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EC CARDIOLOGY
Case Report

Role of CPK-MM in Plantar Fasciitis: Cause and Prognosis

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Received: March 09, 2020; **Published:** March 24, 2020

Abstract

Plantar fasciitis starts with gradual onset of pain at the bottom of heel or the arch of foot and it feels like bruise which is of significant concern. The patient usually experiences severe pain after prolonged walking which generally decreases in intensity after rest. It may go away on its own or it may take six weeks to 12 months. If it persists for longer time, it requires further extensive evaluation. It is important to restrict stepping especially on uneven surfaces until a full history and examination has been completed along with laboratory evaluation. There is the need to identify non-specific pathology that would guide and confirm the need for further diagnostic testing and evaluation. In this report a case of acute plantar fasciitis is discussed where the levels of CPK-MM are directly correlated with the onset and severity of the disease.

Keywords: *Creatine Phosphate; Muscle; Pain; Symptom; Fasciitis*

Introduction

Creatine phosphokinase (CPK) is an enzyme which catalyses the reversible phosphorylation of creatine by adenosine triphosphate (ATP). At neutral pH, creatine phosphate has a much higher phosphorylating potential than does ATP. However, during storage, CPK is rapidly inactivated by the oxidation of the sulfhydryl groups at the active site of enzyme [1].

CPK activity is greatest in muscles and heart tissue. Brain, GIT and urinary bladder contain less activity. Liver and RBCs are devoid of CPK activity. CPK is a dimer, composed of two subunits, each with a molecular weight of 40,000. These subunits are B and M, which are the products of the loci on chromosomes 14 and 19. Three different pairs of subunits exists: BB (CPK-1), MB (CPK-2) and MM (CPK-3). All these isoenzymes are found in the cytosol and are associated with myofibrillar structures [2].

Both M and B subunits have a C-terminal lysine residue. Only M-subunit can be hydrolysed by action of carboxypeptidases. Carboxy-peptidase-B or N sequentially hydrolyses the lysine residues from CPK-MM to produce two CPK-MM isoforms - CPK-MM_2 (one lysine residue removed) and CPK-MM_1 (both lysine residues removed). Loss of lysine residue (positively charged) produces a more negatively charged CPK-MB molecule with greater anodic mobility. There also exists a fourth isoform CPK-Mt, which differs immunologically and in electrophoretic mobility from other isoforms [2].

The appearance of CPK in blood has been generally considered to be an indirect marker of muscle damage, particularly for diagnosis of medical conditions such as myocardial infarction, muscular dystrophy and cerebral diseases. However, there is controversy in the literature concerning its validity in reflecting muscle damage as a consequence of level and intensity of physical exercise. Nonmodifiable factors, for example, ethnicity, age, and gender, can also affect enzyme tissue activity and subsequent CPK serum levels. The extent of effect suggests that acceptable upper limits of normal CPK levels may need to be reset to recognise the impact of these factors. There is a need for standardisation of protocols and stronger guidelines which would facilitate greater scientific integrity. The purpose of this paper is to

examine current evidence and opinion relating to the release of CPK from skeletal muscle in response to physical activity and to examine if elevated concentrations are a health concern [3].

Case Presentation

A 42 year old male presented to the Orthopaedics Department with pain in right heel. The pain was moderate in intensity, on and off for three months. The patient gave history of severe pain with first few steps early morning after awakening. On examination, tenderness was present. Routine biochemical tests were done in the Department of Biochemistry. All values were within normal range except that for vitamin D which was found to be below normal range (Table 1).

Random Blood sugar - 107 mg/dL	S. Chloride - 103.50 mEq/L
Blood urea nitrogen - 13.7 mg/dL	S. Bicarbonate - 24 mmol/L
S. Creatinine - 0.92 mg/dL	Total protein - 6.90 g/dL
S. Uric acid - 4.10 mg/dL	S. Albumin - 4.84 g/dL
S. Calcium - 9.83 mg/dL	S. Globulin - 2.06 g/dL
S. Phosphorus - 3.80 mg/dL	Alkaline phosphatase - 64IU/L
S. Sodium - 136 mEq/L	Total cholesterol - 137 mg/dL
S. Potassium - 4.10 mEq/L	25 OH Vitamin D - 26.41 ng/mL

Table 1*: Levels of various biochemical parameters at the time of diagnosis.*

He was advised to take analgesics SOS and to do regular exercise. He followed the same treatment for 3 months but response rate was not good. After which he was advised to get his CPK-MM levels done. As facility for analysis of CPK-MM was not available in our department, hence, the patient got it done from a private lab. Levels of CPK-MM were found to be raised (Table 2). He was continued on same treatment with some diet modification and supplements. Food items with high sugar levels and fried foods were avoided. Along with dietary restrictions, capsules containing Co-enzyme Q10 and Omega 3 fatty acids were also given. At the time of diagnosis levels of CPK-MM were very high; 487 mg/dL. But with start of therapy, there was improvement in clinical condition as well as the levels of CPK-MM started decreasing (Table 2). During follow up after around 1.5 years (18 months) of diagnosis there was improvement in clinical condition and CPK-MM levels reached less than even half of initial value but did not reach within reference range.

Duration	Levels of CPK-MM
At the time of diagnosis	475 IU/L
After 6 months of diagnosis	283 IU/L
After 12 months of diagnosis	198 IU/L
After 18 months of diagnosis	187 IU/L

Table 2: *Levels of CPK-MM during the course of disease.*

Discussion

Now days, the diagnostic role of CPK-MM has been replaced, to a certain extent, by the muscle protein troponin. However, raised levels of serum CPK are still closely associated with cell damage, muscle cell disruption, or disease. These cellular disturbances can cause CPK to leak from cells into blood serum [4]. Measurement of serum CPK activity and determination of isoenzyme profiles is still an important indicator of the occurrence of muscle cell necrosis and tissue damage due to disease or trauma. There has been extensive discussion in the literature regarding the significance of raised levels of serum CK following physical exercise in relation to degrees of muscle cell dam-

age or disturbance [5]. While the reason for release of CPK-MB into the circulation is clear in cases such as MI, it is less clear why low- to moderate-intensity physical exercise should also result in release of CPK-MM into blood serum [6]. Myofibrillar CPK-MM is bound to the M-line of the sarcoplasmic reticulum of myofibrils and is also found in the space of the I-band sarcomeres providing support for muscle energy requirements. Thus, the enzyme is normally confined to the muscle cell so the question arises: do raised levels of CPK-MM following a period of exercise represent a degree of actual muscle damage and loss of muscle cell integrity, or is there some other molecular explanation that is not permanent cell damage, but a temporal disturbance or disruption to muscle processes [7,8]. This is true, not only for athletic populations but also for individuals who participate in strenuous exercise as part of their lifestyle. In this patient also, slightly higher levels even after treatment may be due to exercise which he was doing as a part of treatment.

CoQ10 is lipid-soluble benzoquinone with similar properties as that of vitamins. It works by having a direct regulatory role on succinyl and the nicotinamide adenine dinucleotide (NADH) dehydrogenases. It acts as a catalyst and plays an integral role in regulating the cytochrome b complex [9]. CoQ10 exerts a therapeutic effect in a variety of disorders like congestive heart failure, diabetes, osteoarthritis, degenerative neurological conditions etc. It supresses pain and prevents cartilage degeneration by inhibiting inflammatory mediators, which play a vital role in disease pathogenesis [10]. More recently, several studies have also shown the anti-inflammatory effects of CoQ10 and found it a good therapeutic option for treating inflammation, dysregulated metabolism, oxidative stress, and mitochondrial dysfunction and thereby it restores CPK-MM activity to baseline levels [11]. The omega3 fatty acid are also beneficial in lowering the inflammation by decreasing the levels of blood markers of inflammation such as C-reactive protein, interleukin 6, and TNF alpha [12].

In this paper, we examined current evidence and opinion relating to the release of CPK-MM from skeletal muscle tissue into blood stream in response to muscle inflammation. The significance of exercise modality on the levels of CPK-MM appears to be related to the magnitude of eccentric contractions involved during the muscular activity and the subsequent extent of muscle disruption. Greater muscle cell disturbance however delays the appearance of a CPK-MM peak compared to less disruption. This may be linked to the time course of inflammation; however, evidence in the literature supporting this theory remains unclear.

Conclusion

As per the case report the CPK-MM is not implicated in the causation of the disease but may be released as a result of inflammation and injury but can be used to monitor the disease progression and response to treatment. However, the molecular mechanisms that result in CPK release from muscle after mild exercise or injury remains unclear. More studies could provide information about the importance of rest periods between periods of active workout and the need for restricted physical activity over the course of the evaluation.

Conflict of interest

None.

Bibliography

1. Schlattner U., *et al*. "Mitochondrial creatine kinase in human health and disease". *Biochimica et Biophysica Acta* 1762.2 (2006): 164-180.

2. Liu CY., *et al*. "Macroenzyme creatine kinase in the era of modern laboratory medicine". *Journal of the Chinese Medical Association* 73.1 (2010): 35-39.

3. Brancaccio P., *et al*. "Creatine kinase monitoring in sport medicine". *British Medical Bulletin* 81-82 (2007): 209-230.

4. Sayers SP and Clarkson PM. "Short-term immobilization after eccentric exercise. Part II: creatine kinase and myoglobin". *Medicine and Science in Sports and Exercise* 35.5 (2003): 762-768.

5. Saks V. "The phosphocreatine-creatine kinase system helps to shape muscle cells and keep them healthy and alive". *Journal of Physiology* 586.12 (2008): 2817-2818.

6. Totsuka M., *et al*. "Break point of serum creatine kinase release after endurance exercise". *Journal of Applied Physiology* 93.4 (2002): 1280-1286.

7. Heled Y., *et al*. "CM-MM and ACE genotypes and physiological prediction of the creatine kinase response to exercise". *Journal of Applied Physiology* 103.2 (2007): 504-510.

8. Brown S., *et al*. "Indirect evidence of human skeletal muscle damage and collagen breakdown after eccentric muscle actions". *Journal of Sports Sciences* 17.5 (1999): 397-402.

9. Soni A., *et al*. "Role of Coenzyme Q10 in current oncology practice: Substance or shadow!" *OncoExpert* 1 (2015): 14-22.

10. Forester BP., *et al*. "Coenzyme Q10 Effects on Creatine Kinase Activity and Mood in Geriatric Bipolar Depression". *Journal of Geriatric Psychiatry and Neurology* 25.1 (2012): 43-50.

11. Khan FY. "Rhabdomyolysis: a review of the literature". *Netherlands Journal of Medicine* 67.9 (2009): 272-283.

12. Prelle A., *et al*. "Retrospective study of a large population of patients with asymptomatic or minimally symptomatic raised serum creatine kinase levels". *Journal of Neurology* 249.3 (2002): 305-311.

Volume 7 Issue 4 April 2020