Original Research

Acute High Intensity Anaerobic Training and Rhabdomyolysis Risk

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ABSTRACT

International Journal of Exercise Science 8(1) : 65-74, 2015. The current popularity of high intensity anaerobic training has caused concerns over the safety and prevalence of conditions such as rhabdomyolysis; thus it is important to understand the possible risks of participating in this type of activity. The purpose of this study was to determine the magnitude of muscle damage associated with a single high intensity anaerobic training session, and the relationship of this response to markers of fitness. Fifteen recreationally trained male participants (age 22.9 ± 4.3 y, mass 87.3 ± 15.6 kg, body fat 16.8 ± 6.4%, $VO_{2\,peak}$ 50.1 ± 7.2 ml · kg^{-1} · min^{-1}) completed a single anaerobic training session consisting of high intensity plyometrics and calisthenics. Prior to the exercise session, participants completed a maximal aerobic capacity test, body composition analysis, and a military physical fitness test (1 min push-ups, 54 ± 14; 1 min sit-ups, 45 ± 11; 1.5 mile run, 12:17 ± 0.067 min). Serum creatine kinase (CK) was measured prior to and 48 h following the exercise session. CK at 48 h (126.3 ± 68.9 U · L^{-1}) did not reach the limits indicating rhabdomyolysis (~881-1479 U/L) but was elevated above resting (CK resting 90.5 ± 53.4). $VO_{2\,peak}$ (L · m^{-1}) had a positive correlation with CK levels ($r = .51$; $p < 0.05$) but body mass or any other indicator of fitness did not correlate. An increase in serum CK levels occurred, but did not reach levels of rhabdomyolysis, suggesting that a single high intensity exercise session is safe for healthy individuals who exercise regularly.

KEY WORDS: Creatine kinase, exercise intensity, anaerobic exercise

INTRODUCTION

It has been documented by the U.S. Armed Forces that there has been a 30 percent increase in reported rates of rhabdomyolysis from 2008 – 2012, presumably due to physical exertion and heat stress (1). High intensity anaerobic training, similar to Crossfit, P90X, and Insanity, is an increasingly popular technique used to increase fitness and athletic performance. These types of methods are commonly used in military settings to prepare the tactical athlete for combat situations and prepare recruits for service (1). The benefits to this training model are the decreased total time needed for training and the ability to train aspects of endurance and strength in the same session. One drawback is a lack of information on the safety of this type of high intensity training. Therefore, investigations on the safety of high intensity anaerobic training are needed.

High intensity anaerobic training is characterized by short durations of high-velocity movements with eccentric loading and limited rest between sets. Musculoskeletal injuries are a concern with any form of exercise. However, an elevated rate of injury is associated with increased exercise intensity and eccentric loading (21, 24). While risk of musculoskeletal injury is an important concern, the risk of exertional rhabdomyolysis associated with this type of exercise may be of greater interest due to the dire implications of rhabdomyolysis (14).

Exertional rhabdomyolysis is associated with strenuous exercise, and can be marked with muscle soreness or pain, swelling of the associated muscle groups, and myoglobinuria (9, 15). Exercise induced muscle damage is common in exhaustive exercise, including distance running, and eccentric exercise such as downhill sprinting, weight training, and plyometric based programs (19, 21). As a result of muscle trauma, there is an increase in circulation of muscle proteins, specifically, but not limited to, myoglobin and creatine kinase (7). The myoglobin in circulation can precipitate in the renal tubules, having a nephrotoxic effect leading to renal failure and myoglobinuria (7, 8, 15). Creatine kinase (CK) levels mirror the increases in circulating myoglobin, promoting the use of serum CK as an indicator of rhabdomyolysis (7). A lack of consistency exists in the amount of serum CK associated with rhabdomyolysis ranging from 881 $U \cdot L^{-1}$ to levels upward of 20,000 $U \cdot L^{-1}$ (4, 6, 15, 21). It has been noted that levels of serum creatine kinase have been observed at 5-10 times the normal limit without a diagnosis of rhabdomyolysis (4, 10, 13, 17, 22). When diagnosing rhabdomyolysis, local and systemic features are examined. The local features include muscle pain, tenderness, and swelling. The Systemic features include "tea" colored urine, fever, and nausea. The "tea" colored urine indicates myoglobinuria or hemoglobinuria, depending on the sediment present (10, 26, 32).

Little is known about the minimum level of physical fitness necessary to participate in high intensity exercise. In sedentary individuals, markers of muscle damage increase rapidly when compared to trained individuals (4). It is proposed that trained individuals have had physiological and mechanical adaptations to the overload associated with eccentric contractions and high intensities (3). Therefore, it is important that the safety of high intensity anaerobic training should be examined in association to overall physical fitness. Acutely detrained athletes may be at risk for rhabdomyolysis as well. These individuals must take caution to gradually increase their workload after a period of detraining (23).

The purpose of this study was to determine the CK response to a single high intensity anaerobic training session and the relationship of this response to markers of fitness. The information gained from this investigation may provide the framework for practical recommendations on the safety of high intensity anaerobic training for individuals with differing levels of fitness.

METHODS

Participants

Fifteen recreationally trained males, aged 20-35 y, recruited from the local university fitness center volunteered to participate in this investigation. All participants reported participating in physical activity lasting at least 30 minutes, 3 or more days per week. Only male participants were used in this study due to potential differences in CK response between males and females (2, 6, 20). The participants signed an Institutional Review Board approved informed consent form prior to starting the research protocol. Each participant was instructed to refrain from vigorous exercise at least 24 hours before the experimental trial and the 48 hours after the trial leading up to the final blood draw after exercise. Prior to completing the experimental exercise session, each participant completed a military style fitness test, VO_2 peak test, ventilatory threshold test, and body composition assessment. VO_2 peak test, ventilatory threshold, and body composition assessment were completed during a single session, while the military fitness test was completed during a separate session. The participants had varied levels of fitness ranging from fair to superior according to relative peak VO_2 and poor to superior according to the 1.5 mile run (28). Each participant completed a single session of high intensity anaerobic training consisting of high intensity plyometrics and calisthenics. Blood draws occurred before the experimental protocol and 48 h after high intensity exercise, CK was measured on a later date.

Protocol

Participants completed a graded maximal treadmill test after at least a 3 h fast. The test protocol started with walking at 4 mph and 1% incline and increased by 1mph every 3 minutes until ventilatory threshold had been exceeded (RER>1.0, Age predicted max HR greater than 85%, and a non-linear rise in ventilation), the protocol was continued until maximum volitional effort. Expired gasses were collected and analyzed using a flow and gas calibrated metabolic measuring system (TrueOne 2400 Parvo medics; Sandy, UT). Ventilatory threshold (VT) was determined using the V-slope method, which was analyzed by the Parvo medics software, and then confirmed by an investigator by visual inspection (12).

The participants completed hydrostatic weighing using an Exertech (La Crescent, MN) electronic load cell based underwater weighing system. Participants were required to fast at least four hours prior to the hydrostatic weighing. Body density was determined from the hydrostatic weighing, converted to percent body fat using the Siri equation (27) which was corrected for estimated residual lung volume (25).

Five ml of blood was drawn using venipuncture technique from an antecubital vein prior to the high intensity anaerobic exercise session, as well as 48 h after the session, and used to measure serum CK levels. Forty-eight hours has been shown to be a peak time for creatine kinase response (2, 16, 29). The blood samples were allowed to clot for 30 minutes at room temperature. The blood was then centrifuged at 2,000 rpm to separate the serum. Serum was then divided into appropriate aliquots and stored at $^{-}80$ °C until CK was assayed using a commercially available kit from BioAssay Systems (Hayward, CA) according to

Table 1. High intensity exercise protocol and dynamic warm-up.

Warm-up		
Exercise	**Distance (m)**	**Description**
Jog	51.6	Lightly ran the length of the court and back
High Knees	25.8	While jogging, lifting the knees through for an increased range of motion
Butt Kicks	25.8	While jogging, bringing the heels up towards the glutes for an increased range of motion
Knee to Chest	12.9	While walking, pulling the knee to the chest. This was done alternating.
Lunge w/ twist	12.9	Taking an increased step, bringing the back knee to the ground while twisting the torso
Squat and spin	12.9	Deep squat then rotating progressing down the court
Elbow to instep/hamstring	12.9	Lunge motion bring the elbow to the instep of the lead foot, then lean back and touching the toes
Inch worm/push up	12.9	Legs straight, while touching the toes. Hand walking to a push up position. Ankle walk to the original position.
High kicks	12.9	Kicking the leg as high as possibly, swing the leg through an wide range of motion
A-skips	51.6	Same as butt kicks, but done with a skip for an increased speed
High skips	51.6	Skip done for maximum height not done for speed
Side-side sprint	51.6	Side shuffle for 3 strides, then turn and sprint the length of the court
Jog to sprint	51.6	Start at a jog and increase speed to a sprint

Exercise	**Sets**	**Time (s)**	**Description**
Line Jumps (2 legs) Forward	4	15	Jumping over a line front to back as quickly as possible
Lateral bounds	3	20	Jumping lateral back and forth for maximum distance and speed
Broad Jumps	3	15	Jumping as far and as fast as possible
Med ball Squat/Throw SS Knee Tucks	3	20	Throwing the medicine ball has high as possible starting a squat position, once the 20 sec has been completed the participants had to jump bringing their knees as high as possible for as many repetitions as possible.
Med ball Side Throw	3	20	Starting from a squatting position, rotating and throwing the medicine ball against the wall, after 20 secs the participants switched to opposite side
Burpee	3	20	Starting in a push-up position, bring the feet to where the hands are placed, and then jumping
Partner Push-ups	2	20	Participants were across from each other in push up position, proceed down for a normal push up but at the top portion would reach out and slap hands with their partner, alternating hands after every push up.

15-20 seconds rest between sets to achieve 1:1 work to rest ratio; 1 min rest between exercises.

manufacturer instructions and read on a photometric plate reader (Fisher Scientific, Waltham, Ma).

The participants completed an Air Force style fitness test. The test consisted of, in order, maximal push-ups in 1 minute, maximal sit-ups in 1 minute, and a 1.5 mile

Table 2. Participant descriptive data and relationship with creatine kinase (CK) at 48 h and CK change over 48 h.

	Descriptive Variable (mean ± SD)	**CK 48 h (r=)**	**CK Δ 48 h (r=)**
Age (years)	23 ± 4	-	-
VO_2 peak (L · min^{-1})	4.29 ± 0.50	0.508*	0.241
VO_2 peak (mL · kg · min^{-1})	50.1 ± 7.2	0.100	0.039
Ventilatory Threshold (% VO_2)	67.1 ± 7.2	0.016	-0.258
Ventilatory Threshold (mL·kg·min^{-1})	33.8 ± 6.6	0.086	-0.102
Height (cm)	27.6 ± 1.1	-	-
Body Mass (kg)	87.4 ± 15.6	0.222	0.101
Fat Free Mass (kg)	64.1 ± 25.3	0.120	0.289
Fat Mass (kg)	23.3 ± 19.1	0.022	-0.299
Body Fat %	16.8 ± 6.4	-0.316	-0.197
Push-ups (in 1 min)	54 ± 14	0.074	0.021
Sit-ups (in 1 min)	45 ± 11	0.303	0.060
1.5 Mile (min:sec)	11:27 ± 1:36	-0.095	0.006

(SD) standard deviation, *$p < 0.05$ correlation between markers of fitness and CK

run. The participants were allowed between 3-5 minutes of rest between exercises. The maximal push-up test started with arms at full extension. The participants then descended to at least a 90 degree bend in the elbow, then ended at full extension. Participants were allowed rest, but had to do so with arms fully extended. The maximal sit-up test required the participants to cross arms in front of the chest, with the hands placed on their shoulders. The participants had to touch elbows to mid-thigh on each repetition, and feet were held during the test. The participants were allowed to rest in the up position of the sit-up. The 1.5 mile run was completed on a 200 m flat indoor track.

The participants completed a single bout of high intensity anaerobic training. The session used a 1:1 work to rest ratio between each set with one minute rest between exercises. Each set consisted of maximal effort ranging from 15-20 seconds. This protocol was selected because it is similar in length and structure to other common high intensity interval training protocols (11, 29). The sessions were completed in groups of 3-6 participants and lasted approximately 19 minutes. The session was completed on a multipurpose court (15 m width by 25.8 m length), and started with a dynamic warm-up, and progressed into high intensity plyometrics, medicine ball throws, and calisthenics (Table 1).

Statistical Analysis

Statistical analysis was performed using SPSS version 21 (IBM, Armonk, New York). Creatine Kinase was analyzed between pre-exercise and 48 h post-exercise using a dependent t-test. Pearson's r correlations were used to determine association between markers of fitness and creatine kinase. A probability of type I error of less than 5% was considered significant ($p < 0.05$).

RESULTS

Fifteen male participants completed the testing protocol associated with this study. Descriptive and fitness data for the maximum treadmill test, hydrostatic weighing, and the military physical fitness test are presented in Table 2.

Correlations of CK with fitness are shown in Table 2. There was a significant correlation between absolute $VO_{2\ peak}$ ($L \cdot min^{-1}$) and CK 48 h post-exercise ($p = 0.027$). There were no other correlations of fitness and creatine kinase levels at 48 h post-exercise ($p > 0.05$; Table 2). There were no correlations of fitness and pre-post CK response following exercise ($p > 0.05$; Table 2).

Mean CK increased 62% ± 52% from pre-exercise to 48 h post exercise ($p = 0.008$; Figure 1), but did not reach criterion values associated with rhabdomyolysis.

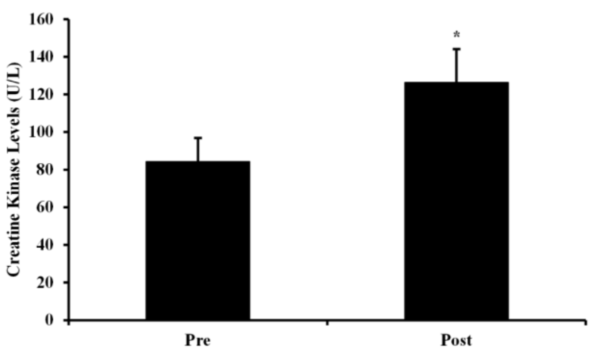

Figure 1. CK levels pre-exercise and 48 hours post-exercise. Data are mean ± SD,* $p < 0.05$.

DISCUSSION

The primary aim of the study was to identify the magnitude of muscle damage associated with a single bout of high intensity anaerobic training by examining serum CK levels pre- and post-exercise, with the intention of determining the risk of rhabdomyolysis. The present study demonstrates the well-documented rise in CK levels following a bout of high intensity exercise. The rise in CK did not reach the lower limits indicative of rhabdomyolysis, supporting the notion that a single bout of high intensity anaerobic training may not produce the damage necessary to cause rhabdomyolysis. The secondary aim of this study was to determine the relationship of CK response to markers of fitness. There were no meaningful relationships between CK response and fitness from the selected fitness markers (Table 1) in the current participants, all of whom were involved in exercise training but had varied levels of physical fitness.

CK is used as a marker of skeletal muscle microtrauma, because it mirrors myoglobin release into circulation (4, 7, 17). Exercise induced metabolic factors including lowered pH, insufficient mitochondrial respiration, and free radical production may initiate proteolytic activity, resulting in increased cell permeability and allowing cellular contents to enter circulation (4). Therefore, increased cell permeability explains the rise in serum CK levels. The normal response to exercise is an increase in blood CK levels, which can indicate muscle damage. Muscle soreness and swelling are also associated with muscle damage and rhabdomyolysis (7, 13, 22). While muscle soreness and swelling were not directly measured in the current study, many participants reported soreness in the days following the high intensity exercise session. It should be noted that subjects did not report discolored urine and symptoms of muscle soreness are often present in individuals without rhabdomyolysis (13). There are no clear standards of CK levels specifically indicating rhabdomyolysis (6, 8, 20). However, it has been reported that CK levels indicative of rhabdomyolysis are 881-1479 U · L^{-1} (20), with CK levels in some cases of rhabdomyolysis exceeding 2000 U · L^{-1} (22). The highest CK level observed in the present study was 315 U · L^{-1}, well below levels indicative of rhabdomyolysis.

All participants in the current study exercised on a regular basis, and individuals who participate in strenuous exercise on a regular basis have elevated resting CK values (6, 8). The constant elevation in resting CK levels make reference intervals difficult to determine. Normal resting CK levels are variable but can range from 35 – 175 U · L^{-1} (4), the current study observed resting CK levels at 84.2 ± 48.9 U · L^{-1}. The resting levels observed would support that the participants did exercise on a regular basis. The current study used a plyometric based exercise protocol with limited amounts of rest. Plyometric exercises induce eccentric overload of the muscle tissue and have been shown to cause severe muscle damage, which may increase the risk of rhabdomyolysis (21). Despite the risk for severe muscle damage, plyometric exercise programs have been recommended for the athletic population to elicit strength gains and protect against muscle damage (3, 24). Following the exercise protocol used in this study, CK levels did not reach levels indicative of rhabdomyolysis, supporting the safety of plyometric based programs in individuals who regularly engage in exercise training.

The risk of rhabdomyolysis may be different following prolonged high intensity aerobic exercise. Events such as marathons can result in rhabdomyolysis, and CK levels can reach 20,000 U · L^{-1} with myoglobinuria present (4, 7, 20, 26). Professional cyclists participating in the 21-day Giro d'Italia road race demonstrated CK levels increasing from start (188.3 ± 85.1 U · L^{-1}) to finish (356.7 ± 212.1 U · L^{-1}). CK did not reach levels indicative of rhabdomyolysis, and renal function was not impaired during this extreme cycling event (8). After examining the CK levels reported following different types of exercise, along with the results of this study, it can be observed that CK levels vary greatly, which support the discrepancies between reference levels and makes diagnosis of rhabdomyolysis using CK difficult.

Previous research has demonstrated that body mass and lean body mass is correlated with CK levels (6, 30), however, the current study did not support this correlation despite the body weight dependent measure of VO2peak (L · min^{-1}) having a positive correlation with CK levels. No correlation was found in any other measured indicator of fitness. The current study examined correlations between fitness markers with the change in CK post exercise (CK response). The current study found no correlations between fitness markers and CK response following exercise. Individuals with a history of no exercise for at least 6 months, have a greater increase in CK levels than compared to trained individuals following exercise (17). Recommendations indicate that sedentary individuals should exercise at low to moderate intensities to avoid a dramatic increase of serum CK (19). Studies investigating CK levels of sedentary individuals following 20 minutes of treadmill running at 40% of VO_2 max and 80% of VO_2 max found CK levels of 101.6 ± 43.7 U • L^{-1} and 216.4 ± 85.6 U • L^{-1}, respectively, suggesting a relationship between CK and intensity (19). The current study's findings are in agreement with these results, in that CK levels increased following exercise but did not reach levels of rhabdomyolysis. The post-exercise CK levels (126.3 ± 68.8 U • L^{-1}) from the current study were very similar to the sedentary group exercising at 40% of VO_2 max (101.6 ± 43.7 U • L^{-1}) despite the history of regular exercise in the participants and the high intensity plyometric training used in the current protocol. Recommendations have been made for rest between exercise bouts to avoid a possible compounding effect of CK levels and to allow the body to clear the components associated with muscle damage (4, 6). It appears that CK levels between 300 to 600 U · L^{-1} does not impair renal function in highly trained cyclists, implying that repeated bouts of exercise do not put a trained individual at risk for rhabdomyolysis (8). The highest CK level observed in the current study was 315 U · L^{-1} which is well below 600 U · L^{-1} upper limit. Thus, CK values above 600 U · L^{-1} may be required before symptoms of rhabdomyolysis arise.

Limitations of the study include a small sample size that consisted of trained males between the ages of 20-35 years old. More research is needed to determine how an exercise protocol similar to the one used in this study would affect a group of sedentary individuals or highly trained athletes. This study demonstrates only the acute effects of a single bout of exercise and does not take into account the effect of frequency of the particular exercise. More research is needed to determine if frequency of this protocol would cause or trend towards levels of rhabdomyolysis. Myoglobin was not measured in this study which is another marker of rhabdomyolysis. However, CK has been shown to peak during the 48 h time whereas myoglobin measurements peak much sooner. There is also conflicting evidence as to the more accurate marker of rhabdomyolysis between CK and myoglobin (5, 18, 31).

In conclusion, an increase in serum CK levels occurred following high intensity anaerobic exercise, but did not reach levels supporting a diagnosis of rhabdomyolysis, suggesting that a single bout of high intensity training is safe for healthy individuals who exercise regularly. Additionally, no relationships were found between CK and fitness or anthropometric markers indicating that within the fitness range of the current study participants, fitness is not related to CK and thus risk for rhabdomyolysis. The physiological benefits of high intensity exercise likely outweigh any risk of rhabdomyolysis in a healthy population who exercise regularly. More research is needed in sedentary individuals with repeated bouts of high intensity exercise to determine safety for a sedentary population.

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