Short communication

Serum creatine kinase level is a poor predictor of muscle function after injury

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Serum creatine kinase and dorsiflexion torque levels were measured in New Zealand White rabbits 1, 2, 7, 14, or 28 days after a single bout of eccentric exercise (n=26). No significant correlation was observed between creatine kinase activity and torque across time periods (P>0.15) and the regression relationship described only about 8% of the experimental variability. These data demonstrate that there exists a poor correlation between serum creatine kinase levels and skeletal muscle function after eccentric exercise.

Studies of eccentric contraction-induced muscle injury employ a wide variety of both human and animal models. A parameter that is often used to estimate the degree of muscle injury after exercise is serum creatine kinase level (Byrnes, Clarkson, White, Hseih, Frykman, Maughan, 1985; Evans et al., 1985). Based on measurements of this parameter, investigators have shown that creatine kinase levels are significantly elevated after eccentric exercise (Byrnes et al., 1985; Evans et al., 1985), the perception of soreness after eccentric exercise is out of phase with serum creatine kinase levels (Newham, 1988), and that a protective effect of previous training can be demonstrated by comparing creatine kinase levels to untrained control values (Evans et al., 1985; Newham, Jones, Clarkson, 1987). It is often assumed that the level of creatine kinase activity is somehow related to the magnitude of muscle injury, although this idea has not been explicitly tested (Kyrolainen, Takala, Komi, 1998; McHugh, Connolly, Eston, Kremenic, Nicholas, Gleim, 1999).

We measured serum creatine kinase levels in New Zealand White rabbits subjected to noninvasive eccentric exercise of the ankle dorsiflexors and measured serum creatine kinase and dorsiflexion torque values 1, 2, 7, 14, or 28 days after a single bout of eccentric exercise (Lieber, Schmitz, Mishra, Fridén, 1994). Twenty-six animals were subjected to eccentric exercise of the dorsiflexors by rotating the ankle from 100° to 70° of dorsiflexion over a 400 ms time period while directly stimulating the muscles via the peroneal nerve. This pattern was repeated every 2 s for 30 min, resulting in 900 eccentric contractions of the dorsiflexors. At the end of a predetermined time period maximum dorsiflexion torque was measured directly by activating the peroneal nerve transectaneously and measuring dorsiflexion torque with a dual mode ergometer (Aurora Scientific, Inc., Model 6400, Aurora, Ontario). In addition, a blood sample was collected in an inert gel serum separator microtainer and immediately centrifuged for measurement of creatine kinase activity using a Kodak Ectocam system DT60 (Eastman Kodak, Rochester, New York).

These data revealed that serum creatine kinase levels provided poor predictive power in estimating skeletal muscle function (Fig. 1). No significant correlation was observed between creatine kinase activity and torque (P>0.15). The regression relationship calculated (Torque (Nm)=0.000184 × CK (IU/L) + 0.643 Nm) described only about 8% of the experimental variability (i.e., r²=0.075).

These data demonstrate that there exists a poor correlation between serum creatine kinase levels and skeletal muscle function after eccentric exercise. It may not be surprising that this relationship is relatively poor since a muscle fiber’s permeability to intramuscular enzymes may or may not be correlated with cellular contractile function. For example, we previously demonstrated that numerous muscle fibers subjected to eccentric exercise that retained their ability to exclude plasma fibronectin demonstrated significant structural abnormalities such as loss of intracellular desmin, myofibrillar disruption, and Z-disk
Serum CK level and muscle injury

Fig. 1. Relationship between serum creatine kinase (CK) and maximum dorsiflexion torque. Data are presented for torque measured 1, 2, 7, or 14/28 days after a single eccentric exercise bout. Note the approx. 6-fold variation in serum CK levels between measurements obtained 1 or 7 days after exercise (filled arrows) with a corresponding approx. 10% difference in maximum tetanic tension (open arrows).

Disintegration. These fibers would be considered injured but would not necessarily contribute to the total pool of serum creatine kinase. Thus, while serum creatine kinase levels may provide a gross indication of skeletal muscle injury, differences between serum creatine kinase levels do not necessarily provide any relative indicator of muscle injury magnitude. This is seen clearly in our data when creatine kinase levels and dorsiflexion torque measured 1 day after eccentric exercise are compared to those measured 7 days after exercise (Fig. 1). For the 1 day subjects, CK levels (3846±276 IU/L) were over 6 times those obtained for the 7 day subjects (618±162 IU/L; Fig. 1, filled arrows) and yet dorsiflexion torque for the 1 day subjects (0.584±0.024 Nm) was only 10% less than torque measured on the 7 day subjects (0.646±0.025 Nm; Fig. 1, open arrows). For these data, a significant difference between CK activities (P<0.001) was accompanied by no significant difference between torque values (P>0.2). We thus encourage investigators to use caution when attempting to infer muscle functional properties based on serum enzyme levels.

Our results using the rabbit model may not reflect the results that would be obtained using a human model. This is because the rabbit dorsiflexors in this study were maximally activated both during eccentric exercise and subsequent testing. There is evidence that, during human eccentric exercise, muscle activation levels are submaximal (Wестинг, Сегер, Thorstensson, 1990) and, during testing, joint torque levels may be confounded by the perception of pain (Newham, Mills, Quigley, Edwards, 1983). Thus, it is difficult to make a detailed comparison between the results of this study and those obtained from human studies when the neural activation patterns are so qualitatively different.

Perspective

The results from this study provide strong evidence against using serum creatine kinase levels to make statements about the magnitude of muscle injury. We would suggest that elevated creatine kinase levels provide evidence of muscle injury in a “binary” fashion – injured or not injured. However, the absolute values of the serum creatine kinase levels do not provide further information regarding the extent of the injury.

Key words: eccentric contraction; muscle damage; creatine kinase; muscle function.

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References


