

# GLUTAMINE SUPPLEMENTATION IN RECOVERY FROM ECCENTRIC EXERCISE ATTENUATES STRENGTH LOSS AND MUSCLE SORENESS

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The purpose of this study was to examine the effect of glutamine supplementation on indices of recovery following eccentric exercise. In a randomized single-blind placebo-controlled design, 15 physically active males (mean age,  $21 \pm 1.5$  years; mean height,  $1.81 \pm 0.07$  m; mean body mass,  $78.4 \pm 9.2$  kg) were assigned to a control or glutamine intervention group. Each participant performed 100 drop jumps from 0.6 m followed by ingestion of  $0.3 \text{ g} \cdot \text{kg}^{-1}$  body mass of maltodextrin mixed with 750 mL of distilled water and lemon flavoring (Control) or with an additional  $0.3 \text{ g} \cdot \text{kg}^{-1}$  L-glutamine (Glutamine) at 0, 24, 48, and 72 hours post-exercise. Knee-extensor concentric peak torque at angular velocities of  $0.52$  and  $3.14 \text{ rad} \cdot \text{s}^{-1}$ , perceived muscle soreness, and plasma creatine kinase activity were measured at 0, 1, 24, 48, 72, and 96 hours post-exercise. L-glutamine supplementation resulted in a greater preservation of peak torque over the 96-hour measurement period at both  $0.52 \text{ rad} \cdot \text{s}^{-1}$  (Control,  $75 \pm 16\%$ ; Glutamine,  $85 \pm 15\%$  of pre-exercise values,  $p=0.03$ ) and  $3.14 \text{ rad} \cdot \text{s}^{-1}$  (Control,  $79 \pm 16\%$ ; Glutamine,  $90 \pm 12\%$ ,  $p=0.01$ ). Muscle soreness was significantly lower over 96 hours with L-glutamine supplementation (Control,  $4.6 \pm 2.5$  units; Glutamine,  $3.6 \pm 2.5$  units,  $p=0.03$ ). L-glutamine supplementation did not affect the magnitude or temporal nature of the creatine kinase response. As a therapeutic intervention, glutamine supplementation was effective in attenuating strength loss and muscle soreness following eccentric exercise-induced muscle damage. [*J Exerc Sci Fit* • Vol 9 • No 2 • 116–122 • 2011]

**Keywords:** L-glutamine, muscle damage, soreness, strength, treatment

## Introduction

Exercise-induced muscle damage is associated with impaired muscle function, delayed-onset muscle soreness, and increased levels of muscle proteins in the circulation (Byrne et al. 2004; Clarkson & Hubal 2002; Warren et al. 1999). Symptoms of muscle damage are most pronounced and recovery is longest when exercise is unaccustomed and high-force eccentric muscle actions are involved (e.g., resistance exercise, plyometrics, downhill running), but is also evident after prolonged

low-force stretch-shortening cycle exercise such as distance running (Chambers et al. 1998; Nicol et al. 1996; Eston et al. 1995; Gibala et al. 1995; Golden & Dudley 1992; Warhol et al. 1985; Sherman et al. 1984). Prophylactic and therapeutic nutritional interventions involving protein, protein hydrolysate, mixed amino acids, selective amino acids, and branched-chain amino acids have been demonstrated to be effective in reducing some or all of the symptoms of muscle damage following isolated eccentric muscle actions (Buckley et al. 2010; Jackman et al. 2010; Nosaka et al. 2006; Sugita et al. 2003), resistance exercise (Kraemer et al. 2006), downhill running (Etheridge et al. 2008), and endurance exercise (Greer et al. 2007; Saunders et al. 2004; Coombes & McNaughton 2000). Reductions in soreness (Jackman et al. 2010; Greer et al. 2007; Nosaka



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et al. 2006), strength loss (Buckley et al. 2010; Etheridge et al. 2008; Greer et al. 2007; Kraemer et al. 2006; Sugita et al. 2003), and blood markers such as creatine kinase (CK) (Greer et al. 2007; Kraemer et al. 2006; Nosaka et al. 2006; Saunders et al. 2004; Coombes & McNaughton 2000) have been observed. The mechanism(s) by which protein or amino acid supplementation attenuates symptoms of muscle damage are unclear. Greater amino acid availability (Jackman et al. 2010; Nosaka et al. 2006), extra energy intake from supplementation (Jackman et al. 2010), increased protein synthesis and/or decreased protein breakdown producing a positive net protein balance (Etheridge et al. 2008; Kramer et al. 2006) have been suggested as potential underlying mechanisms.

A potential therapeutic nutritional supplement that has yet to be investigated following exercise-induced muscle damage is the non-essential amino acid glutamine. Glutamine is the most abundant amino acid in human muscle and plasma, fulfilling numerous cell regulatory roles and acts as a fuel source for intestinal cells and leukocytes (Roth 2008; Wernerman 2008; Castell 2003; Walsh et al. 1998). In critical illness, endogenous production of glutamine from skeletal muscle becomes insufficient, resulting in depletion of glutamine in muscle and plasma, which serve as reliable prognostic markers (Roth 2008; Wernerman 2008). Glutamine supplementation in clinical contexts has been demonstrated to restore plasma glutamine and improve net protein balance and immune system function (Roth 2008; Wernerman 2008; Castell 2003).

In healthy individuals following very prolonged exercise (i.e., >2 hours), the plasma concentration of glutamine has been demonstrated to decrease significantly, by as much as 20–30% (Castell 2003; Walsh et al. 1998). Evidence documenting the influence of eccentric exercise-induced muscle damage on plasma glutamine concentration is equivocal (Gleeson et al. 1998; Miles et al. 1990). In the 9 days of monitoring after eccentric exercise, Miles et al. (1990) observed a significant 24% reduction in plasma glutamine from  $437 \mu\text{mol} \cdot \text{L}^{-1}$  pre-exercise to  $332 \mu\text{mol} \cdot \text{L}^{-1}$  at day 3 post-maximal eccentric exercise of the elbow and knee flexors and extensors. Conversely, Gleeson et al. (1998) observed no change in plasma glutamine for up to 10 days following 20 electrically stimulated submaximal ( $\approx 40\%$  isometric maximal voluntary contraction) eccentric actions of the knee extensors. The discrepancy in the above two studies may relate to the greater muscle activation, force, and number of eccentric muscle actions in the study of Miles et al. (1990). Recent

evidence has demonstrated an acute reduction in muscle glutamine concentration following resistance exercise (Blomstrand & Essen-Gustavsson 2009). Two hours following 40 leg-press repetitions at 80% of one repetition maximum, Blomstrand and Essen-Gustavsson (2009) observed significant reductions in vastus lateralis muscle glutamine concentrations of 34% and 29% in type I and II fibers, respectively.

Therefore, potential exists for glutamine homeostasis to be disturbed following eccentric exercise, manifested as a reduction in muscle and/or plasma glutamine concentration (Blomstrand & Essen-Gustavsson 2009; Miles et al. 1990). In such a context, oral glutamine supplementation may restore glutamine homeostasis and maintain a positive net protein balance and/or reduce the inflammatory response to eccentric exercise resulting in attenuation of exercise-induced muscle damage and indirect markers such as strength loss, soreness, and CK activity. Plasma glutamine can be elevated acutely with oral glutamine ingestion (Castell & Newsholme 1997; Ziegler et al. 1990). For example, an oral dose of  $0.1 \text{ g} \cdot \text{kg}^{-1}$  body mass (i.e.,  $\approx 7 \text{ g}$ ) results in a 50% increase in plasma glutamine by 30 minutes, followed by a return to baseline values in 1–2 hours (Castell & Newsholme 1997). Clinical intravenous doses of glutamine are typically 20–25 g per day (Wernerman 2008), and exercise studies have employed oral ingestion doses of up to 45 g per day for 6 weeks without adverse effects (Gleeson 2008; Candow et al. 2001).

Therefore, the aim of this study was to evaluate the efficacy of oral glutamine supplementation as a therapeutic nutritional intervention in an experimental model of eccentric exercise-induced muscle damage. We hypothesize that daily glutamine supplementation post-eccentric exercise will reduce muscle damage and attenuate the associated symptoms (i.e., strength loss, soreness, and CK activity), thereby improving recovery from this form of exercise.

## Methods

### Participants

Fifteen physically active males volunteered with informed consent to participate in this study, which had been approved by the ethics committee of the School of Sport and Health Sciences at the University of Exeter. Volunteers were free from musculoskeletal injury and had not taken any dietary supplement within the past 6 months. Volunteers were randomly assigned in a single-blind manner to a control group ( $n=8$ ) or glutamine

**Table.** Physical characteristics of the study participants\*

	Control group (n = 8)	Glutamine group (n = 7)
Age (yr)	22.1 ± 3.6	23.3 ± 2.9
Stature (m)	1.86 ± 0.05 <sup>†</sup>	1.78 ± 0.07
Mass (kg)	80.9 ± 9.5	84.9 ± 6.3

\*Data presented as mean ± standard deviation; <sup>†</sup>significantly greater stature for control group ( $p = 0.02$ ).

intervention group ( $n = 7$ ). The Table illustrates the volunteers' physical characteristics. Volunteers had an equivalent body mass, but the stature of the control group was greater than that of the glutamine group. Volunteers were instructed to avoid therapeutic treatment of any symptoms of muscle damage and to maintain their normal diet throughout the experiment.

### **Experimental design**

One week prior to the first experimental trial, volunteers attended a familiarization session whereby demonstrations of the testing procedures were provided with volunteers undertaking no eccentric exercise. The experimental design consisted of baseline testing followed by repeated testing of the same parameters at 1, 24, 48, 72, and 96 hours following muscle-damaging exercise. Baseline values of plasma CK activity, muscle soreness, and knee extensor peak torque were established. Volunteers then immediately performed 100 drop jumps (10 sets, 10 reps, 1-minute recovery) from a height of 0.6 m (Highton et al. 2009). They were instructed to achieve 90° of knee flexion followed by a jump for maximum height. Volunteers received verbal encouragement throughout the protocol to maintain maximal effort.

### **L-glutamine supplementation**

Immediately following the muscle damage protocol, volunteers ingested 0.3 g · kg<sup>-1</sup> body mass of maltodextrin mixed with 750 mL of distilled water (Control) or with an additional 0.3 g · kg<sup>-1</sup> body mass of L-glutamine (Glutamine; Myprotein.co.uk, Manchester, UK). The two beverages were lemon flavored, masked in an opaque container, and were indistinguishable in taste and appearance. Volunteers ingested the same beverage following the completion of testing at 24, 48, and 72 hours. The glutamine dose of 0.3 g · kg<sup>-1</sup> body mass represented an average daily intake of 26 g · d<sup>-1</sup> (≈100 kcal) for 4 consecutive days post-eccentric exercise. This dose has previously been demonstrated to acutely elevate

(≈2 hours) plasma glutamine (Ziegler et al. 1990) and is consistent with doses employed in clinical and exercise studies without any adverse effects (Wernerman 2008). Based on the dose-response relationship for oral glutamine, it is reasonable to propose that the dosage would have acutely elevated plasma glutamine immediately post-eccentric exercise and at 24-hour intervals for 4 days following eccentric exercise.

### **Knee extensor peak torque**

Prior to each testing session, volunteers were given time to stretch and complete a 5-minute warm-up on a Monark cycle ergometer (Monark Exercise Ab, Vansbro, Sweden) at 50 revolutions per minute and a resistance of 1 kp. Maximal voluntary concentric knee extensor peak torque was determined at angular velocities of 0.52 and 3.14 rad · s<sup>-1</sup> using an isokinetic dynamometer with a passive knee flexion return to the start angle (Biodex 3; Biodex, Shirley, NY, USA). The system was calibrated for each volunteer prior to each trial according to the manufacturer's instructions. Volunteers produced five maximal actions at each angular velocity with a 1-minute recovery separating the two velocities. The highest peak torque during the five repetitions at each angular velocity was used as the criterion variable.

### **Muscle soreness**

Muscle soreness was evaluated with a visual analog scale consisting of a 10-cm horizontal line, utilizing verbal anchors "no soreness" on the left to "maximal soreness" on the right. Volunteers performed an unloaded squat movement from full knee extension to 90° knee flexion with return to full knee extension, and were then asked to place a vertical mark on the horizontal line on the scale that corresponded to their perception of muscle soreness. Soreness was quantified by measuring the distance in centimeters from the left hand end of the scale to the volunteer's mark.

### **Plasma CK activity**

Plasma CK activity was measured from a 30-μL fingertip capillary blood sample. Plasma CK activity was analyzed by spectrophotometry (Jenway, Dunmow, UK) in accordance with the manufacturer's guidelines (Randox, Co. Antrim, UK). The normal resting value of plasma CK activity is <200 μL.

### **Statistical analyses**

Data were analyzed with SPSS version 15.0 (SPSS Inc., Chicago, IL, USA). Data are presented as mean ± standard deviation unless otherwise stated. Peak torque was

expressed relative to the pre-exercise peak torque. Peak torque, soreness, and CK data were analyzed with separate two-factor (time  $\times$  experimental group) repeated measures ANOVA. Values for plasma CK activity were transformed to natural log to satisfy the assumptions of the analysis. An alpha level of  $p < 0.05$  was accepted as a statistically significant difference between experimental conditions. Follow-up tests on time main effects were performed using paired sample t-tests applying the Bonferroni correction procedure, and independent-sample t-tests were used for group main effects. The relationship between peak torque and muscle soreness was investigated with the Pearson product moment correlation coefficient and expressed as the coefficient of determination (i.e.,  $R^2$ ).

## Results

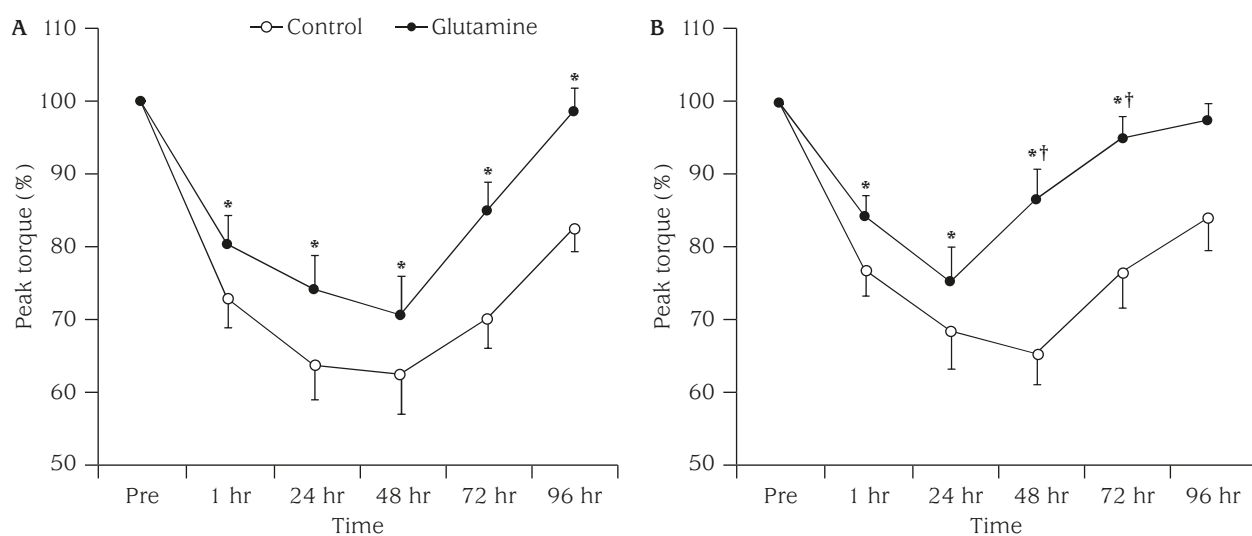
### Knee extensor peak torque

No differences in concentric peak torque were evident before eccentric exercise at both  $0.52 \text{ rad} \cdot \text{s}^{-1}$  (Control,  $263 \pm 45 \text{ N} \cdot \text{m}$ ; Glutamine,  $260 \pm 32 \text{ N} \cdot \text{m}$ ,  $p = 0.90$ ) and  $3.14 \text{ rad} \cdot \text{s}^{-1}$  (Control,  $160 \pm 50 \text{ N} \cdot \text{m}$ ; Glutamine,  $170 \pm 22 \text{ N} \cdot \text{m}$ ,  $p = 0.64$ ). Figure 1A illustrates that peak torque at  $0.52 \text{ rad} \cdot \text{s}^{-1}$ , expressed relative to pre-exercise values, was reduced significantly by 23% at 1 hour ( $p < 0.001$ ) and was still significantly reduced by 9% at 96 hours ( $p = 0.01$ ). Figure 1B illustrates that peak torque at  $3.14 \text{ rad} \cdot \text{s}^{-1}$  was reduced significantly by 19% at 1 hour

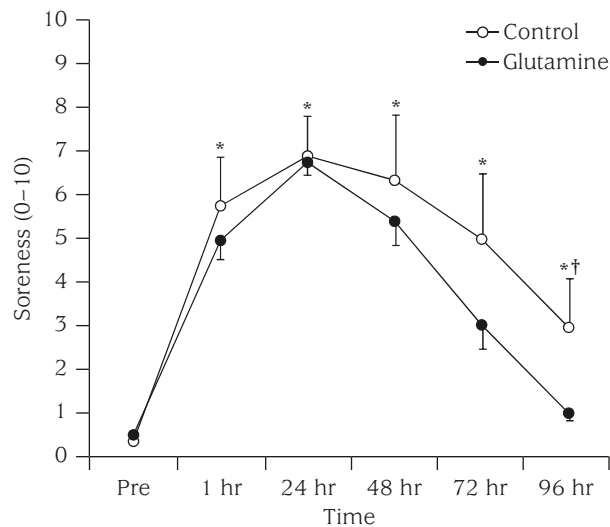
( $p < 0.001$ ) and by 14% at 72 hours ( $p = 0.005$ ), but had recovered by 96 hours. Glutamine supplementation resulted in significantly greater peak torque over the 96-hour measurement period at both  $0.52 \text{ rad} \cdot \text{s}^{-1}$  (Control,  $75 \pm 16\%$ ; Glutamine,  $85 \pm 15\%$ ,  $p = 0.03$ ) and  $3.14 \text{ rad} \cdot \text{s}^{-1}$  (Control,  $79 \pm 16\%$ ; Glutamine,  $90 \pm 12\%$ ,  $p = 0.01$ ). Glutamine supplementation resulted in significantly greater peak torque at 48 hours ( $p = 0.004$ ) and 72 hours ( $p = 0.009$ ) at  $3.14 \text{ rad} \cdot \text{s}^{-1}$ . Peak torque at  $3.14 \text{ rad} \cdot \text{s}^{-1}$  had returned to baseline by 72 hours with glutamine supplementation but was still significantly reduced at 96 hours ( $p = 0.008$ ) in the control group.

### Muscle soreness

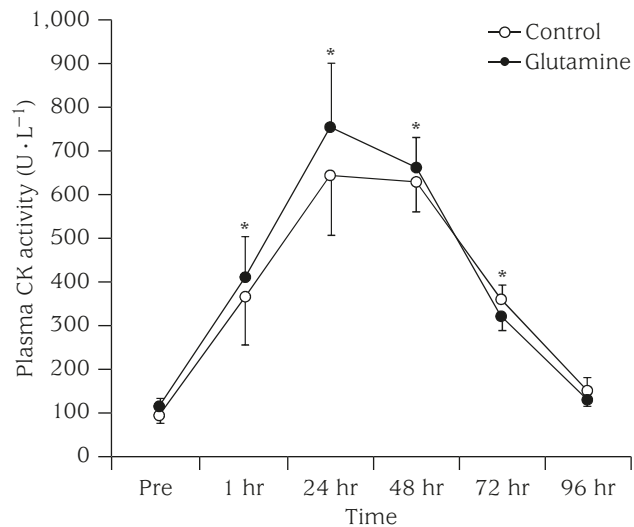
No difference in soreness was evident before eccentric exercise (Control,  $0.4 \pm 0.2 \text{ cm}$ ; Glutamine,  $0.5 \pm 0.3 \text{ cm}$ ,  $p = 0.35$ ). Figure 2 illustrates that soreness increased significantly at all time points following eccentric exercise. Glutamine supplementation resulted in significantly less soreness over the 96-hour testing period (Control,  $4.6 \pm 2.5 \text{ cm}$ ; Glutamine,  $3.6 \pm 2.5 \text{ cm}$ ,  $p = 0.03$ ). Glutamine supplementation did not affect the timing or magnitude of the peak soreness experienced (i.e., at 24 hours: Control,  $6.9 \pm 0.9 \text{ cm}$ ; Glutamine,  $6.8 \pm 0.7 \text{ cm}$ ,  $p = 0.70$ ), but diminished soreness more rapidly, resulting in significantly less soreness at 96 hours ( $p = 0.001$ ). Soreness was not associated ( $p > 0.05$ ) with the magnitude of strength loss apart from a weak negative relationship observed at 1 hour post-exercise ( $R^2 = 0.27$ ,  $p = 0.05$ ).



**Fig. 1** Concentric knee-extensor peak torque (expressed as a percent of pre-exercise peak torque) at: (A)  $0.52 \text{ rad} \cdot \text{s}^{-1}$ ; (B)  $3.14 \text{ rad} \cdot \text{s}^{-1}$ . \*Significant difference from baseline for both conditions,  $p \leq 0.01$ ; †significant difference between conditions at time point,  $p < 0.01$ .



**Fig. 2** Muscle soreness on active movement of the knee extensors. \*Significant difference from baseline for both conditions,  $p < 0.01$ ; †significant difference between conditions at the time point,  $p < 0.01$ .



**Fig. 3** Plasma creatine kinase activity following eccentric exercise. \*Significant difference from baseline for both conditions,  $p < 0.01$ .

### Plasma CK activity

Figure 3 shows that plasma CK activity was significantly elevated above baseline at 1 hour ( $p = 0.01$ ), 24 hours ( $p < 0.001$ ), 48 hours ( $p = 0.001$ ), and 72 hours ( $p = 0.005$ ), reaching peak values at 48 hours. No differences were apparent between groups for the magnitude and temporal nature of the CK response.

### Discussion

The major findings of this study are that oral glutamine supplementation, immediately post and for 72 hours after eccentric exercise, resulted in significantly less strength loss and muscle soreness compared with a placebo. To our knowledge, this study represents the first test of the effectiveness of glutamine supplementation as a therapeutic nutritional supplement in an experimental model of eccentric exercise-induced muscle damage.

Glutamine supplementation was effective in reducing muscle damage on the basis of strength measurements. Maximal voluntary contraction provides the most effective means of evaluating the magnitude and time course of damage resulting from eccentric exercise (Warren et al. 1999). Glutamine supplementation reduced the average decrement in knee extensor strength by 10% over 96 hours during both low (25% *cf.* 15%) and high (21% *cf.* 10%) angular velocities of movement. At the high angular velocity, strength returned to

pre-exercise levels by 72 hours with glutamine supplementation but remained significantly reduced in the control group at 96 hours. Therefore, glutamine supplementation afforded a small but meaningful protection against strength loss, resulting in a more rapid return to the pre-damage state at the higher velocity of movement.

Our findings are in agreement with a number of recent studies reporting positive effects of protein or selected amino acid supplementation on muscle strength following eccentric exercise (Buckley et al. 2010; Etheridge et al. 2008; Nosaka et al. 2006). The mechanism(s) underlying improved muscle function in the present and previous studies are not understood. Our study along with previous studies did not employ an isoenergetic control and although the additional energy intake from glutamine was small ( $\approx 100 \text{ kcal} \cdot \text{d}^{-1}$ ), it is a potential explanatory factor (Jackman et al. 2010; Nosaka et al. 2006). Central and peripheral mechanisms have been demonstrated to contribute to strength loss (Hubal et al. 2007; Prasartwuth et al. 2005), with peripheral mechanisms accounting for the majority of the immediate and prolonged loss of strength (Hubal et al. 2007). Suggested peripheral mechanisms of strength loss include impaired excitation-contraction coupling (Ingalls et al. 1999), sarcomere length redistribution (Proske et al. 2001), and leukocyte accumulation (Paulsen et al. 2010; Raastad et al. 2003; MacIntyre et al. 1996). A possible mechanism of glutamine action is attenuating the inflammatory response to eccentric exercise.

A local inflammatory response is observed in skeletal muscle post-eccentric exercise (Peake et al. 2005), with the timing and magnitude of leukocyte infiltration associated with decrements in muscle function (Paulsen et al. 2010; Raastad et al. 2003; MacIntyre et al. 1996). Glutamine is known to maintain protein balance and plays many cell regulatory and immune system roles (Roth 2008; Wernerman 2008; Castell 2003; Walsh et al. 1998). Glutamine supplementation may improve muscle function by attenuating the local inflammatory response to eccentric exercise (Paulsen et al. 2010; Raastad et al. 2003; MacIntyre et al. 1996). Recent animal evidence from rats provides tentative support for such a hypothesis. Cruzat et al. (2010) reported that glutamine supplementation increased rat skeletal muscle and plasma glutamine concentrations and attenuated the inflammatory response to exercise. In animals supplemented with  $1.5 \text{ g} \cdot \text{kg}^{-1}$  glutamine for 21 days, Cruzat et al. (2010) observed higher muscle glutamine concentrations pre- and post-exercise and lower plasma concentrations of proinflammatory cytokines (i.e.,  $\text{PGE}_2$  and  $\text{TNF-}\alpha$ ) following 2 hours of swimming. The authors suggested that myocyte intracellular glutamine transport is accompanied by an increase in cell water and volume which may increase resistance to mechanical trauma and subsequent inflammatory responses. A basic hypothesis is that glutamine supplementation maintained glutamine homeostasis and dependent physiological functions post-eccentric exercise when glutamine utilization was increased. Since glutamine is synthesised by branched-chain amino acid metabolism, it is possible that protein or amino acid supplementation ensures adequate glutamine synthesis and release at a time of increased utilization following eccentric exercise (Parry-Billings et al. 1990).

Glutamine supplementation did not affect the magnitude of muscle soreness experienced but resulted in a more rapid dissipation of soreness evident as a significantly lower soreness at 96 hours. This finding is in general agreement with two recent studies reporting positive effects of selected amino acid supplementation on muscle soreness following eccentric exercise (Jackman et al. 2010; Nosaka et al. 2006). Nosaka et al. (2006) reported reduced soreness of the elbow flexors at 24 and 48 hours post-eccentric exercise when a supplement containing 12 amino acids (3.6 g) including L-glutamine was ingested pre, immediately post, and on eight more occasions over 4 days post-eccentric exercise. Jackman et al. (2010) observed reduced soreness of the knee extensors at 48 and 72 hours post-eccentric exercise when a 7.3-g branched-chain amino

acid supplement was ingested four times daily (starting immediately pre-exercise) for 3 days. In contrast to the present study, both of the aforementioned studies resulted in a significantly lower peak magnitude of soreness. Unlike the above studies, our supplementation regimen did not include a pre-exercise supplement. Future research may wish to investigate the efficacy of an additional pre-exercise glutamine supplement. Currently, there is no general consensus on the underlying mechanisms of muscle soreness following eccentric exercise, although damage and/or inflammation of the extracellular matrix are a potential etiological factor (Cramer et al. 2007; Clarkson & Hubal 2002).

The lower muscle soreness with glutamine supplementation could have attenuated strength loss via a reduction in conscious or reflex inhibition affecting voluntary activation during maximal voluntary contractions. Reduced voluntary activation is mainly observed in the first 24 hours after eccentric exercise (Prasartwuth et al. 2005) when soreness was comparable between the glutamine and placebo groups. Glutamine supplementation resulted in significantly lower soreness at 96 hours, whereas strength loss was significantly reduced at the higher movement velocity at 48 and 72 hours, and no meaningful associations between soreness and strength were evident at any time point. Therefore, our evidence does not suggest that the preservation of strength was related to the reduced muscle soreness.

In conclusion, our findings provide initial support for the efficacy of oral glutamine supplementation in promoting recovery from eccentric exercise-induced muscle damage. Further research is warranted to investigate glutamine homeostasis post-eccentric exercise, the influence of glutamine supplementation on homeostasis, and to confirm the efficacy of oral glutamine supplementation in improving recovery from exercise-induced muscle damage. Glutamine supplementation attenuated the magnitude of strength loss, improved the time course of strength recovery, and diminished muscle soreness more rapidly in comparison with an isocarbohydrate placebo.

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