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Effects of 30 days of creatine ingestion in older men

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Abstract In this investigation we evaluated the effects of oral creatine (Cr) supplementation on body composition, strength of the elbow flexors, and fatigue of the knee extensors in 20 males aged 60–82 years who were randomly administered Cr or placebo (P) in a double-blind fashion. Subjects ingested either 20 g of Cr or P for 10 days, followed by either 4 g of Cr or P, respectively, for 20 days. Tests were conducted pre-supplementation and following 10 and 30 days of supplementation. Leg fatigue was determined using an isokinetic dynamometer; subjects performed 5 sets of 30 maximal voluntary contractions at $180° \cdot s^{-1}$, with 1 min of recovery between sets. The strength of the elbow flexors was assessed using a modified preacher bench attached to a strain gauge. There was a significant interaction ($P < 0.05$; group × time) in leg fatigue following supplementation. However, this interaction appears to have resulted from a combination of the improved fatigue score by the Cr-supplemented group and the decreased fatigue score by the P-supplemented group, because when the simple main effects were analyzed for the groups individually, there was no significant difference over time for either of the groups. There were no significant differences in body mass, body density, or fat-free mass as assessed by hydrostatic weighing, or strength between the Cr-supplemented or P-supplemented groups. These data suggest that 30 days of Cr-supplementation may have a beneficial effect on reducing muscle fatigue in men over the age of 60 years, but it does not affect body composition or strength.

Key words Creatine monohydrate · Ergogenic aid Sarcopenia · Aging · Fatigue

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Introduction

With aging there are decreases in muscle mass, strength, and exercise performance (Rogers and Evans 1993). Muscle wasting can lead to immobility, increased risk of falls, and disease, but maintaining a high level of physical activity may reduce such risks (Fiatarone and Evans 1993). Since Harris et al. (1992) demonstrated elevated creatine (Cr) and phosphocreatine muscle levels following oral Cr monohydrate supplementation ($\approx 20\ g \cdot day^{-1}$ for 5 days), many, but not all (Barnett et al. 1996; Redondo et al. 1996; Terrillion et al. 1997; Thompson et al. 1996) investigators have shown that in young subjects, Cr has positive effects on muscle mass (Balsom et al. 1993; Earnest et al. 1995; Greenhaff et al. 1994a; Vandenberghe et al. 1997), strength (Earnest et al. 1995; Vandenberghe et al. 1997), and performance of high-intensity exercise (Casey et al. 1996; Earnest et al. 1995; Greenhaff et al. 1993b; Jacobs et al. 1997; Rossiter et al. 1996). Only two investigations have examined the potential benefits of Cr supplementation in a healthy elderly population (Bermon et al. 1998; Rawson et al. 1998).

Older people have reduced levels of muscle phosphocreatine (Möller et al. 1980). Furthermore, vegetarians or low meat eaters, as is the case with some elderly populations, have reduced levels of serum Cr (Delanghe et al. 1989) and possibly reduced muscle Cr levels (Balsom et al. 1993; Harris et al. 1992). We have demonstrated previously that older men supplemented with Cr for 5 days experienced a small increase in body mass, a marginal improvement in exercise performance, and no changes in strength (Rawson et al. 1998). The 0.5-kg increase in body mass was less than that reported to occur in younger subjects (1–4 kg; Volek and Kraemer 1996). Gordon et al. (1995) demonstrated improved exercise performance and increased muscle Cr and phosphocreatine levels in older men (age range 43–70 years) suffering from chronic heart failure who underwent a “Cr loading” phase of $20\ g \cdot day^{-1}$ for 10 days.

Since only small changes were found in our previous investigation of 5 days of Cr supplementation (Rawson et al. 1998), the hypothesis of the present investigation was that a longer period of Cr loading and a greater maintenance dose would be effective in increasing body mass and improving exercise performance in healthy older men.

Methods

Subjects

Twenty healthy male subjects whose age ranged from 60 to 82 years volunteered for this study. Each subject signed a physical activity readiness questionnaire and an informed consent document consistent with the University's policy on human subject testing. Furthermore, subjects received written approval from their physician. The ten subjects in the Cr group were [mean (SE)] 66.7 (1.9) years of age and weighed 84.2 (4.0) kg. The ten subjects in the control group were 66.9 (2.2) years of age and weighed 84.5 (4.3) kg. The study was double-blind, placebo controlled.

Supplementation

Subjects received containers containing either chewable Cr monohydrate tablets (Cr group; Createam, NutraSense, Shawnee Mission, Kan., USA) or an equivalent volume of a similar-tasting and look-alike dextrose placebo (P group). Subjects in the Cr group ingested 5 g of Cr and 7 g of dextrose four times per day for 10 days, followed by 4 g of Cr and 6.8 g of dextrose once per day for 20 days. Subjects in the control (P) group ingested 25 g of dextrose four times per day for 10 days, followed by 20 g of dextrose for 20 days. Subjects in both groups also ingested one serving of Gatorade 30 min following ingestion of the supplement at four equal intervals throughout the day. The addition of a glucose solution to a Cr-loading program has been shown to significantly enhance muscle Cr uptake, which is considered to be due to insulin-stimulated transport (Green et al. 1996).

Experimental design

Subjects were tested prior to supplementation (visits 1 and 2), following the 10-day loading period (visit 3), and again following a 20-day maintenance period (visit 4). Criterion measures were body mass, body composition, arm isometric strength, and leg fatigue. All tests were conducted on the four visits, with the exception of hydrostatic weighing which was conducted on visits 2, 3 and 4 and were conducted within 1 h of the previous appointment time to minimize diurnal variations. Subjects were instructed to report to the laboratory having abstained from physical activity for at least 48 h and having fasted from the previous night.

On visit 1, the protocol for the arm strength and the leg fatigue tests were carefully explained and sufficient time was given for familiarization with the test protocols. Height and body mass were also recorded at this time. On visit 2, subjects were weighed and then repeated the maximal strength test and leg fatigue protocols, and body composition was assessed using hydrostatic weighing. Subjects were randomly assigned to a Cr group or a P group. During visits 3 and 4 the measurements were reassessed.

For 3 days prior to the study, during days 7, 8, and 9 of supplementation, and again during days 27, 28, and 29 of supplementation subjects recorded their food and fluid intake. Subjects were asked to avoid changes in their diet for the duration of the study and were given instruction on how to record accurately the quantity and type of food consumed. Diet records were analyzed using Nutritionist IV for Windows Version 4.1 (First Data Bank, San Bruno, Calif., USA). After the end of the study subjects were asked to complete a physical activity questionnaire (Modified Baecke questionnaire for older adults) to assess any potential differences in activity levels.

Arm isometric strength

The isometric strength of the elbow flexors was assessed using a modified preacher bench (standard weight-lifting equipment) attached to a strain gauge and interfaced with a computer (Jackson Evaluation System, Lafayette Instrument Co., Lafayette, Ind., USA). Subjects were seated on the bench with the elbow of the dominant arm fixed at 90°. Three maximal isometric contractions, with a 1-min rest between trials, were recorded and averaged as the criterion score.

Leg fatigue

Subjects completed 5 sets of 30 knee extensions at $180° \cdot s^{-1}$ on an isokinetic dynamometer (Biodex Medical Systems, Shirley, N.Y., USA). Each contraction began with the knee at 90° knee flexion, continued to the point of full knee extension, and ended with the leg actively returned to the starting position. The peak torques for each of the 5 sets of 30 repetitions were recorded, summed and used to assess work and fatigability. One bout of 30 maximal voluntary contractions at this velocity has been shown to result in marked phosphocreatine degradation in both type I and type II skeletal muscle fibers of the quadriceps muscle group (Tesch et al. 1989). A similar exercise protocol has been shown to increase performance in young individuals following Cr supplementation (Greenhaff et al. 1993b).

Body composition

Body mass was assessed using a calibrated electronic scale with a precision of 0.2 kg (Befour, Saukville, Wis., USA). Subjects were weighed without shoes and wore the same clothing on all the testing days. Changes in body composition were estimated using hydrostatic weighing. Subjects wore nylon swimsuits and urinated immediately before the test. Ten trials were taken for each subject and the last three averaged to determine underwater weight. Residual lung volume was estimated from age and height (Goldman and Becklake 1959). Underwater weight was used to assess changes in body density, fat-free mass, and percent body fat.

Analytical approach

All data were analyzed using Statistica for Windows Version 5.1 (StatSoft, Tulsa, Okla., USA). A repeated-measures analysis of variance (ANOVA) and an intraclass R coefficient were used to assess the reliability of the baseline measures. The reliability of body mass, arm isometric strength, and leg fatigue was $R = 0.99$, 0.97, and 0.95, respectively. A repeated-measures ANOVA with a grouping factor was used to compare the pattern of change between groups pre- to post-supplementation (group × time interaction term). Main effect analyses and post-hoc tests were used to locate differences when the ANOVA revealed a significant interaction. All data are presented as the mean (SE). The level of significance was set a priori at $P < 0.05$.

Results

Nutritional data, physical activity, and compliance

No significant differences were detected between groups at any point prior to or during the study regarding energy intake, macronutrients, or the proportion of proteins, fats, and carbohydrates ingested (Table 1). There were no significant differences between groups in physical activity as assessed by questionnaire.

Due to travel obligations one subject in the Cr group was tested after 28 days of supplementation, one subject in the P group could not make his 30-day exercise test but agreed to continue supplementation for 1 extra week (37 total days), and one subject was unable to participate in the leg fatigue test due to a leg injury that occurred outside the study. Side effects reported by subjects in the Cr group during the investigation included gastrointestinal discomfort ($n = 1$), a skin rash ($n = 1$), and muscle cramping of the plantar flexors ($n = 1$). There were no side effects reported by subjects ingesting the P.

Body composition

There was a significant increase over time in body mass ($P < 0.05$). Although this difference was not statistically significant between groups, the mean increases in body mass were 0.78 (0.3) and 0.32 (0.3) kg for the Cr and P groups, respectively (Table 2). There were no significant differences both between groups and over time in body density, fat-free mass, or percent fat as assessed by hydrostatic weighing (Table 2).

Arm isometric strength and leg fatigue

There were no significant differences (group × time) in arm isometric strength as both groups demonstrated only small increases (Cr = + 1.7 kg, P group = + 1.2 kg; Table 2).

The sum of peak torque values for each repetition of each bout were summed and used to represent leg muscle fatigue. There was a significant interaction ($P < 0.05$; group × time) in leg fatigue following Cr supplementation. After 10 days of supplementation, the Cr group showed an 8% increase [+ 488 (246) Nm] in performance on the leg fatigue test, while that of the P group remained unchanged [−21 (178) Nm; Fig. 1]. Over the course of the 30-day supplementation period the Cr group demonstrated a 9% increase [+ 510 (316) Nm] in performance on the leg fatigue test, while the P group showed a 5% performance decrement [−450 (353) Nm]. When the main effects were analyzed for the groups individually, there was no significant difference over

Table 1 Nutritional assessments made during the 3 days immediately prior to the study (Pre), during days 7, 8, and 9 of supplementation (Post 10), and during days 27, 28, and 29 of supplementation (Post 30). Values are the means (SE) for ten subjects in the creatine-supplementation (Cr) group and nine subjects in the placebo-supplementation (P) group. (Please note that energy intake is given in Kcal, where 1 cal = 4.195 Joule)

Variable	Pre	Post 10	Post 30
Energy intake (Kcal)			
Cr group	2067.8 (202.4)	2273.1 (182.2)	2059.8 (156.4)
P group	2145.4 (110.6)	1987.6 (156.9)	2175.4 (278.4)
%Protein			
Cr group	18.0 (1.7)	15.4 (1.2)	14.5 (1.0)
P group	15.2 (1.5)	14.1 (1.4)	13.5 (1.0)
%Carbohydrate			
Cr group	48.8 (2.6)	57.0 (4.1)	57.0 (3.7)
P group	58.1 (3.5)	60.5 (3.5)	55.3 (3.8)
%Fat			
Cr group	29.1 (3.0)	24.7 (2.3)	25.7 (3.0)
P group	22.2 (2.0)	21.0 (1.8)	25.7 (3.2)

Table 2 Body composition and strength measurements before (Pre) and after 10 (Post 10) and 30 days (Post 30) of Cr or P supplementation. Values are means (SE) for ten subjects in the Cr group and ten subjects in the P group. (*BM* Body mass, *FFM* fat-free mass, *%Fat* percentage of body fat, *STR* arm isometric strength)

Variable	Pre	Post 10	Post 30
BM (kg)			
Cr group	84.2 (4.0)	85.1 (4.0)	84.9 (4.1)
P group	84.5 (4.3)	85.0 (4.2)	84.8 (4.2)
FFM (kg)			
Cr group	65.8 (3.0)	66.4 (3.1)	66.4 (2.8)
P group	62.7 (2.7)	63.4 (2.5)	62.8 (2.6)
%Fat			
Cr group	21.9 (1.6)	21.9 (1.6)	21.8 (1.6)
P group	25.6 (1.5)	25.1 (1.5)	25.7 (1.4)
STR (kg)			
Cr group	51.5 (3.6)	52.6 (3.5)	53.2 (3.8)
P group	51.5 (3.9)	51.3 (4.1)	52.7 (4.1)

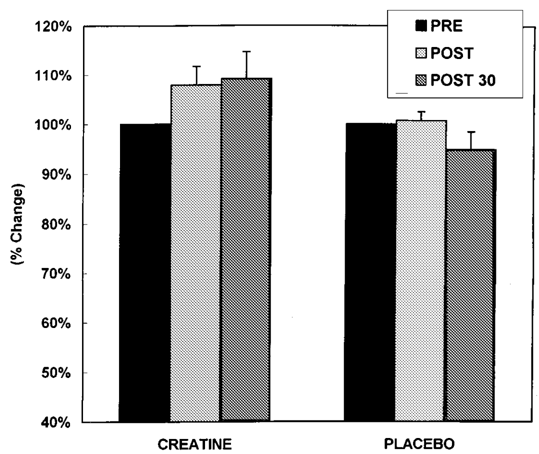

Fig. 1 Effect of 30 days of creatine (Cr) supplementation on leg fatigue. Leg fatigue is expressed as a percentage change in the total peak torque generated during the five sets of exercise. Values are the means ± SE of ten subjects in the Cr group and eight subjects in the placebo (P) group. There was a significant interaction (group × time) in percentage change of leg fatigue following Cr supplementation ($P < 0.05$). Subjects ingested either 20 g of Cr (5 g of Cr four times per day for 10 days) or a dextrose P for the same duration. Following this loading phase, subjects ingested either 4 g of Cr or the P, respectively, once per day for 20 days (PRE presupplementation, POST following 10 days of supplementation, POST 30 following 30 days of supplementation)

time for either of the groups (Cr group $P = 0.09$, P group $P = 0.18$). Thus, although there was a significant interaction term (group × time) in the full model ANOVA, this interaction appears to have been the result of a combination of the improved fatigue score by the Cr group and the decreased fatigue score by the P group.

Perceived benefits

At the end of the study subjects were asked to complete a survey regarding their experience in the study. Out of the 20 subjects, 9 were able to correctly identify which treatment they received, 8 were unsure, and 3 misidentified which treatment they received. Six subjects reported an increased feeling of muscle strength or less difficulty performing their daily activities. These 6 subjects were all in the Cr group. However, when considering each of the criterion measures individually for these six subjects, five subjects showed an increase in body mass (range 1–3%), three showed an increase in arm strength (range 8–13%), and four demonstrated reduced leg fatigue (range 4–14%). One of these six subjects showed an increase in all three measures. Changes in the criterion measures and the perceived benefits for each subject are presented in Table 3.

Discussion

The performance of short-term intense exercise relies upon pre-exercise muscle phosphocreatine levels and the rate of phosphocreatine resynthesis between bouts of exercise. Cr supplementation increases pre-exercise phosphocreatine availability, increases phosphocreatine resynthesis, and attenuates ATP degradation (Greenhaff et al. 1993a; Greenhaff et al. 1994a, b). The improvements in performance resulting from these metabolic changes could potentially offer benefits to an elderly population. Increases in energy production during activities may allow elderly people the opportunity to exercise more vigorously or may aid in recovery from injury. Satolli and Marchesi (1989) demonstrated more rapid recovery from injury in patients supplemented with phosphocreatine.

Following the Cr loading phase, subjects in the Cr group demonstrated an increase in the sum of peak torques across all five sets of +488 Nm, while subjects in the P group experienced a small decrease of −21 Nm. Across all 30 days of supplementation the Cr group experienced a mean increase in the sum of peak torques of +510 Nm, while the P group demonstrated a performance decrease of −450 Nm. The interaction term in the analysis showed that the Cr-supplemented group incurred some benefit compared to the P group. However, the 9% decrease in leg fatigue that was observed following 30 days of Cr supplementation was not significant when the main effect was analyzed over time ($P = 0.09$). These results are in agreement with our previous investigation in which subjects who ingested Cr for 5 days also showed marginal improvements in performance (3%), but with no significant difference when the simple main effect was analyzed (Rawson et al. 1998). Thus, older subjects exhibit only a small improvement in muscle fatigue following Cr supplementation when compared to younger subjects (Casey et al. 1996; Earnest et al. 1995; Greenhaff et al. 1993b; Jacobs et al. 1997; Rossiter et al. 1996).

In one investigation, an increase in one-repetition maximal (1-RM) strength was observed when subjects ingested Cr concurrently with a strength-training program (Vandenberghe et al. 1997). These authors reported that subjects in the Cr group not only showed greater increases in fat-free mass, but also maintained

Table 3 Changes in criterion measures, perceived benefits of supplementation, and ability to identify treatment in twenty subjects ingesting Cr or P for 30 days. (*ΔSTR* change in arm strength, *ΔLEG* change in leg fatigue test, *ΔBM* change in body mass). Improved perception of strength and muscle fatigue is denoted by ⊕, and no perceived benefit of strength and muscle fatigue is denoted by ∅. The ability to identify treatment is represented by either Cr, P, or ? (unable to identify)

Subject group	ΔSTR (kg)	ΔPerceived Strength	ΔLEG (Nm)	ΔPerceived fatigue	ΔBM (kg)	Treatment ID
Cr group	+6.2	⊕	−1242	⊕	−0.8	Cr
	+5.2	⊕	−1110	⊕	+1.1	Cr
	−3.6	⊕	+632	⊕	+2.4	Cr
	−3.2	⊕	+1221	⊕	+0.8	Cr
	+8.6	∅	+1203	∅	+0.3	P
	+3.3	∅	+1811	∅	+0.8	?
	+4.7	∅	+462	∅	+0.8	?
	−4.4	∅	+516	∅	+1.6	P
	−3.9	⊕	+348	∅	+0.5	Cr
	+4.5	⊕	+1260	⊕	+0.3	Cr
P group	−2.3	∅	+374	∅	0.0	?
	+0.6	∅	−569	∅	+0.5	Cr
	+2.6	∅	−614	∅	+0.3	P
	−5.3	∅	+1330	∅	+1.3	?
	+3.5	∅	No data	No data	+0.3	?
	+3.9	∅	−254	∅	−0.7	P
	−4.4	∅	−1980	⊕	−1.2	?
	+9.2	∅	No data	∅	+1.9	?
	−0.3	∅	−1268	∅	+0.8	P
	+4.1	∅	−621	∅	0.0	?

more of these gains during a period of detraining plus low-dose supplementation. Earnest et al. (1995) found improved 1-RM strength when subjects were also resistance training during supplementation. The results of the current investigation of 30 days of Cr ingestion, as well as the results of our previous study of 5 days of Cr supplementation (Rawson et al. 1998), support no increase in strength in non-weight-training older subjects.

Although there was a significant increase in body mass in these older subjects ($P < 0.05$), there was no difference in this parameter between groups. Previous investigations of Cr supplementation reported increases in body mass ranging from 1 to 4 kg (Volek and Kraemer 1996), while subjects ingesting Cr in the present study gained only 0.78 kg. There were no significant differences between groups in body density, fat-free mass, or percent fat as assessed by hydrostatic weighing. In our previous investigation, there was a significant increase in body mass in the Cr group following 5 days of Cr ingestion (+0.5 kg), but the increase was still smaller than has been shown to occur in younger subjects.

In the only other study to examine Cr supplementation in elderly men, Bermon et al. (1998) reported no changes in lower limb volume, body mass, or percent fat following 8 weeks of Cr ingestion. In that study, 32 elderly subjects took part in an 8-week resistance-training program with concurrent ingestion of Cr. The authors reported that Cr supplementation did not induce additional strength gains or resistance to fatigue compared to resistance training alone.

Improved performance of high-intensity exercise (Casey et al. 1996; Earnest et al. 1995; Greenhaff et al. 1993b; Jacobs et al. 1997; Rossiter et al. 1996) and increased body mass are consistent findings with Cr supplementation (Balsom et al. 1993; Earnest et al. 1995; Greenhaff et al. 1994a; Jacobs et al. 1997; Mujika et al. 1996; Stroud et al. 1994; Vandenberghe et al. 1997; Volek et al. 1997). Based on data from our investigations of both acute and longer supplementation periods in this population, it is suggested that the older subjects did not take up Cr into their muscles to the same extent as younger subjects. Ku and Passow (1980) reported that the saturable component of Cr transport is dependent upon cell age and is higher in young cells. The uptake and rate of transport of Cr by the muscle is mediated by insulin action (Haugland and Chang 1975; Koszalka and Andrew 1972) and is enhanced in the presence of carbohydrate (Green et al. 1996). Aging is associated with glucose intolerance, and there is a decline in insulin-stimulated glucose transport with age (Dolan et al. 1995) that does not appear to be due to a decline in Glut-4 transporters alone (Youngren and Barnard 1995).

In summary, our results show that 10 days of Cr supplementation of 20 $g \cdot day^{-1}$ followed by another 20 days of supplementation of 4 $g \cdot day^{-1}$ did not affect body mass in men of over 60 years of age, as has been reported for young subjects taking 20 $g \cdot day^{-1}$ for only 5 or 6 days. Also, this Cr supplementation regimen did not alter body composition or strength. However, Cr supplementation may have a beneficial effect on reducing muscle fatigue.

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