Major increase in creatine kinase after intensive exercise

BACKGROUND

Exercise-induced rhabdomyolysis is an increasingly frequent cause of hospitalisation and is much debated in the media. The real incidence of the condition is unknown. We wanted to investigate changes in creatine kinase (CK) levels in healthy students following intensive exercise and to look for a correlation between CK, pain and previous exercise history.
METHOD AND MATERIAL

Twenty-four healthy students performed a single intensive workout and acted as their own controls with testing before and after the exercise session.

RESULTS

All participants displayed an increase in CK levels after the workout, 58 % to above 5 000 IU/l. CK rose from a median of 104 IU/l (72–212) to a median of 6 071 IU/l (2 815–12 275) on day 4, p < 0.001. A negative Spearman’s rank correlation was observed between the frequency of strength training prior to the experiment and the CK increase, rho = -0.477 (p = 0.021).

INTERPRETATION

A major increase in CK levels is a normal phenomenon after intensive exercise, and the amount of the increase is related to previous exercise history. Further studies should evaluate whether patients with exercise-induced rhabdomyolysis should receive the same treatment as those with rhabdomyolysis caused by other mechanisms.
training were then performed on many different muscle groups with high intensity and short breaks (20 seconds of activity, 10 seconds rest). Each exercise was repeated six times before a one-minute break and change of exercise, with eight exercises in total. Finally, a competition was held to stand against a wall for as long as possible with 90-degree hip and knee flexion (‘wall sit’). The participants were asked to drink plenty of fluids after the workout.

The day before and four days after the workout, blood and urine samples were taken to obtain baseline values and maximum values (9). Sampling and analysis of CK and creatinine in blood, as well as urine dipstick testing, were performed by the Department of Medical Biochemistry, St. Olavs Hospital, Trondheim University Hospital. Urine dipsticks positive for blood were used as an indirect index of myoglobinuria.

Before the workout, the participants completed a questionnaire on how often they engaged in strength training and on their regular medication use. On day four, the participants completed a questionnaire on muscle pain after the workout.

Statistical analyses were performed in SPSS Statistics version 25 (IBM SPSS Inc., Chicago, IL). A p-value < 0.05 was considered significant. Normally distributed data are presented as mean (standard deviation), non-normally distributed data as median (interquartile range). A student’s t-test for repeated measures was used for comparison of creatinine before and after exercise, and a Wilcoxon signed rank test for comparison of CK levels before and after exercise. Spearman’s rank correlation was used to analyse the association between previous exercise history, pain and CK increase.

All participants with CK levels > 5 000 IU/l after exercise were offered a follow-up measurement. Eight of 14 completed the follow-up, all of whom showed a decrease in CK levels.

Results

The median age of the participants was 24 (24–27) years. The pre-exercise blood sample haemolysed for one of the participants; baseline CK level could thus not be determined and this participant was excluded from analyses that include CK change. All participants showed an increase in CK levels, from a median of 104 (72–212) IU/l on the day before exercise to a median of 6 071 (2 815–12 275) IU/l on day four, p < 0.001 (Figure 1). Fourteen of 24 participants had CK levels > 5 000 IU/l. Four participants had urine dipsticks positive for blood on day 4. These four individuals had CK levels of 2 815, 5 248, 13 535 and 35 440 IU/l, respectively. Three of them thus had rhabdomyolysis according to the definition of muscle pain, CK > 5 000 and urine dipsticks positive for blood.

![Figure 1](image.png)

**Figure 1** CK levels measured before exercise and on day 4 after exercise, in 24 healthy subjects. The median is represented by the line in the middle of the filled box. The box represents the 25–75 % interquartile range. The whiskers show the range of the data set; the circle shows an outlier.

Strength training history, as measured by the number of strength training sessions per
week, showed a negative Spearman’s rank correlation with the CK increase, \( \rho = -0.477 \) (\( p = 0.021 \)). (Figure 2).

![Figure 2](image)

**Figure 2** Scatter plot showing CK levels in 24 healthy subjects stratified according to number of reported strength training sessions per week. Significant negative Spearman’s rank correlation, \( \rho = -0.347 \) (\( p = 0.097 \)), with a smaller CK increase in participants who engage more frequently in strength training.

Creatinine levels were normally distributed and decreased from a mean of 69.4 (65.5–73.4) µmol/l the day before exercise to 67.0 (62.6–71.3) µmol/l on day four, \( p = 0.013 \). None of the three participants with rhabdomyolysis showed an increase in creatinine levels. We found no correlation between degree of self-reported muscle pain and the CK increase. Ten women were using hormonal contraceptives; only one participant used other regular medications.

**Discussion**

This experiment shows that intensive, varied exercise leads to a marked increase in CK levels, as previously demonstrated in studies using standardised exercise loads (12, 15). A marked increase in CK levels must thus be considered a normal phenomenon after an intensive workout. Moreover, we have shown that previous exercise history correlates negatively with the increase in CK levels. Since CK levels increased in all participants, there is reason to believe that most people with exercise-induced rhabdomyolysis are neither diagnosed nor treated in hospital.

Several risk factors for increased CK levels after exercise have been proposed in the literature: dehydration, overheating, high humidity, medication use, eccentric exercise and limited exercise history (1, 3, 6). It is possible that variables such as sex, age, genetics and ethnicity may also affect the CK increase, but our dataset is too small to allow subgroup analyses. Our participants were encouraged to drink plenty of fluids after the workout, and this most likely explains the statistically, but not clinically, significant fall in creatinine levels.

One weakness of the study is that participants were not restricted from exercising between the study workout and the sampling on day four. Exercise during this period may have led to a further CK increase in some participants. However, the finding of a significant CK increase remains unchanged, even though some participants may have engaged in additional exercise.

Larger clinical trials of patients hospitalised with exercise-induced rhabdomyolysis and treated with various hydration protocols are required to assess the risk of renal damage and determine the best treatment for this condition. We believe there is a need to reevaluate whether euvolaemic and healthy patients with exercise-induced rhabdomyolysis should receive the same treatment as patients with rhabdomyolysis attributable to other factors.
MAIN MESSAGE
An increase in CK levels is a normal phenomenon after strenuous exercise sessions offered by standard fitness centres
The amount of CK increase correlates with previous exercise history

REFERENCES: