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Annals of Biological Research, 2012, 3 (8):4209-4214
(http://scholarsresearchlibrary.com/archive.html)

Annals of Biological Research
Scholars Research Library
ISSN 0976-1233
CODEN (USA): ABRNBW

Central and peripheral fatigue factors after an exhaustive aerobic exercise following creatine supplementation

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ABSTRACT

Fatigue is a complex phenomenon that can be evoked by peripheral and central factors. The effects of creatine supplementation (CrS) on peripheral and central fatigue factors after exhaustive aerobic exercise are not fully understood. Thus the purpose of this study was to investigate central and peripheral fatigue factors after an exhaustive aerobic exercise following CrS. Twenty untrained male subjects participated in a placebo (Plc, n=10)/creatine (Cr, n=10), double-blind study conducted over 7 days period. The Cr group received 20 g (4 × 5 g) creatine monohydrate per day and Plc group received the same dosage of a glucose polymer. Each subject performed a graded treadmill exercise test to complete exhaustion. Blood lactate levels increased (P<0.05) immediately after the exercise in the Cr and Plc groups and there was no significant difference between two groups. While, blood lactate concentration decreased after the exercise in the both groups (P<0.05), the decrease of blood lactate concentration was quickly in the Cr group than the Plc group (P<0.05). Additionally, although serotonin: dopamine ratio was lower in the Cr group immediately after the exercise and during the recovery, no significant difference between two groups was observed. These findings suggest that although CrS effective to reduce blood lactate after an exhaustive aerobic exercise, central fatigue index was not affected by CrS.

Key words: Creatine supplementation, Central fatigue, Peripheral fatigue

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INTRODUCTION

Fatigue is an important factor affecting exercise and sporting performances. It is defined physiologically as the inability to maintain power output [23], and the organism uses it as a defense mechanism to avoid irreversible damage due to excessive exertion [26]. The fatigue that accompanies physical exercise is thought to derive from 1) metabolic changes in muscle that ultimately lead to muscle exhaustion (*peripheral fatigue*) and 2) modifications in the central nervous system (CNS) that diminish motor neuron impulse traffic to muscle (*central fatigue*) [14, 24]. Peripheral fatigue can occur at several site such as the neuromuscular junction, the sarcolemma – T tubules – sarcoplamic reticulum system, and myofilaments [27]. Current research suggests that the primary site of peripheral fatigue usually is within the muscle itself. Accumulation of lactate and the H^+ associated with lactic acid may lead to fatigue by interfering with the contractile process in several places, decreasing the amount of calcium released, interfering with calcium – troponin binding, disrupting the Na^+ – K^+ pump, inhibiting anaerobic glycolysis, or interfering with cross-binding [22, 27]. Central fatigue is also thought to play a significant role in fatigue during exercise [21]. It is suggested that an alternation in brain neurotransmitters, specifically the ratio of brain serotonin to dopamine, is associated with reduce motor unit recruitment [21].

Creatine (Cr) plays an important role in rapid energy provision during muscle contraction and it is demonstrated that creatin supplementation (CrS) can be improve exercise performances [11]. Several studies exploring the effects of

CrS on blood lactate levels have resulted inconsistent findings. Roschel et al. (2010) indicated that Crs for 5 days reduces blood lactate levels during a high intensity intermittent exercise in rats, while these findings have not been confirmed by others in human [7, 9, 29]. For example, Dawson et al. (1995) demonstrated that although CrS for 5 days enhanced single and repeated maximal short sprints, but CrS did not influence on blood lactate levels. However, although a number of studies investigated the role of Cr in preventing peripheral fatigue during high intensity exercise, attempts to determine the effect of CrS on central fatigue factors are very little. By our knowledge there is only one study that has determined the effects of CrS on central fatigue during exercise. Hadjicharalambous et al. (2008) reported that 7 days CrS reduces central fatigue during exercise in the heat. The purpose therefore of the present study was to examine the effects of oral Cr on central and peripheral fatigue factors after an exhaustive aerobic exercise.

MATERIALS AND METHODS

Participants and inclusion criteria

Twenty healthy and sedentary young males volunteers (22.4 ± 0.8 years; mean ± SD) provided written informed consent for the study, which was approved by the Islamic Azad University, Fars Science & Research branch Ethics Committee. All the subjects were asked to complete a personal health and medical history questionnaire, which served as a screening tool. Our participants were not engaged in any systematic exercise programs at least 6 months before the study and none of them had a history of cardiovascular or respiratory disease and/or evidence of musculoskeletal injury. All participants were Cr free prior to the study. The subjects were randomly assigned to one of the Cr group (n=10) or placebo (Plc) group (n=10).

Supplementation protocol

Subjects were given oral supplements over 7 days, either Cr group or Plc group. The Cr group received 20 g (4 packages, each containing 5 g) Cr monohydrate per day (100% pure Cr monohydrate; ON., USA). Plc group received the same dosage of a glucose polymer. Both supplements had similar taste, texture and appearance and were placed in generic packets to ensure double-blind administration. Participants otherwise followed their normal diet but eliminated caffeine and caffeine-containing foods throughout the experimental period to minimize the possible inhibitory effects of caffeine on the ergogenic effect of Cr. At the end of the study all participants gave verbal assurance that they had complied with these instructions.

Exercise Protocol

After the familiarization trials, subjects performed the exhaustive aerobic exercise test (Bruce protocol). The Bruce protocol is a maximal exercise test on the treadmill that speed and incline is increased every three minutes [1]. Each subject performed a graded treadmill exercise test to complete exhaustion. Each participant was equipped with a heart rate monitor (Beurer, Germany) to control the heart rate during the exercise.

Measurements

Anthropometric and body composition measurements

Height and body mass were measured, and body mass index (BMI) was calculated by dividing body mass (kg) by height (m^2). Waist circumference was determined by obtaining the minimum circumference (narrowest part of the torso, above the umbilicus) and the maximum hip circumference while standing with their heels together. The waist to hip ratio (WHR) was calculated by dividing waist by hip circumference (cm) [1]. Fat mass, body fat percent, lean body mass and intracellular and extracellular water were assessed by bioelectrical impedance analysis using a Body Composition Analyzer (Boca X_1, Korea). All the measurements were obtained before and after the CrS period.

Estimated urine creatinine

Urine creatinine was determined using 24 h urine collections. The urine samples were collected on the day preceding supplementation (baseline) and after 7 days CrS period. The urine creatinine concentration determined using a spectrophotometric enzymatic creatinine Kit (Roche Diagnostics Ltd., East Sussex, UK).

Biochemical analyses

Blood samples were collected at rest, immediately after the exhaustive aerobic exercise, and 10 min and 20 min of recovery from the exercise. Blood samples immediately analyzed in the Shiraz Namazi Hospital. Plasma lactate levels were determined in duplicate via a spectrophotometric enzymatic lactate Kit. The plasma serotonin and dopamine level were measured in duplicate using an enzyme-linked immunosorbent assay (ELISA) kits (Casabio Biotech Co. LTD.; China). The sensitivity of kits for serotonin and dopamine were less than 62.5 and 0.25 ng/ml respectively. Central fatigue index was calculated by dividing serotonin to dopamine concentrations.

Statistical Analysis

Data were analyzed using SPSS software for windows (version 13, SPSS, Inc., Chicago, IL). 2 × 4 repeated measures ANOVA was used to evaluate time-course change in variables. Post hoc analyses (Bonferroni) were then performed when warranted and independent t-test was used to compute differences in the variables. Mean values of two groups before and after CrS were compared by paired-samples t-test and independent-samples t-test for the variables. The significance level of this study was set at $P < 0.05$.

RESULTS

Change in anthropometric, body composition and urine creatinine variables

Anthropometric and body composition characteristics of the subjects at baseline and after CrS are presented in Table 1. Before the CrS, there were no significant differences in any of variables among the two groups. After CrS, body mass, BMI, lean body mass and urine creatinine increased (P<0.05) in the Cr group compared to the Plc group, while no significant change in anthropometric and body composition variables were found in the Plc group after the CrS.

Table 1. Anthropometric, body composition characteristics and urine creatinine levels (mean ± SD) of the subjects before and after CrS

Variables	Plc group (n=10)		Cr group (n=10)	
	Pre	Post	Pre	Post
Body mass (kg)	71.7 ± 6.7	71.6 ± 6.8	71.8 ± 10.3	73.1 ± 9.9*
BMI (kg/m^2)	23.66 ± 2	23.67 ± 2	23.3 ± 3.01	23.8 ± 2.8
Fat mass (kg)	16.3 ± 5.7	15.3 ± 4.7	15.4 ± 6.9	14.9 ± 6.2
Body fat (%)	21 ± 5.5	20.9 ± 5.4	20.6 ± 6	19.9 ± 5.7
Lean body mass (kg)	53.3 ± 4	53.4 ± 4	53.9 ± 5.7	54.6 ± 4.9*
Intracellular water (%)	37.2 ± 2.4	37.1 ± 2.3	37.1 ± 2.6	37.5 ± 2.5
Extracellular water (%)	17.9 ± 1.2	17.8 ± 1.1	18.01 ± 1.5	16.4 ± 4.8
Urine creatinine (mg)	183.2 ± 102.1	116.1 ± 54.1	204.7 ± 58.9	251 ± 70.6*

** P<0.05 for between-group differences*

Change in Blood lactate levels

Change in blood lactate concentrations before, immediately after the exhaustive aerobic exercise, 10 min and 20 min of recovery from the exercise are shown in figure 1. The results showed that blood lactate levels increased (P<0.05) immediately after the exhaustive aerobic exercise in the Cr and Plc groups and there was no significant difference between two groups. Although 10 min of recovery from the exercise blood lactate concentrations decreased (P<0.05) in both groups compared to the end of exercise, the decrease of blood lactate concentration was quickly in the Cr group than the Plc group (P<0.05). Similarly, the blood lactate concentration 20 min of recovery from the exercise decreased (P<0.05) in both groups compared to the end of exercise and compared to the 10 min of recovery from the exercise; but the decrease of blood lactate concentration was quickly in the Cr group than the Plc group (P<0.05). Despite decrease of blood lactate in the Cr and Plc groups after the exercise, blood lactate concentration was higher than the rest level in the both groups (P<0.05).

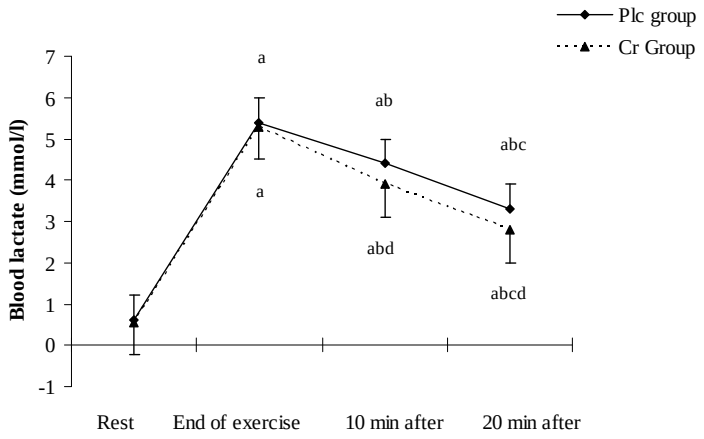

Figure 1. Change in blood lactate concentrations before, immediately after the exhaustive aerobic exercise, 10 min and 20 min of recovery from the exercise.

(a) Significant difference with rest blood lactate concentration (P<0.05).
(b) Significant difference with blood lactate concentration immediately after exercise (P<0.05).
(c) Significant difference with blood lactate concentration 10 min of recovery from the exercise (P<0.05).
(d) Between-group differences (P<0.05).

Changes in central fatigue index (Brain serotonin: dopamine ratio)

Change in brain serotonin: dopamine ratio before, immediately after the exhaustive aerobic exercise, 10 min and 20 min of recovery from the exercise are shown in figure 2. As shown in figure 2, serotonin: dopamine ratio decreased (P<0.05) in Cr group immediately after exercise, increased (P<0.05) 10 min of recovery from the exercise and decrease (P<0.05) again 20 min of recovery from the exercise in the Cr group. Although serotonin: dopamine ratio was lower in the Cr group immediately after the exercise and during the recovery, no significant difference between two groups was observed.

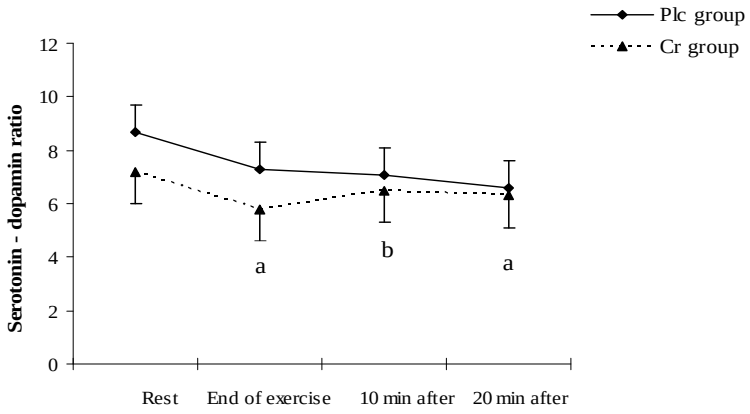

Figure 2. Change in serotonin – dopamine ratio blood before, immediately after the exhaustive aerobic exercise, 10 min and 20 min of recovery from the exercise.

(a) Significant difference with rest serotonin – dopamine ratio (P<0.05).

(b) Significant difference with serotonin – dopamine ratio immediately after exercise (P<0.05).

DISCUSSION

The results of present study showed that Cr increased after CrS in the Cr group (P<0.05), thus each changes in this group might resulted from Cr effect. After CrS, body mass, BMI and lean body mass increased (P<0.05) in the Cr group compared to the Plc group. Various studies have shown an average of 1–2 kg of total body mass increases with 20 g/day of CrS for 5–7 days [16, 31]. Kreider (1998) indicated that short duration (5–7 days) of CrS at 20–25 g/day typically leads to increases of up to 1.6 kg in total body mass. In our subjects, we observed a significant 1.2 ± 0.7 kg increase in body mass in the Cr group after Cr loading, with body mass remaining unchanged in the Plc group (– 0.2 ± 0.6 kg; Table 1). The increase in body mass has previously been attributed to an increase in total body water, caused by water retention in skeletal muscle cells due to increased cellular osmolarity [30]. Interestingly, cell swelling has been identified as a universal anabolic signal, stimulating protein synthesis and net protein deposition [18]. In agreement with this, Ingwall (1976), using differentiating skeletal muscle cells in culture, showed that muscle-specific protein synthesis is stimulated by Cr. However, this has not been confirmed in subsequent studies *in vitro* [10, 33]. Nonetheless, Parise et al. (2001) suggest that net muscle protein anabolism following short-term CrS can be explained by a reduction in protein catabolism rather than an increase in protein synthesis.

The results demonstrated that although blood lactate concentration decreased after the exercise in the both groups (P<0.05), the decrease of blood lactate concentration was quickly in the Cr group than the Plc group (18.5% *VS* 26.4% decreases 10 min after the exercise; 38.8% *VS* 47.1% decreases 20 min after the exercise; P<0.05). The half – life of lactate is about 15 – 25 min after the exercise regardless of the starting level and near–resting levels are achieved in about 30 – 60 min, regardless of the starting level [27]. Our results showed that blood lactate concentration in Cr group is achieved to its half – life about 20 min after the exercise, while in Plc group only 38.8% of lactate removes from the blood after 20 min of recovery from the exercise. After exercise, the lactate removal from blood may depend on the slow-twitch fiber content of muscle, the lactate concentration in blood, and the intensity of the recovery exercise [2]. The rate of lactate removal from the blood partly depends on amount of lactate present after the exercise or the mass action effect. By means that as more lactate appears in the blood, lactate removal from the blood is faster [27, 3]. On the other hand, blood lactate levels reflect the balance between lactic acid production (appearance) and clearance (removal) [27]. Lactate moves between lactate – producing and lactate – consuming sites through intracellular and extracellular lactate shuttles [5]. Lactate transport across cellular membranes occurs by facilitated exchange down concentration and hydrogen ion (pH) gradients using lactate transport proteins known as monocarboxylate transporters (MCTs) [5]. Lactate moves between the cytoplasm, where it is produced, and mitochondria by MCT1 and lactate removes from the fast-twitch and fast oxidative glycolytic muscle fibers by MCT4 [3]. Bonen although, indicated that exercise training can increase the expression of both

MCT1 and MCT4 in human muscle, the effect of CrS on these proteins is unclear [4]. By according to our results, it seems that CrS may effective to increase MCTs activity, however further studies are needed to examine the effects of CrS on MCTs expression and activity.

As shown in figure 2, although serotonin: dopamine ratio was lower in the Cr group immediately after the exercise and during the recovery, no significant difference between two groups was observed. Serotonin has been linked to fatigue because of its documented role in sleep, feelings of lethargy and drowsiness, and loss of motivation, whereas increased dopamine neurotransmission favors feelings of motivation, arousal, and reward. It is suggested that an increase in the ratio of brain serotonin to dopamine, is associated with reduce motor unit recruitment and central fatigue during exercise [21]. However, the effect of Cr on exercise performance is well understood, its biochemical role in prevention of central fatigue is not. It was found for example, that oral CrS improved mental function and reduced mental fatigue by increasing the oxygen utilization in the brain [32]. In addition, several pharmacological studies suggested that oral CrS has been found to increase brain dopamine synthesis in the substantianigra of mice by protecting against striatal dopamine depletion [15] and/or by enhancing tyrosine hydroxylase activation (Matthews et al. 1999). In addition, an improvement in mental function and diminished central fatigue was observed during performing a mathematical calculation following oral CrS [32]. In contrary to our results, Hadjicharalambous et al. (2008) reported that 7 days CrS reduces central fatigue index during exercise in the heat. Their observations indicated that CrS is effective to reduce free – tryptophan: tyrosine ratio. These discrepant results may be attributed to differences in timing in blood sampling, variation in the exercise protocols and differences in subject populations. It must be noted that the subjects in the study of Hadjicharalambous et al. (2008) were endurance-trained athletes, the exercise performed in the heat and blood samples were taken during and the end of exercise. Consequently, more studies are warranted to examine the effect of Cr on central fatigue during exercise.

CONCLUSION

In summary, despite the effectiveness of CrS to reduce blood lactate after exhaustive aerobic exercise, CrS has no effect on central fatigue. Additional research is needed to examine the effect of CrS on central fatigue factors and on mechanisms by which Cr helps to remove lactate from the blood.

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