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Original Research Paper

Biochemistry

COMPARISON OF CARDIAC MARKERS CK-MB CARDIAC TROPONIN I AND MYOGLOBIN FOR DIAGNOSIS OF MYOCARDIAL INFARCTION.

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ABSTRACT

BACKGROUND- This study was conducted to compare the diagnostic efficiency of CK MB, cardiac troponin and myoglobin in patient of acute coronary syndrome. Early identification of acute coronary event will help in initiating early and timely treatment thereby reducing the mortality associated with MI.

METHODOLOGY-This study was conducted as a hospital based cross sectional study at Department of Medicine in collaboration with Department of Biochemistry, LNMC and associated J.K. Hospital, Bhopal during the study period of 18 months. All the patients diagnosed with MIand matched healthy controls were included in 1:1 ratio. Clinical history was recorded in detail. All the participants were subjected to detailed general and systemic examination along with routine and special investigations.

RESULTS- A total of 267 cases of MI were included with mean age of 54.7±13.6 years whereas mean age of 267 controls was 53.9±12.8 years. About 179 (67.04%) cases and 174 (65.2%) controls were males. Our study revealed that within 72 hour of onset of symptoms, Troponin I has highest sensitivity and specificity with overall highest diagnostic accuracy followed by CK-MB and myoglobin.

CONCLUSIONS- Based upon the findings of present study, it could be concluded that Troponin I is the best marker for early diagnosis of acute coronary event, however, when the patient present early during the first 6 hours of onset of symptoms, myoglobin is a sensitive assay.

KEYWORDS : myoglobin, Troponin I, CK-MB, MI, diagnostic efficiency

INTRODUCTION

Myocardial infarction commonly known as "heart attack" is a medical emergency characterized by acute chest discomfort or chest pain which may radiate to shoulder, arm, jaw or neck.[1,2] MI results from decreased or complete cessation of blood flow to the portion of heart or myocardium leading to irreversible damage to myocardium.[3] Acute Myocardial infarction represents one of the most common cause of mortality globally. Majority of MI cases are secondary to underlying coronary artery disease (CAD).[4]

The underlying pathophysiological mechanism leading to myocardial infarction include decreased coronary blood flow which is not sufficient to meet the oxygen demand of the myocardium resulting in cardiac ischemia. The etiopathogenesis of reduced coronary flow is multifactorial and atherosclerosis is most common cause.[5,6] Myocardial infarction was initially categorized into two forms transmural (affecting entire thickness of myocardial muscles) and non-transmural (typically epicardium is spared). Later, the new nomenclature was introduced in 1980 based upon ECG in which Q wave MI was classified as transmural MI but autopsies failed to confirm such association. Thus, in 1990, a new classification ST segment elevation MI (STEMI) and non-STEMI (NSTEMI) was adopted.[7]

Though ECG is helpful in establishing diagnosis of acute myocardial infarction, but ECG during the initial stages of MI may be non-diagnostic. Thus, the role of biomarkers in early diagnosis of myocardial infarction continue to evolve after the incorporation of cardiac biomarkers in the definition of MI. Various cardiac biomarkers used in evaluation and diagnosis of MI include cardiac troponin (Trop T and Trop I), creatine kinase-MB (CKMB), homocysteine, myoglobin, Lactate dehydrogenase, C-reactive protein etc.[8-10] The present study was therefore conducted at tertiary care centre to compare the diagnostic efficiency of CK MB, cardiac troponin and myoglobin in patient of acute coronary syndrome. Early identification of acute coronary event will help in initiating early and timely treatment thereby reducing the mortality associated with MI.

METHODOLOGY

This study was conducted as a hospital based cross sectional study at Department of Medicine in collaboration with Department of Biochemistry, LNMC and associated J.K. Hospital, Bhopal during the study period of 18 months i.e. from 1st March 2019 to 30th August 2021. Sample size was estimated using the formula

$$n=\frac{(Z\alpha)^2 x P x Q}{D^2}$$

Where, $Z\alpha=1.96$ when α is 5%, $(Z\alpha)^2=4$; P = prevalence of CVD in India = 21.1[11]

$Q = 100–P = 78.9$; D = allowable error = 5%

$$n=\frac{4 x 21.1 x 78.9}{5^2}$$

$n=266.3=267$

All the patients diagnosed with MI belonging to more than 18 years of age were included whereas patients with muscle damage and chronic renal disease were excluded from the study. Matched healthy controls were also included in 1:1 ratio. After obtaining ethical clearance from Institute's ethical committee all the patients fulfilling the inclusion criteria were enrolled in the study and written consent was obtained from all of them. Detailed history regarding sociodemographic variables were obtained using questionnaire. Clinical history regarding mode of presentation, duration of symptoms, previous history of hospitalisation, co-morbid conditions, addiction, lifestyle etc. was obtained from all the study participants and entered in questionnaire. Past history or relevant family history, if any was noted. Further all the participants were subjected to detailed general and systemic examination. All the four systems were examined thoroughly with special emphasis on examination of cardiovascular system and any positive abnormal findings were noted. All the patients were subjected to routine and special investigations at the time of admission including complete blood picture, LFT, RFT, lipid profile, chest X-ray, ECG and cardiac biomarkers i.e. CK MB, Troponin I and Myoglobin

STATISTICAL ANALYSIS – Data was compiled using MS Excel and analysed using IBM SPSS software version 20. Categorical data was expressed as frequency and

proportions whereas continuous data was expressed as mean and standard deviation. Diagnostic accuracy of all the biomarkers were calculated and expressed as sensitivity, specificity, positive predictive value and negative predictive value.Continuous variables between cases and controls were compared using independent t test. P value less than 0.05 was considered statistically

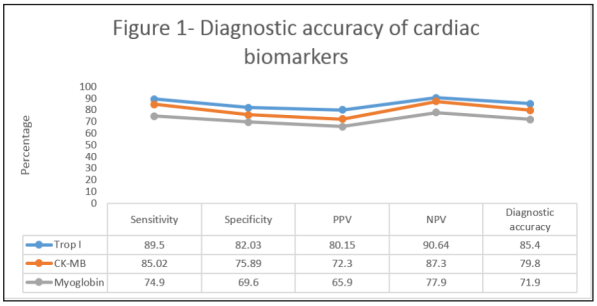
RESULTS

A total of 267 cases of MI were included with mean age of 54.7±13.6 years whereas mean age of 267 controls was 53.9±12.8 years. About 179 (67.04%) cases and 174 (65.2%) controls were males. The two groups were comparable with respect to age and gender (p>0.05).

Table 1- Trop I, CKMB and Myoglobin levels in

		MI		Total
		Present (Cases)	Absent (control)	
Trop I (ng/ml)	>0.04 (Raised)	214	25	239
	<0.04 (Normal)	53	242	295
CK-MB (ng/ml)	>4.9 (Raised)	193	34	227
	<4.9 (Normal)	74	233	307
Myoglobin (ng/ml)	>72 (Raised)	176	59	235
	<72 (normal)	91	208	299
Total	267	267	534	

A 2x2 table was constructed for all the 3 cardiac biomarkers for calculating diagnostic accuracy of the cardiac biomarkers.



Our study revealed that within 72 hour of onset of symptoms, Troponin I has highest sensitivity and specificity with overall highest diagnostic accuracy followed by CK-MB and myoglobin.

DISCUSSIONS

Myocardial infarction is one of the most common medical emergency encountered in emergency department.[1]As the condition is associated with high morbidity and mortality, early diagnosis and immediate management is of utmost importance. The age of the first coronary event is estimated to be 65.6 years in males and 72 years in females. Mortality due to MI may be observed in approximately 30% cases.[12]In India the prevalence of MI is reported approximately a decade earlier as compared to developed nations. In India, mortality due to cardiovascular disease were attributed in 28.1% cases in 2016.[13]ECG helps in establishing definitive diagnosis, but the changes in ECG take time to appear. Various cardiac biomarkers used in evaluation and diagnosis of MI include cardiac troponin (Trop T and Trop I), creatine kinase-MB (CKMB), homocysteine, myoglobin, Lactate dehydrogenase, C-reactive protein etc.[8-10]Various biomarkers are available for diagnosis of MI. The ideal Cardiac enzyme or biomarkers need to be highly specific, highly sensitive and easily detectable as early as possible in the disease process.[8-10] The present study thus aimed to compare the diagnostic efficiency of CK MB, cardiac troponin and myoglobin in patient of acute coronary syndrome.Myoglobin is a heme protein which is often observed in a patient with acute MI as early as within one to three hours of onset of myocardial infarction event. This cytoplasmic oxygen binding protein is present in skeletal and cardiac muscles and is eliminated by the kidneys. Its sensitivity for diagnosis of MI is high whereas its low specificity is limiting factor.[14] The MB isoform of creatine kinase isoenzyme (previously called creatine phosphokinase) is a mitochondrial enzyme specific for myocardium.The CKMB activity can be detected within 3 to 9 hours after MI, reaches maximum levels in 10-20 hours and thereafter, it starts declining reaching normal levels after 72 hours.[15] Troponins are the regulatory protein which is composed of three isoforms- troponin C, troponin I and Troponin T. Of them, Troponin C does not act as cardiac biomarkers but play a very important role in calcium binding. On the other hand Trop T as well as Trop I inhibit binding of tropomyosin binding and ATPase activity respectively.[16] Both these cardiac troponins have higher sensitivity and specificity for predicting the myocardial infarction and outcome of patients with MI.[17]We included 267 cases with confirmed MI and 267 healthy controls and observed three cardiac biomarkers at the time of admission. The mean age of cases as well as controls was more than 50 years and majority of participants were males irrespective of presence or absence of MI. Our study findings were supported by findings ofKorkmazet al, in which mean age of patients with MI was 55 ± 15 years and 55% were males.[18]

The standard cutoff values were taken for detection of these cardiac biomarkers and a 2x2 table was constructed for each biomarker to assess the activity of these cardiac markers in presence or absence of MI. We observed that majority of patients presented after 6 hours of onset of symptoms. We performed the cardiac biomarker assays at the time of admission irrespective of onset of symptoms. Mean duration since onset of symptoms and hospitalization was 10.3±3.6 hours for cases. The sensitivity, specificity, NPV, PPV and overall diagnostic accuracy of Troponin I was maximum for diagnosis of MI. The sensitivity of Troponin I was 89.5% whereas that of CKMB and Myoglobin was 85.02% and 74.9% respectively. We observed that the patients who presented early had higher myoglobin levels and as the time lapse was seen, trop I and CK-MB performed better. deWinteret al however documented higher sensitivity (87%) of myoglobin as compared to CK MB and Trop T in initial 5 hours of onset of symptoms at a cutoff value of 90 μg/L.[19] Literature suggest that myoglobin rises immediately after the acute cardiac event , peaks at 12 hours and then decline. Though it is a sensitive marker, but its specificity is low.[20] Wu et al observed that the sensitivity of myoglobin is highest in initial 6 hours of onset of MI, whereas CKMB is sensitive marker for 48 hours and after 48 hours, Troponin I is the sensitive marker, and its sensitivity tend to decline after 72 hours.[21] Chiu et al documented sensitivity of myoglobin and CK-MB as 92.3% and 96.2%, respectively during 4 to 8 hours of onset of symptoms, whereas Troponin I and CK MB had sensitivity of >93% at 8 to 24 hours. However, the sensitivity of Troponin I remained highest after 72 hours of onset.[22]

CONCLUSION

Based upon the findings of present study, it could be concluded that Troponin I is the best marker for early diagnosis of acute coronary event, however, when the patient present early during the first 6 hours of onset of symptoms, myoglobin is a sensitive assay.

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