Creatine Kinase Response to Various Protocols of Resistance Exercise

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Reference Data

ABSTRACT
Little is known about the muscle enzyme response to resistance exercises with various protocols. This study evaluated serum creatine kinase (CK) activity in response to resistance exercise with different protocols. Twelve subjects performed exercises with accommodating resistance at different speeds, or accommodating, variable, and fixed resistances to failure. Venous blood samples were evaluated for serum CK preexercise, postexercise, and 24 hrs postexercise. Subjects also reported ratings of perceived soreness (RPS) 24 hrs postexercise. Results showed no significant difference in CK response, and conflicting results for RPS depending on the protocol. It is concluded that the exercises used in the current study were not sufficiently stressful or different enough from each other to elicit a significant CK response.

Key Words: isokinetic, muscle, perceived soreness

Introduction
Muscles are often sore after an initial bout of resistance exercise, or after exercises with high-force eccentric components. Cellular muscle fiber disruption is a popular hypothesis for the cause of this muscle soreness (14, 30). The presence of muscle enzymes in the blood are considered markers of muscle tissue damage. These enzymes would not ordinarily be present in the blood if not for a disruption in the integrity of the muscle cell membrane. One of the most commonly studied of these enzymes is creatine kinase (CK).

Resistance exercises may involve a variety of protocols including altering the amount of resistance, volume of work, form of resistance, or speed of the maneuver. The muscle enzyme activity from resistance exercises has been evaluated (4, 13, 19, 31), but many of these studies have evaluated the CK response only from eccentric exercises (3, 8, 20). Studies evaluating the CK response to concentric exercises, or exercises with other manipulations in the protocol, are limited.

The purpose of the present study was to evaluate the serum CK response to fatiguing resistance exercises with different protocols.

Methods

Subjects
Twelve healthy male college students with resistance exercise experience served as subjects. None were competitive lifters, and all were sedentary for at least 2 weeks prior to the study. Their descriptive characteristics (± SE) were as follows:

- Age 21.9 yrs ± 0.7
- Height 179.5 cm ± 1.6
- Body mass 83.8 kg ± 3.1
- Body fat 14.7% ± 1.3
- Lean mass 71.5 kg ± 2.8
- VO₂peak 38.7 ml·kg⁻¹·min⁻¹ ± 2.8

Body composition was estimated using skinfold measurements (16). Peak oxygen uptake was predicted by maximal cycle ergometry. Subjects were informed of the nature of the investigation and each provided informed written consent prior to the investigation.

Experimental Design
To begin the study, each subject performed a graded exercise test (GXT) on a cycle ergometer with a standard protocol (26). This GXT (a) served as a medical screening to ensure subject safety, (b) helped predict peak oxygen uptake, and (c) was used to compare the CK response and perceived soreness values of aerobic exercise to similar values from resistance exercises. The subjects then completed a maximal isokinetic pretest to assess their peak torque production. The torque data were used to calculate the amount of resistance required for the other forms of resistance.

After satisfactorily completing the GXT and the isokinetic pretest, the subjects were randomly divided into 2 subgroups in which each would perform 3 resistance exercises. During each of the 3 remaining resistance exercise days they performed 1 set of resistance exercises to failure. They were prompted to give maximal effort for each repetition until unable to continue.
Each testing session took place on 1 day and was separated by 1 week. The subjects were instructed to remain sedentary on the days between testing sessions.

**Exercise Protocols**

Subgroup 1. All of the exercises for Subgroup 1 (n = 6) were done on the Kin-Com® 125E+ isokinetic testing device (Chattecx Corp., Hixson, TN). The subjects performed a maximal number of concentric flexion and extension repetitions at the knee until unable to continue. Each performed maximally to failure at 50, 100, and 200° per sec to ensure muscle fatigue and soreness. The sequence of the speeds was balanced and was different for each subject. Subsequent statistical analysis demonstrated no order effect. Range of motion was limited from 90 to 0° of flexion (full extension).

Isokinetic resistance was chosen as the form of resistance in part because of the ease with which dual-concentric exercise could be provided; another reason was to control for speed. However, since isokinetic resistance provides accommodating resistance, the slower isokinetic speeds that allow the muscle to produce more force will result in relatively greater amounts of resistance from the apparatus. Since it is possible to continue generating repetitions by decreasing force production, the torque output was monitored and the subjects were encouraged to put forth maximal effort with each repetition. We are confident that they did maintain force production until failure, and that torque did not decrease during the last few repetitions of the set.

Subgroup 2. With Subgroup 2 (n = 6) we manipulated the form of resistance rather than the speed of the exercise. The exercises involved concentric leg extension and eccentric leg flexion at the knee. They were done with accommodating resistance (Acc) on the Kin-Com® isokinetic testing device, with variable resistance (Var) on a David® leg extension machine (David International, Helsinki, Finland), and with fixed resistance (Fix) on a Universal® leg extension machine (Kiddle Inc., Cedar Rapids, IA). With each form of resistance the subjects performed as many repetitions as possible at a resistance calculated from their pretest. All exercises were done at the same speed of 60° per sec, and range of motion was again limited to an arc of 90°. The sequence of resistance exercises was balanced and was different for each subject. Subsequent statistical analysis demonstrated no order effect for these exercises. The subjects in this subgroup also put forth maximum effort until momentary muscular failure.

Both groups performed all exercises with only the leg that corresponded to hand dominance. To reduce the effects of any diurnal variations, testing was always conducted at the same time of day.

**Data Collection.** A trained phlebotomist obtained blood samples by venipuncture from a superficial vein at the cubital fossa. Samples (10 ml) were drawn immediately preexercise, immediately postexercise, and 24 hrs postexercise. Each Vacutainer™ tube was labeled with a code number known only to the principal investigator. Samples were allowed to coagulate at room temperature and were then placed on ice for storage and transportation. Samples were centrifuged at 2,000 rpm for 10 min in a refrigerated centrifuge at 5°C (International Equipment Co., Needham Heights, MA). Serum supernatant was removed from the test tube by pipette and placed into 2.5-ml cryovials for storage. Labeled cryovials were stored at −80°C for not more than 1 month before being analyzed.

All serum samples were allowed to thaw to room temperature and were analyzed at the same time. Creatine kinase reagent was reconstituted and warmed to room temperature before a standard assay was performed according to the procedure outlined by Szasz et al. (29). Change in absorbence per minute (ΔA per min) was determined by spectrophotometry (Gilford, Medfield, MA) at a wavelength of 340 nm. Creatine kinase values (CK U/L) are reported at a standard temperature of 30°C. Subjects also reported a subjective rating of perceived muscle soreness (RPS) 24 hrs postexercise, from a 15-point interval perception scale (an original Borg scale modified for soreness) (2).

**Statistical Treatment.** Individual analyses of variance with repeated measures were used to analyze the data for each variable (CK and RPS). Tukey post hoc tests were used to determine differences between significant main effects. Statistical significance was set at an alpha level of p ≤ 0.05. Data are presented as group means (±SE).

**Results**

Subgroup 1

For Subgroup 1, the analyses of variance for the CK and RPS data showed no significant difference between any of the treatment conditions (speeds). There were also no significant differences for RPS data over time. However, there was a significant main effect for CK data over time. Post hoc analysis revealed a significant difference for the 200° per sec variable. The post-24-hr value was significantly different from both of the other times. Mean values for CK are presented in Table 1 and Figure 1. Mean values for RPS were 8.7 (1.4), 8.0 (1.1), 7.8 (1.0), and 7.0 (0.7) for GXT, 50, 100, and 200° per sec, respectively. The values for RPS are shown in Figure 2.

Subgroup 2

In Subgroup 2, the analysis of variance for CK demonstrated no significant difference between any of the exercises for group or time. Mean values for CK are shown in Table 1 and Figure 3. However, a significant main effect for RPS was present for Subgroup 2, with Acc being significantly different from the other 2 other conditions. Soreness from the GXT was also significantly different.
Table 1
Mean Serum Creatine Kinase (U/l)
by Subgroup and Condition

<table>
<thead>
<tr>
<th>Condition</th>
<th>Pre</th>
<th>Post</th>
<th>24 Hrs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$M$</td>
<td>$SE$</td>
<td>$M$</td>
</tr>
<tr>
<td>Subgroup 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GXT</td>
<td>75.4</td>
<td>12.3</td>
<td>58.1</td>
</tr>
<tr>
<td>50°/s per sec</td>
<td>79.4</td>
<td>13.7</td>
<td>73.3</td>
</tr>
<tr>
<td>100°/s per sec</td>
<td>85.5</td>
<td>23.6</td>
<td>91.6</td>
</tr>
<tr>
<td>200°/s per sec</td>
<td>73.3</td>
<td>16.7</td>
<td>73.3</td>
</tr>
<tr>
<td>Subgroup 2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GXT</td>
<td>203.7</td>
<td>86.0</td>
<td>197.5</td>
</tr>
<tr>
<td>ACC</td>
<td>82.5</td>
<td>16.5</td>
<td>81.5</td>
</tr>
<tr>
<td>VAR</td>
<td>179.2</td>
<td>71.0</td>
<td>179.2</td>
</tr>
<tr>
<td>FIX</td>
<td>89.6</td>
<td>20.9</td>
<td>89.6</td>
</tr>
</tbody>
</table>

![Figure 1](image1.png)
Figure 1. Mean serum creatine kinase (U/l) for Subgroup 1.

![Figure 2](image2.png)
Figure 2. Mean subjective ratings of perceived soreness for Subgroup 1.

![Figure 3](image3.png)
Figure 3. Mean serum creatine kinase (U/l) for Subgroup 2.

![Figure 4](image4.png)
Figure 4. Mean subjective ratings of perceived soreness for Subgroup 2.

from Fix and VAR. Mean values for RPS were 9.3 (1.1), 9.2 (0.7), 6.8 (0.5), and 6.7 (0.5) for GXT, ACC, VAR, and Fix, respectively. The RPS values for Subgroup 2 are shown in Figure 4.

Discussion

Although creatine kinase is a well accepted marker of muscle tissue disruption, the association between the severity of damage and the magnitude of CK response remains unclear (3). The response times between muscle soreness and the physiological markers of muscle disruption (such as CK) also remain unclear (5, 30). Creatine kinase has been reported to peak anywhere from immediately postexercise (28) to 14 days postexercise (15). However, these discrepancies may be due to the mode of exercise employed.

Studies on CK response to resistance exercises have reported less of a response with isometric exercise than with other forms of resistance (4, 13, 31). Much of the
research on CK response to dynamic resistance exercise has evaluated concentric versus eccentric contractions (3, 8, 20). Eccentric resistance exercises have been shown to produce a greater response in enzyme activity than their concentric counterparts. Nute and coworkers reported the CK response to high and low intensity eccentric resistance exercises, and to high and low intensity concentric exercises (25). No significant differences were seen in CK or muscle soreness between intensity levels for either concentric or eccentric exercises. However, both peak muscle soreness and CK values reported at 24 hrs postexercise were significantly less with the concentric than with the eccentric exercises (25).

Kraemer and colleagues reported CK response data from 6 heavy-resistance exercise protocols. The exercises were divided into 2 subgroups (strength vs. hypertrophy protocols), each containing 3 variations. Creatine kinase peaked at 24 hrs for all exercises in both groups. However, what was most surprising was that at 24 hrs postexercise the 10-RM protocol (which had lighter resistance) produced a significantly greater CK response than any other protocol, including those with heavier eccentric loads. Kraemer et al. hypothesized that CK response may be related to cortisol response, which was higher in the 10-RM 1-min rest protocol, and may exert a catabolic effect on muscle tissue remodeling (19).

In both subgroups of the present study some subjects showed only slight increases in CK from preexercise values while others showed no change in CK. The latter, who were classified as nonresponders, showed no change in CK regardless of the treatment imposed. It is possible that the concentric-only activity the subjects in Subgroup 1 performed did not impose enough muscle damage to create a significant CK response. Franklin and colleagues found increased CK levels as a result of concentric-only isokinetic exercise (10); their subjects achieved peak CK levels at 12 hrs postexercise, with peak values being 31% higher than preexercise values.

Other investigators have attributed muscle soreness, particularly delayed onset muscle soreness, to the eccentric portion of the exercise (11, 12). Most theories for this soreness have included inflammation, myofibrillar disruption, and connective tissue damage hypotheses (27). In addition to the theories of mechanical strain (Z-band streaming and sarcomere disruption) and spasm, damage from free radicals is emerging as a popular hypothesis.

In the present study, changes in soreness were reported with the aerobic exercise despite no measurable changes in CK. Spiteri and colleagues have also reported no changes in CK at 1, 2, 4, 6, and 24 hrs after a maximal cycle ergometer test (28). Yet Manfredi and co-workers reported significantly elevated CK levels in older men up to 10 days after cycling (21). In Subgroup 2 of the present study, where the resistance exercises had an eccentric phase, we were still unable to observe any significant differences in CK. We feel that the exercises did not differ enough from each other to elicit a significant CK response.

It is possible that the successive exercise effect on the CK response was underestimated. Soreness and CK are both known to become attenuated with successive bouts of exercise (6, 7, 9, 15, 18, 22, 24). Triffletti et al. (31) suggest that this adaptation in response to isometric exercise lasts 2 to 3 weeks, whereas it is thought to last longer with more eccentric exercises. Since the eccentric activity in the current study was limited, we assumed that this successive exercise effect would be short-lived. We are unaware of any research describing the duration of the exercise effect for the types of exercises in the current study.

It is also possible that CK may not be a sensitive enough indicator for the relatively minor disruption that is thought to occur from these mostly noneccentric exercises. Also, the subjects in this study may not have reached peak CK levels at 24 hrs postexercise. Although 24 hrs is generally the time point for analyzing CK levels, there is much discrepancy regarding time to peak response, and the time course of the CK response to concentric-only resistance exercise has not been established. Byrnes et al. (3) reported that peak CK responses occurred at 25 hrs postexercise for concentric/eccentric exercises, compared to 10 hrs postexercise for the same exercises with only a concentric phase.

To account for this unknown information, an unpublished pilot study was conducted prior to the present study to determine the time to peak CK response for velocity-specific ACC, VAR, and Fix resistance exercises (17). Serial venous CK samples were obtained every 12 hrs for 72 hrs. Five of the 6 subjects peaked at 24 hrs; the 6th subject demonstrated a biphasic response, with the first peak occurring at 24 hrs, followed by a higher peak occurring at 48 hrs (17).

A biphasic response was first reported in rats (1) and was later reported in humans by Newham and colleagues (23). Newham et al. reported peak CK at 24 hrs, followed by the second peak of the biphasic response between 4 to 7 days postexercise. If a biphasic response occurred in the subjects of the current study, with the second peak occurring after 24 hrs postexercise, it would have gone undetected. If such a response occurred after 72 hrs postexercise, it would also have been undetected in the pilot study. Another possible explanation for the lack of a significant CK response is the relatively small sample size. But given the invasive nature of this study, a larger sample size was not feasible.

**Summary**

Muscle soreness may be experienced after certain resistance exercises and is thought to result from muscle fiber disruption or connective tissue damage. Most stud-
ies that have evaluated these factors have used only eccentric exercises. However, other exercises and forms of resistance are frequently used, particularly in clinical situations. The results from Subgroup 1 suggest there are no differences in RPS or CK, due to the speed of the isokinetic exercise. However, the results from Subgroup 2 suggest that while RPS was affected by the different exercises, the serum enzyme response was not.

Practical Applications

Elevations in CK occur as a result of certain exercises, especially eccentric resistance exercises. It is known that different exercises will produce different magnitudes of enzyme response. Likewise, it is known that the time to peak response also varies with the mode of exercise. The data from the present study suggest that muscle fiber disruption, as indicated by CK, may not be due to a particular form of resistance or isokinetic speed, although soreness may. This information may be useful when prescribing resistance exercises, especially during injury rehabilitation or in other clinical settings.

References


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