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BIO-MARKERS ASSAY IN ACUTE MYOCARDIAL INFARCTION- A CROSS SECTIONAL STUDY

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ABSTRACT

Acute myocardial infarction (AMI) is diagnosed with history of chest pain, ECG, enzyme bio markers. Many persons may not present with typical chest pain and have atypical presentations. The aim of the present study was to study the levels of various enzymatic markers in AMI and determine the efficacy of CK-MB in terms of early detection when compared to that of the other know routine enzymatic markers of AMI. The present study included 50 cases with AMI and 40 control subjects. We observed that within six hours of hospital admission, cases with AMI showed a significant increase of both Total CK and CK -MB.

KEY WORDS: Acute Myocardial Infarction, markers, creatinine kinase.

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INTRODUCTION

The term acute myocardial infarction haunts the modern society in spite of the diagnostic & treatment sophistication. What was previously a disease of the 50s age group, now not even sparing the teens. Any disease the time of accurate diagnosis stands between life & death which is of paramount importance in acute MI. Cardiac muscles are metabolically very demanding and cessation of blood supply even for short period can result in necrosis & there is no regeneration. Acute myocardial infarction (AMI) is diagnosed with history of chest pain, ECG, enzyme bio markers. Many persons may not present with typical chest pain as seen in diabetic autonomic neuropathy and considering India being one of the leaders in patients with diabetes mellitus (DM), there is the possibility of large quantum of patients being deceived by clinical symptoms & signs of MI. In nearly half of the patients ECG may be equivocal initially thereby delaying diagnosis & initiation of treatment. So we should rely on enzyme biomarkers which is neither subjective as chest pain nor electro physiological parameter to supplement, to establish or exclude the diagnosis. Inadequate or complete cessation of oxygen supply to a part of the myocardium result in wide range of structural changes in cardiac cell, function and metabolism thus leading to mechanical, electrical and biochemical disturbances in the affected part of the myocardium, which may be either transient or permanent depending on the duration of ishaemia. Loss of functional integrity of sarcolemma liberates the cytoplasmic cell constituents from the affected cardiac cell into the circulation which can be analyzed biochemically including the Myoglobin, Contractile protein myosin, Regulatory proteins -Tropomyosin, Troponin T, Troponin C, Troponin I, Cytoplasmic enzymes -Creatine kinase (CK), Lactate dehydrogenase (LDH), Aspartate amino transferases(AST).[1,2] TnC has no potential as a cardiac marker, because its amino acid sequence in both skeletal and cardiac muscle is identical. Aspartate amino transferases (AST) is moderately elevated in cirrhosis, skeletal muscle disease, after trauma or surgery, cholestatic jaundice, severe hemolytic anemia, hence not specific for MI. Total CK is markedly elevated in MI, muscular dystrophy, rhabdomyosis and a moderate elevation occur in muscular injury, after surgery, alcoholism. Creatine Kinase-MB (CK-MB) an isoenzyme of CK is considered to be a more specific indicator of AMI and it has been recognized that the amount of enzyme released correlates with the size of the infarct CK-MB has the advantage over AST and LDH in that it is not present in extra cardiac tissues. LDH is markedly increased in (more than 5 times the upper adult reference limit) in MI, circulatory failure with shock and hypoxia, acute leukemia, lymphomas; moderately increased in viral hepatitis, malignancy, skeletal muscle disease, pulmonary embolism. Cardiac Troponin-T (TnT) is a polypeptide subunit of the myofibrillar regulating Troponin complex and is a unique myocardial protein. Cardiac Troponin I (TnI) is a monomer with a molecular mass of 24 kDa. It is an inhibitory polypeptide subunit of the myofibrillar regulating Troponin complex. TnI is uniquely located in the myocardium and is the most specific cardiac injury biomarker. Myoglobin is a water soluble conjugated protein. The clinical value of determination of myoglobin in AMI is limited because of the lack of specificity resulting from the fact that myoglobin is a constituent of skeletal muscle and is readily detected in serum following damage to skeletal muscle. From the above enzyme biomarkers it is evident that TnT, TnI , CK-MB are more cardiac specific than the others in cardiac injury. The Pattern of elevation of cardiac markers in acute MI is shown in table I. Out of these TnI was found to increase as early as 3 hrs from the onset of myocardial injury/pain & clearly ahead in terms of onset time and cardiac specific. In this study we studied the different enzyme levels in AMI patients established by clinical signs & symptoms, ECG and normal healthy subjects.

Table 1
Pattern Of Cardiac Markers Elevation In Acute Myocardial Infarction

Marker	Time to Initial Elevation (hours)	Time to Peak Elevation (hours)	Time to Return to Normal (days)
CK-TOTAL	4-8	12-24	2-3
CK – MB	3-6	12-18	<1
MYOGLOBIN	1-4	6-10	1
AST	6-8	24-48	4-6
LDH	12-24	48-72	7-12
CTn I	3-6	12-24	3-10
CTn T	4-6	24-48	7-14

AIM & OBJECTIVES OF THE STUDY

The aim of the present cross-sectional work was to study the level of enzymes AST, CK, CK-MB, LDH in both normal controls and at 6 hours in those presenting with AMI. To determine the efficacy of CK-MB in terms of early detection when compared to that of the other know routine enzymatic markers of AMI.

MATERIALS AND METHODS

This was a cross-sectional study where ninety male subjects were chosen in the age group of 40-60 years. Out of them forty were normal healthy males and they formed the normal control group. Fifty of them were patients with AMI, admitted to the Cardiology Department of Government General Hospital formed the study group. Those individual with diabetes mellitus, impaired renal function or having clinical features of hyperlipidemia were excluded from the study. Institutional Ethical committee clearance was obtained. The study group consisted of fifty patients with ECG evidence of AMI. Subjects in the control group did not have any history of chronic ailment and were free from symptoms and clinical signs of coronary heart disease. All the subjects were BMI (Body Mass Index) matched. Blood samples were collected by venipuncture within six hours of admission. About 5ml was allowed to clot and the serum was separated after centrifugation. The analysis of Total CK, CK-MB, LDH, serum AST was done immediately. Statistical Analysis was done by Excel 2007.

RESULTS AND DISCUSSION

The results are showed in table 2 as mean, SD unless otherwise specified. The diagnosis of AMI was based on the patient's history, clinical signs and symptoms, electrocardiographic tracings and serum levels of cardiac biomarkers. World Health Organization has recommended that the diagnosis of AMI be based on fulfillment of at least two of the following three criteria.

1. Clinical history of severe ischemic type of chest pain with duration of twenty minutes.
2. Changes on serial electrocardiograph tracings.
3. Initial rise and subsequent fall in serum levels of cardiac biomarkers.

Table 2
Mean & SD of Cardiac injury bio markers in cases & controls

MARKERS	GROUP	N	MEAN	SD	P-VALUE
Total-CK (U/L)	Controls	40	41.36	18.18	t = 30.72 P=0.001
	Cases	50	1058.21	233.20	
CK-MB (U/L)	Controls	40	1.44	1.37	t = 13.35 P=0.001
	Cases	50	124.50	65.18	
LDH (U/L)	Controls	40	134.39	12.65	t = 0.46 P=0.65
	Cases	50	133.04	14.67	
AST (U/L)	Controls	40	23.11	4.24	t = 1.95 P>0.06
	Cases	50	25.047	5.33	

The reference level obtained for Total CK, CK-MB, LDH, AST, are 41.36 $\pm$18.18, 1.44 $\pm$1.37, 134.39 $\pm$ 12.65, 23.11 $\pm$4.24. These levels are found to correlate well with the levels obtained by Christenson et al.[3] According to our study, there is an increase in Serum Total CK to the

level of 1058.21 ± 233.20 U/L as compared to controls who had 41.36 ±18.18 U/L. This study shows a twenty five fold significant increase of CK in cases of MI with a p value of 0.001, which is highly significant. The reference range for CK -MB is 1.44 ±1.37 U/L. In our study cases with AMI showed levels upto 124.50 ±65.18 U/L, which is highly significant with a p value of 0.001. The total CK activity in serum begins to raise within 4-8 hours reaches a peak value between 24-48 hours and then rapidly returns to normal by 3-5 days *(24, 25)*. Average elevation of total CK activity is 7-12 times the upper limit. An earlier peak around 8-12 hours occurs with early reperfusion.[4] Hence within six hours of hospital admission, cases with AMI showed a significant increase of both Total CK and CK -MB. Serum LDH levels increase only 12 hours after AMI and reaches its peak between 48-72 hours and returns to normal within 7-10 days, hence serum LDH cannot be taken as an early biomarker for AMI. In this study serum LDH showed no increase in AMI patients within six hours of hospital admission, with the levels of serum LDH for the cases and controls being 133.04 ±14.67 and 134.39 ± 12.65 respectively, with a p value of 0.65, which is not significant. Serum levels of AST when estimated in both cases and controls showed no increase in our study. AST starts to rise after 6-8 hours in AMI and peaks at 18-24 hours and returns to normal within 4-6 days. So this finding correlated with our study with the values for cases and controls being 25.07 ± 5.33 and 23.11 ± 4.24 respectively, with a p value of > 0.06, which is not significant. In summary there is a significant increase of Total CK and CK-MB in cases within six hours of AMI. Hence CK-MB can be used as an early specific biochemical marker for AMI. Thus cardiac marker enzymes/proteins should be used for early diagnosis of MI thus enabling earlier intervention and therapy.[5]

CONCLUSION

AMI continues to be one of the most common causes for mortality and morbidity worldwide, and hence there is a need to diagnose the condition at an early stage for appropriate management. Approximately one third of the patients with AMI do not present with classical chest pain and non diagnostic electrocardiograph tracings are recorded in approximately half of the patients presenting to the emergency department with chest pain, therefore in the majority of patient clinician must obtain serum cardiac marker measurement to either establish or exclude the diagnosis of AMI. Assay for measuring serum levels of biomarker of cardiac injury, remain an important tool for diagnosing patient with suspected MI. Elevated serum levels of other commonly used biomarker are not specific for cardiac injury because these markers are present in other tissue types throughout the body.

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