Effect of exercise on serum creatine kinase in carriers of Duchenne muscular dystrophy

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SUMMARY In order to evaluate the effect of exercise on serum creatine kinase levels, blood samples were obtained from 17 normal females and 12 Duchenne muscular dystrophy carriers before and 9 hours after moderately strenuous exercise. The results revealed that after exercise serum creatine kinase levels may be better indicators of carrier status than resting levels. The mean serum creatine kinase levels before and after exercise, as well as the mean increases, were found to be significantly greater in Duchenne muscular dystrophy carriers than in normal control subjects.

Numerous studies have been concerned with the identification of carriers of Duchenne muscular dystrophy. Past investigators have focused on the rise in serum enzymes, abnormal muscle ultrastructure, myopathic changes of the electromyogram, derangement in muscle protein synthesis, and muscle weakness. Other studies reported aberrations in the electrocardiogram, red blood cell morphology, membrane protein peak II phosphorylation activity, and lymphocyte capping, in carriers of this X linked neuromuscular disorder. Unfortunately, many of these pathological findings are not observed in all carriers of Duchenne muscular dystrophy, some of the tests are cumbersome or invasive in nature, and other studies which have not been duplicated await confirmation.

At present, serum creatine kinase determination is the most widely used method for carrier detection though it has been proposed that pyruvate kinase may be a more sensitive indicator. Since there is considerable variation in serum creatine kinase levels among known carriers, several enzyme determinations are usually made in the attempt to establish carrier status. During the days before testing, undue motor activity is usually avoided because it has been shown that moderately heavy exercise will result in increased serum creatine kinase levels.

This study was directed towards the evaluation of the hypothesis that the serum creatine kinase concentration several hours after a measured exercise would constitute a more effective carrier detection method.

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Subjects and methods

Seventeen healthy female volunteers, between the ages of 20 and 41, who did not have clinical muscle weakness, participated in this study as controls. Obligate, probable, and possible carriers known to us through contacts with Duchenne muscular dystrophy patients followed at the Child Development Center were invited to take part in this investigation. Both control and study populations were asked to refrain from unusual exercise for 2 days before testing. The study design, rationale, and test procedure were explained and the subjects gave written informed consent.

On the morning of the test, the participants’ weight was recorded, a venous blood sample was drawn, and the subjects were asked to pedal a Schwinn EX-1 Bicycle Ergometer to produce 5000 to 6000 kilopond-metres of work within a 10 to 12 minute period. The exercise load setting, which was 900 kilopond-metres/minute at the beginning was reduced to 600 and later to 450 kilopond-metres/minute when the subjects became exhausted at the initial higher exercise levels. After completion of the exercise, the participants were permitted to go about their usual daily activities with restriction only of undue exercise. Based on the evaluation of previous reports, we obtained a second venous blood sample, approximately 9 hours after completion of the exercise.

All blood specimens were centrifuged and the serum was frozen. Serum creatine kinase determinations were carried out within 48 hours at 37°C, according to the method of Szasz et al.21 22
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Results

Table 1 presents the age, weight, total exercise load, and serum creatine kinase activity immediately before and 9 hours after exercise of 17 normal appearing control females. Equivalent data for female relatives of patients with Duchenne muscular dystrophy are shown in Table 2. In genetic terms, these include definite, probable, and possible carriers. However, based on pedigree evaluations and previous significantly increased serum creatine kinase levels, it is assumed that the subjects listed in Table 2 are Duchenne muscular dystrophy carriers. Table 3 contrasts the mean serum creatine kinase levels before and 9 hours after exercise as well as the mean increases of serum creatine kinase between the controls and carriers. These data indicate that the after exercise values may be more discriminating than the before exercise levels and the net change between the first and second blood samples.

A graphic presentation of a discriminant function analysis is depicted in the figure. A log log transformation was used because of the extreme skewness of the distributions. The X near the centre of the graph indicates a mid-point between the means of the two groups. The classification boundary is shown by the broken line, which is the boundary that would be expected to produce the minimum misclassification. Since the calculated boundary is more horizontal than vertical, it implies that the after exercise value is more important than the before exercise value in making the discrimination.

Table 1 shows the age, weight, total exercise load, and serum creatine kinase (CK) determinations in normal appearing control subjects.

Table 2 shows the age, weight, total exercise load, and serum creatine kinase (CK) determinations in female relatives of patients with Duchenne muscular dystrophy.

Table 3 shows the comparison between serum creatine kinase (CK) levels of controls and carriers.

*According to pedigree evaluation subjects 7 to 12 are possible carriers of Duchenne muscular dystrophy. Because of their significantly raised serum kinase levels they are considered to be definite carriers in this study.
Discussion

In this study we investigated the possibility of improving the discriminating ability of serum creatine kinase by taking blood samples before and 9 hours after a measured exercise load. As previous reports indicate, the amount of exercise is an important consideration. Emery reported preliminary results similar to ours, stressing the need for further study of the effects of standard exercise. Thomson measured creatine kinase increases after a more leisurely walk than Emery’s subjects. He was not able to demonstrate a significant exercise effect. Hughes et al. found no significant difference in bicycle exercise effects in carriers compared with controls. However, these subjects exercised somewhat less than ours, and the creatine kinase determinations were not made between 4 and 20 hours after exercise when the maximum exercise effects would be expected. In the study of Nuttal and Jones, normal untrained female subjects displayed increased creatine kinase levels 8 to 16 hours after strenuous weight lifting. The exercise load given to the subjects in our study was probably between the latter two in difficulty. Although two of our control subjects had large increases in their creatine kinase after exercise, the results did not exceed the normal range (15 to 135 IU) in our laboratory. The exercise load of our subjects seems to be sufficient to improve the discriminating ability of creatine kinase levels. While these preliminary data provide evidence that after exercise serum creatine kinase determinations are of greater value in identifying carriers of Duchenne muscular dystrophy than randomly obtained levels, we propose a large scale study to investigate further and substantiate our result.

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