. Nosaka, M. Wada, and S. Katsuta. Loss of sarcoplasmic reticulum membrane integrity after eccentric exercise. *Acta Physiol. Scand.* 161:581–582. 1997.

Acknowledgments

This investigation was supported by the National Strength and Conditioning Association-Student Research Grant, NSCA Dr. Michael Pollock Memorial Research Grant (a research grant donated by Hammer Strength, a Life Fitness Company), the Gatorade Sports Science Institute-Student Research Grant, and the NutraSense Company. The authors would like to acknowledge Konrad Chmiel for his assistance with this study.