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Biochemistry

A STUDY OF SERUM CK-MB LEVEL IN NON DIALYSED CHRONIC KIDNEY DISEASE PATIENTS

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ABSTRACT Chronic kidney disease is associated with early increased risk of cardiovascular morbidity and mortality. CK-MB the traditional marker for myocardial ischemia loses its specifity in renal failure because of non cardiac source of this enzyme.

AIMS:The aim of the study was to measure and compare the level of serum CK-MB in non dialysed chronic kidney disease patients and in healthy controls.

MATERIAL AND METHOD: 50 healthy controls and 50 non dialysed chronic kidney disease patients on conservative treatment attending Nephrology department, Gauhati Medical College and Hospital, during September 2015-August 2016 were included in this study. Quantitative analysis of urea, creatinine, CK-MB were done by photometric method.

RESULTS: Serum CK-MB levels were significantly higher in the cases as compared to controls (p value <0.0001).

CONCLUSION: Non specific modest elevation of CK-MB can cause false positive results in absence of myocardial ischemia in CKD patients. So CK-MB should be interpreted with caution in these patients.

KEYWORDS : serum CK-MB, non dialysed chronic kidney disease

INTRODUCTION

Chronic kidney disease (CKD) is characterized by progressive loss of renal function. The NKF-K/DOQI (National Kidney Foundation) guidelines stratify CKD from stage 1 at the milder end of the spectrum to stage 5 with kidney failure or GFR <15ml/min/1.73m2. [1]

The incidence of cardiovascular disease is seven- to tenfold greater in patients with CKD than in non-CKD age- and gender matched controls.[2] The spectrum of cardiovascular pathology predominant among patients with CKD (hypertensive cardiomyopathy, arrhythmias, heart failure, valvular disease, and peripheral vascular disease) differs from that predominant in the general population (atheromatous coronary artery disease).[3]CK-MB is one of the diagnostic marker for acute coronary syndrome in the general population. Creatine kinase(CK) is a dimer composed of two subunits, each with a molecular weight of about 40,000 Da. These subunits (B and M) are the products of loci on chromosomes 14 and 19, respectively. Because the active form of the enzyme is a dimer, only three different pairs of subunits can exist: BB (or CK-1), MB (or CK-2), and MM (or CK-3). Serum CK is increased in nearly all patients when injury, inflammation, or necrosis of skeletal or heart muscle occurs. CK-MB owing to the phenomenon of "fetal reversion," in which fetal patterns of protein synthesis reappear. [4] Thus serum CK-MB isoenzyme may increase in such circumstances. This explanation may also account for the elevated CK-MB values sometimes observed in chronic renal failure (uremic myopathy). Changes in serum CK and its MB isoenzyme following acute myocardial infarction have been the mainstay of diagnosis for many years.[5] However, it is now more advantageous to use more cardiac-specific nonenzymatic markers, such as cardiac troponin I or T.

The present study was undertaken to study the elevated CK-MB levels in renal insufficiency as compared to healthy controls.

AIMS AND OBJECTIVES

To measure the level of serum CK-MB in non dialysed chronic kidney disease patients and in healthy controls and to find out if there was any significant increase in CK-MB levels.

MATERIALS AND METHODS:

The study was carried out in Department of Biochemistry and Nephrology department, Gauhati Medical College and Hospital. All the studies and investigations were carried out after obtaining informed consent and after approval by the Institutional Ethics Committee. Clinically diagnosed Chronic Kidney disease patients of either sex, above 18 years of age, on conservative treatment and healthy controls were included. Blood samples were analysed for glucose, urea, creatinine and CK-MB. Demographic data were determined by existing standards, medical records and proper history taking.

Patients with the following were excluded –

1. Previous ischemic heart disease.
2. Trauma.
3. Hypothyroidism.
4. Cerebrovascular diseases.
5. Muscular dystrophies and dermatomyositis.

The subjects were divided into two groups. Group I included 50 normal healthy individuals. Group II included age and sex matched 50 non dialysed chronic kidney disease patients. Serum creatinine levels were estimated using modified Jaffes method. The normal range is 0.7-1.4 mg/Dl. Blood urea was estimated using Urease –GLDH (Glutamate Dehydrogenase) method. Normal range at our laboratory is 15-40 mg/dL. Plasma Glucose was estimated based on Trinder's GOD/POD method. Normal range of Plasma Glucose (Fasting): 70 - 110 mg/dl. CK-MB was estimated by VITROS CKMB Slide method.

The VITROS CKMB Slide is a multilayered, analytical element coated on a polyester support.A drop of patient sample is deposited on the slide and is evenly distributed by the spreading layer to the underlying layers.

This layer contains surfactants; N-acetylcysteine (NAC), which activates CK without pretreatment of the sample; and goat antihuman CK-M antibodies, which inhibit CK-MM (muscle) activity and ~50% of the CK-MB (heart) activity. The remaining CK activity represents 50% of the total CK-MB isoenzyme concentration plus any CK-BB (relatively rare). In the reagent layer, creatine kinase in the sample catalyzes the conversion of creatine phosphate and adenosine diphosphate (ADP) to creatine and adenosine triphosphate (ATP). In the presence of glycerol kinase, glycerol is phosphorylated to L-α-glycerophosphate which is then oxidized to dihydroxyacetone phosphate and H2O2 in the reaction catalyzed by L-α-glycerophosphate oxidase. Finally, leuco dye is oxidized by hydrogen peroxide in the presence of peroxidise to form a dye. The low wavelength light cutoff filter on the slide support minimizes the blank rate effects of incident light during dye development. The rate of change in reflection density is converted to enzyme activity. All parameters were analyzed by fully automated analyzer.

The results obtained were statistically analyzed and compared between the two groups. Baseline characteristics of the study participants are expressed in mean ± SD. Unpaired student's t- test was used to analyze differences in baseline characteristics. The results were considered significant when the probability (p value) was less than 0.05. Statistical analysis was done using GraphPad InStat version 3.00.

All the statistical graphs were prepared using Microsoft Excel 2010.

RESULT:

SEX DISTRIBUTION

Out of total number of subjects in the case and control group, 33 (66%) were males and 17 (34%) were females.

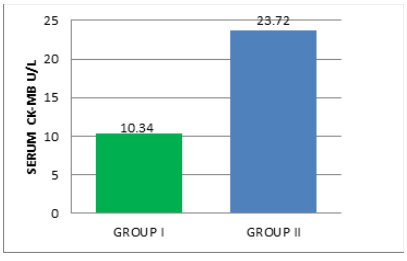
TABLE 1: Serum CK-MB, Blood Urea and Creatinine levels in studied groups

PARAMETERS	GROUP I (mean±SD)	GROUP II (mean±SD)	p value
SERUM CK-MB (U/l)	10.34±5.03	23.72±16.52	<0.0001 *
UREA (mg/dl)	31.86±8.31	56.28±13.57	<0.0001 *
CREATININE (mg/dl)	0.81±0.21	2.77±1.00	<0.0001 *

*extremely significant(<0.0001)

The present study demonstrated that serum CK-MB levels were elevated in non dialysed chronic kidney disease patients when compared with healthy controls and this increase was statistically significant (p<0.0001).Chronic kidney disease patients had higher CK-MB levels (mean 23.72±16.52 SD) than controls (mean 10.34±5.03 SD).

Figure 1: Comparison of means of serum CK-MB in studied groups



DISCUSSION

The present study demonstrated that serum CK-MB levels were significantly elevated in non dialysed CKD patients. Chronic kidney disease patients had higher CK-MB levels (mean 23.72±16.52 SD) than controls (mean 10.34±5.03 SD). Blood urea and serum creatinine were statistically increased in CKD patients. Green TR [6] demonstrated 88% increase in CK-MB level in renal failure patients in a longitudinal study over a 3year period. Mclaurin et al [7] showed a 30 % increase in CK-MB levels in dialysis patients. Golam K. Alam & Davi B. Lieb [8] demonstrated a 30% increase in CK MB in renal failure patients. Similarly Iliou MC et al [9] documented a 7% increase in CK MB levels in CKD patients.

The possible causes of elevation include:

Increased reexpression of fetal CK MB in myopathic skeletal muscles in renal patients.[4] Abnormal protein metabolism and muscle wasting in CKD which can be a source of increased CK MB in these patients. Hyperphosphatemia in CKD also can cause myocardial damage.[10]

Patients with CKD have a higher prevalence of traditional risk factors compared to the general population (e.g.: diabetes, hypertension, older age, smoking history and abnormal lipid profiles).[11] The prevalence of asymptomatic coronary artery disease is 20% to 40% among persons with chronic renal failure. CK-MB, the traditional marker for myocardial injury, loses its specificity in the setting of renal failure. [12]

In the general population, an elevation of CK-MB has a sensitivity for diagnosing acute myocardial infarction of 46.4% at 4 hours and 91.5% at 6 hours after onset.[13] However, in chronic renal failure patients, nonspecific modest elevations of CK-MB can cause false-positive results at rates of 20% to 30% in the absence of myocardial injury. [14]

CONCLUSION

Non specific modest elevation of CK-MB can cause false positive results in absence of myocardial ischemia in CKD patients. So CK-MB should be interpreted with caution in these patients. Prospective studies to fully elucidate the best marker for detection of myocardial injury and prognosis in this patient population are required.

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References

1. Levey AS, Coresh J, Balk E, Kausz AT, Levin A, Steffes MW et al. National Kidney Foundation Practice Guidelines for Chronic Kidney Disease: Evaluation, Classification, and Stratification. Ann Intern Med 2003; 139 (2): 137-47.
2. Wheeler DC, Townend JN, Landray MJ. Cardiovascular risk factors in predialysis patients: baseline data from the Chronic Renal Impairment in Birmingham (CRIB) study. Kidney Int Suppl 2003;S201-3.
3. Baigent C, Burbury K, Wheeler D. Premature cardiovascular disease in chronic renal failure. Lancet 2000;356:147-52.
4. Burtis CA, Ashwood ER, Burns DE,editors. Teitz textbook of Clinical Chemistry and Molecular Diagnostics. 5th ed. Philadelphia: Elsevier; 2012.p. 569-571.
5. Dolci A, Panteghini M. The exciting story of cardiac biomarkers: from retrospective detection to gold diagnostic standard for acute myocardial infarction and more. Clin Chim Acta 2006;369:179-87.
6. Green T.R., Golper T.R. Diagnostic value of creatine kinase and creatine kinase MB isoenzyme in chronic hemodialysis patients : a longitudinal study Clin. Nephrol. 1986; 25 (1): 22-27.
7. Mary D. Mclaurin, Fred S. Apple, Ellen M. Voss, Charles A. Herzog and Scott W. Sharkey., Cardiac Troponin I, Cardiac Troponin T and Creatine kinase MB in dialysis patients without ischemic heart disease evidence of Cardiac Troponin T expression in skeletal muscle Clin. Chemistry 1997; 43: 6; 976-982.
8. Golam K. Alam, David B. Lieb. Biochemical markers of Myocardial Ischemia in renal failure. Hospital physician December 2002; 27-31.
9. Iliou M.C., Fumeron C. Factors associated with increased serum levels of cardiac troponins T and I in chronic hemodialysis patients: Chronic Hemodialysis and New Cardiac Markers Evaluation (CHANCE) study. Nephrol. Dial. Transplant 2001; 16; 1452-1458
10 Hruska KA, Mathew S, Lund R, Qui P, Pratt R. Hyperphosphatemia of Chronic Kidney Disease. Kidney international. 2008;74:148-157.
11 Burtis CA, Ashwood ER, Burns DE,editors. Teitz textbook of Clinical Chemistry and Molecular Diagnostics. 5th ed. Philadelphia: Elsevier; 2012.p.1547
12. George SK, Singh AK. Current markers of myocardial ischemia and their validity in end-stage renal disease. Curr Opin Nephrol Hypertens 1999;8:719-22.
13. Zimmerman J, Fromm R, Meyer D. Diagnostic marker cooperative study for the diagnosis of myocardial infarction. Circulation 1999;99:1671-7.
14. Pierce GF, Jaffe AS. Increased creatine kinase MB in the absence of acute myocardial infarction. Clin Chem 1986; 32: 2044-51.