

Correlation of Creatine Kinase and Myoglobin Concentrations in Patients Suffering from Debilitated Conditions Related to Myopathies

ABSTRACT

Aim

The present study describes the determination of a possible correlation between CK and myoglobin levels, in addition to the hypothesis that increase in myoglobin concentrations may precede changes in CK levels in patients suffering from myopathies.

Method

The inclusion period for this cohort study was from December 2005 to December 2007. Patients who met the laid down and referred criteria were eligible for the study, which includes patients aged > 20 years to < 75 years (both gender) and had a diagnosis of myopathies as per description. Standard protocols were followed for blood samples collection and estimation of aldolase, CK AST, ALT, CK and myoglobin levels. Regression correlations were determined and results were compared as per R2 and significance level $P < 0.05$.

Results

A total of 48 patients were included in the study, males = 32 (66.66%) and females = 16 (33.33%). Except for both CK and myoglobin, the rest of the enzymatic components were not found to be linearly correlated showing R2 factor less than 0.0012. Notably CK and myoglobin levels, when plotted through regression, were leading with exceptional correlation, with R2 0.491 for total patients, R2 0.512 for males and 0.532 for females.

Conclusion

It was suggested that by combining both CK and myoglobin estimation in patients with myopathies especially dermatomyositis or polymyositis, it provides better overall impression of muscle damage and related conditions.

Short Title

Correlation of CK and Mb levels in myopathies.

Keywords

Myopathies, Dermatomyositis, Polymyositis, Regression R2, Creatine Kinase, Myoglobin Concentrations.

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INTRODUCTION

It is a known fact that myopathies are neuromuscular disorders depicted by the primary manifestation of muscle weakness related to dysfunctional muscle fiber. Moreover, myopathies can be inherited (such as the muscular dystrophies) or acquired (such as common muscle cramps). Generally, myopathies are grouped as congenital myopathies, muscular dystrophies, mitochondrial myopathies, glycogen storage diseases of muscle, dermatomyositis (DM), myositis ossificans, familial periodic paralysis: polymyositis (PM), including body myositis, and related myopathies and tetany. In this context the analysis of muscle enzymes such as creatine kinase (CK), transaminase enzymes including aspartate transaminase enzymes or aldolase, including myoglobin determines the presence and extent of myopathies¹⁻⁵. It is well documented that concentration of circulating CK is the laboratory parameter most widely used to diagnose and follow the patients with DM or PM or related myopathies because of its high dimension of sensitivity, relative muscle specificity, and good correlation with disease activity and muscle strength^{2,6-8}. However, it was argued that independent assessment relating only to serum CK levels might never be an alternate for a systematic review of the patient, which includes muscle strength and functional assessments, as done for the measurements of myositis disease activity². Moreover, there are certain other consistent attribute regarding CK levels, one of which is its continual elevated concentration at some point in the illness, thus making it prone to bias. Therefore, to aid in the diagnosis and treatment in myopathies, researchers, scientists and clinicians searched for other parameters as well and noted that myoglobin is one of such biochemical markers⁹. There were few significant preliminary studies reported earlier on the importance of determination of serum myoglobin levels in patients of PM, DM and generic myopathies, in addition to serum enzyme such as CK, suggesting that changes of myoglobin levels may facilitate or even precede alterations of creatine kinase and clinical features^{1,2,10-12}. Therefore, the present study was undertaken to determine possible correlation between CK and myoglobin levels, in addition to the hypothesis that increase in myoglobin concentrations may precede changes in CK levels in patients suffering from myopathies.

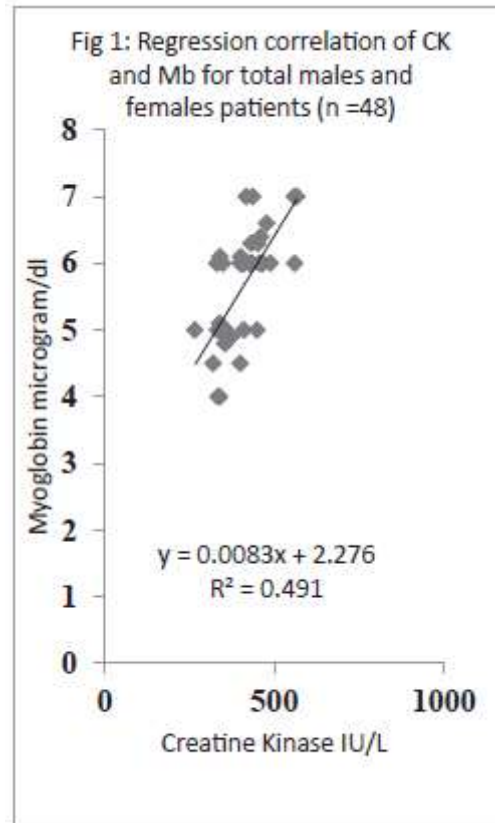
MATERIALS AND METHODS

Study Design

The inclusion period for this cohort study was from December 2005 to December 2007, of which data were collected retrospectively from November 2006 to Dec 2005 and prospectively from Dec 2006 to Dec 2007. The study was a collaborative venture between departments of biochemistry lab services and Physiotherapy services. Patients who met the following criteria were eligible for the study. Thus, the inclusion criteria were patients aged > 20 years to < 75 years and had a diagnosis of myopathies as per description^{5,13}. Importantly, patients must not have had any proximal muscle weakness. Muscle strength was checked according to the eight manual muscle testing (8-MMT)⁵. Exclusion criteria were patients aged group < 18 years and > 75 years with proximal muscle weakness (8-MMT score \leq 72) and known immunosuppressive condition including other clinical conditions such as infections, hypothyroidism, hepatitis, chronic haemolysis, recent myocardial infarction (less than three months), or recent leg or arm trauma⁵.

Data Collection

Data of a total of 46 patients (males = 32, females = 16) were obtained and compiled as per criteria. Where possible, data was also collected from LIS and HIMS archives. Following data were collected: age, gender, description of myopathies, disease duration and previous history of CK myoglobin levels or any other muscle enzyme or related components.

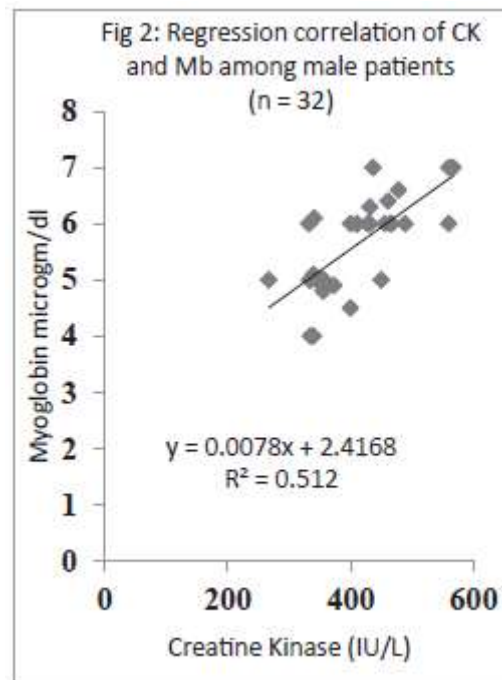


Blood Sample Collection and Analysis

Blood tests including serological testing for antinuclear antibodies (ANA) and RA factor, aldolase, creatine kinase, C reactive protein and myoglobin measurements were performed following internationally recognized and prescribed methodology and as per protocols noted earlier^{1,5,10}. Blood samples were collected by venipuncture on Li-heparinate 5 mL tubes from patients after 72 h of resting and an overnight fasting. Plasma aldolase, CK enzyme levels and myoglobin were performed by enzymatic methods at admittance and at the diagnosis of myopathy. Aldolase was determined by standard commercial kit from Randox on Monza (semi-automatic analyzer-Randox- UK). AST, ALT, CK and CRP were measured on Hitachi 912 (Roche Diagnostics-Basel) using commercial kits and both internal and external quality controls. Myoglobin was measured on Hitachi 912 (Roche Diagnostics-Basel) by Tina-Quant Myoglobin Gen.² (Roche)-immunoturbidimetric- latex- bound anti-myoglobin antibodies method. The ranges for myoglobin (Mb) were Men: 2.3-7.2 µg/dL Women: 1.9-5.1 µg/dL. Normal reference ranges of all analytes are plasma aldolase, 0-16 years: <14.5 U/L and > 17 years: <7.7 U/L; CK, males > 18 years: 52-336 U/L, females > 18 years: 38-176 U/L; CRP, < 8.0 mg/L; AST, 8-48 U/L; and ALT, 7- 45 U/L, respectively.

RESULTS

The results are summarized in Figures 1-3. Briefly a total of 48 patients were included in the study, males = 32 (66.66%) and females = 16 (33.33%). Levels of CK, CRP, aldolase, AST, ALT and myoglobin were measured, and

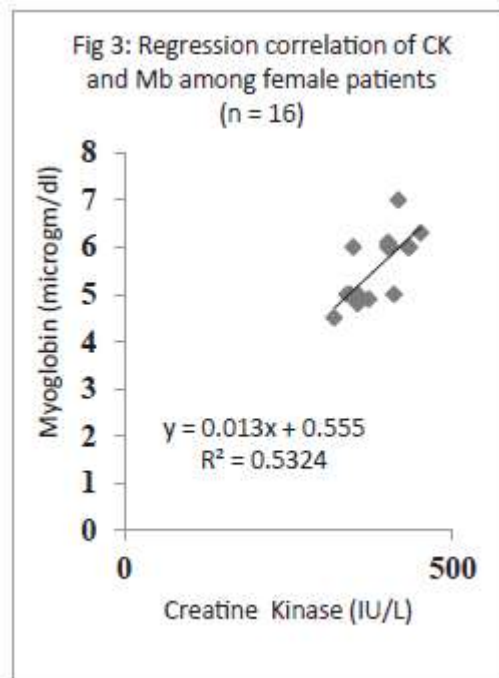


except both CK and myoglobin, the rest of the component were not found to be linearly correlated showing R2 factor less than 0.0012. The mean CK levels for males was 401.43 ± 72.50 IU/L (range 267-567), for females was 397.37 ± 60.25 IU/L (ranges 320-560) and for total patients, 400.80 ± 96.20 IU/L, where as myoglobin concentrations were 5.58 ± 1.10 $\mu\text{g/dl}$ (range 4-7), 5.56 ± 1.23 $\mu\text{g/dl}$ (4.5-7) and 5.59 ± 1.45 $\mu\text{g/dl}$ for males and females and total patients. Notably CK and myoglobin levels, when plotted through regression, were leading with exceptional correlation, with R2 0.491 for total patients (Fig 1), R2 0.512 for males (Fig 2) and 0.532 for females (Fig 3), thus depicting 49%, 51% and 53% existing correlation with elevating levels of both components. This also shows the positive correlation between these parameters and strongly significant ($p < 0.01$). The results profoundly suggest that by means of the myoglobin assay no additional clinically relevant information needed as far analysis of related components were concerned, ever since myoglobin and creatine kinase levels showed around 49% to 53% positive correlation with occupying muscle disorders.

DISCUSSION

It was documented that the levels of several enzymes such as aldolase, lactate dehydrogenase (LD) and its isoforms 5 and 1, and transaminases (both serum glutamic oxalacetic transaminase [SGOT]/aspartate aminotransferase [AST], serum glutamic pyruvic transaminase [SGPT]/alanine aminotransferase [ALT]) and carbonic anhydrase III in serum were noted to be increased in patients with myopathies during active muscle disease^{1,2,5,10,11}. However the extent of increase in all of these enzyme activities occurs less frequently and to a smaller extent as compared to CK levels^{2,14-16}. Furthermore, the enzyme components namely LD isoenzyme 5 is associated with skeletal muscle^{2,16} but elevations in the levels of LD isoenzymes 1,2, and 3 may occur with chronic myositis as well^{17,18}. On the other hand, carbonic anhydrase III, which is located in type I muscle fibers, is also frequently elevated in patients with IIM and

other diseases associated with skeletal muscle damage^{2,19,20}, thus illustrating non-significant clinical correlation.



In this regard, two previous studies suggested the importance of estimating CK and myoglobin in patients with myopathies that noted would be more beneficial when correlated with each other than any other enzymatic or muscle components^{1,10,21}. It was also reported earlier that serum Mb and CK levels have similar values as indicators of muscle damage in primary and secondary skeletal muscle disorders. Nonetheless, it was argued that, the serum Mb level helps more in the detection of carriers, however is not more sensitive than CK measurement²¹. Additionally, it was documented that muscle damage due to excessive exercise leads to an increase in myoglobin levels thus depicting its sensitivity as a direct parameter for assessing acute muscle damage¹. Nevertheless, combining both CK and myoglobin estimation in patients with dermatomyositis or polymyositis provides better overall impression of muscle damage^{1,21}. Henceforth, the present study describes correlation studies of CK and myoglobin levels of a total of 48 patients (males = 32 (66.66%) and females = 16 (33.33%)) where levels of CK, CRP, aldolase, AST, ALT, CK and myoglobin were measured to assess its correlating abilities more significantly towards muscle damage and myopathies. It was noted that except CK and myoglobin the rest of the component were not found to be linearly correlated where R2 factor was less than 0.0012. Notably CK and myoglobin levels, when plotted through regression, were leading with exceptional correlation, with R2 0.491 for total patients, R2 0.512 for males and 0.532 for females, thus depicting 49%, 51% and 53% existing correlation with elevating levels of both components. The mean CK levels for males was 401.43 ± 72.50 IU/L (range 267-567), for females was 397.37 ± 60.25 (ranges 320-560) IU/L and for total patients, 400.80 ± 96.20 IU/L, whereas myoglobin concentrations were 5.58 ± 1.10 μ g/dl (range 4-7), 5.56 ± 1.23 μ g/dl (4.5-7) and 5.59 ± 1.45 μ g/dl for males and females and total patients. Supporting our findings, the two previous studies mentioned earlier^{1,10,21} reported the significance of combining CK estimation with that of myoglobin concentration. Giampietro et al categorically stated that myoglobin and creatine kinase have proved to be the best indicators of the hypothyroid myopathy, since they are sensitive for the early detection of muscle involvement due to the metabolic disorder and are closely correlated to the metabolic conditions of patients^{10,22}. Regarding muscle-derived CK activity in patients with PM/DM, the levels of CK and other muscle-derived enzymes in serum are generally useful in following myositis activity and responses to therapy, although the magnitude of the elevation does not always correlate with

global disease activity (Rider and Miller, 1995; Straus et al., 1989)^{2,6}. Past and present studies also suggested inclusion of other enzymatic components for the same purpose. For example in a cohort study, it was found that elevated plasma aldolase at inclusion was an accurate marker that helped to identify SSc patients. However, other components such as AST and CRP were not able to predict subsequent Myo-SSc occurrence⁵. The reason provided for defiant elevation in serum CK levels in patients with myositis was due to increases in the MM-isoenzyme fraction which is released from skeletal muscle². Persistent elevation of MB levels is commonly seen in patients with skeletal muscle damage but not in patients with myocardial infarction^{2,8,23}. The levels of macro-CK type 1, a complex of a CK isoenzyme and immunoglobulin, are elevated in patients with myositis in comparison with the levels in patients with heart disease, infections, malignancies, and other disorders^{2,24,25} although the correlation of macro-CK levels with disease activity remains to be determined. In a very significant study reported earlier by Diószeghy and Mechler, serum creatine kinase (CK) and myoglobin (Mb) levels were measured in patients with different neuromuscular diseases, carriers of X-linked Duchenne-type muscular dystrophy and normal volunteers²¹. The highest levels were found in Duchenne dystrophy and both values decreased in parallel with age. In patients suffering from limb-girdle dystrophy the increases in CK activity and Mb concentration were also pronounced, thus supporting the outcome of our cohort as well. It was thus concluded that by combining both CK and myoglobin estimation in patients with myopathies especially dermatomyositis or polymyositis, it provided a better overall impression of muscle damage and related conditions

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