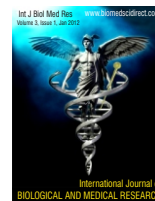


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Original Article

Sensitive Troponins Overpower Complex CPK-MB

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ABSTRACT

Annually, several million patients seek care in the emergency department because of chest pain or other symptoms suggesting an acute coronary syndrome (ACS), but only about 10% are subsequently confirmed to have acute myocardial infarction (AMI). Blood testing for biomarkers of myocardial injury plays an increasingly important role for the evaluation, diagnosis, and triage of patients with chest pain. The guidelines for the diagnosis of myocardial infarction (MI) have recently changed and prominently incorporate the results of cardiac marker testing in the clinical definition of MI. We review these updated guidelines for MI definition as it pertains to cardiac biomarker testing and further compare the differing biology and release kinetics of clinically relevant biomarkers. Finally, we define the contemporary use of cardiac biomarker testing for patients with chest pain, including appropriate integration of point-of-care testing into (POCT) day-to-day clinical use. Ideally, sensitive and specific serum myocardial markers could provide the basis for early detection as well as determine the status of reperfusion following thrombolytic therapy. The present study examined the utility of cardiac troponin I (cTnI), and CK-MB, for the sensitive and specific detection of AMI in 54 consecutive patients presenting to the emergency department (ED) with chest pain. In addition, cardiac troponin T (cTnT) samples were measured to following thrombolytic therapy to assess reperfusion. However, cTnI was the most specific serum marker (specificity 91.9% compared to CK-MB 85.6%). In the reperfusion study, cTnT and CK-MB's, relative increases were greater more significant. Within the reperfused group, the relative increase of cTnT was greater than CK-MB at 90 min following thrombolytic therapy. These findings show the clinical utility of cardiac-specific troponins as markers for the early detection of AMI and monitoring of reperfusion following thrombolytic therapy. With so many advances in the knowhow of myocardial pathology, it becomes mandatory to suggest new parameters and to compare them to highlight the biochemical support that has gone miles since its inception. The study population consisted of 70 patients. Patients from both sexes, with clinical history of typical chest pain for more than 30 minutes in duration with evidence of acute changes of myocardial infarction on ECG were included in the study. This study was conducted to compare the sensitivity of creatine kinase-MB (CK-MB), cardiac troponin T (CTnT) and cardiac troponin I (CTnI) for detection of AMI. Data analysis was performed with Statistical Package for Social Sciences 11.5 (SPSS 11.5). The sensitivity of CK-MB was 90% and 48% as compared to CTnT and CTnI respectively. The sensitivity of CTnT was 46% and 69% as compared to CK-MB and CTnI respectively while the sensitivity of CTnI was 100% as compared to both CK-MB and CTnT. It is concluded that cTnI is the preferred, more precise, dependable and cost effective serum marker for detection of AMI as compared to CTnT and CK-MB.

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1. Introduction

Current cardiac marker technologies, particularly the serum troponins, can now detect extremely small amounts of myocardial

necrosis (<1.0 g), which, in the setting of an ACS, may be associated with increased risk of complications compared with patients without myonecrosis. The increased risk associated with even minor amounts of myonecrosis has led to the concept that any amount of myocardial necrosis should be defined as a myocardial infarction² with the caveat that some patients previously designated as having severe stable or unstable angina may be diagnosed as having had a small AMI. This change in perspective

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will lead to an increase in the number of cases of AMI that are recognized (improved sensitivity). Presumably, fewer false-positive diagnoses will occur (improved specificity) owing to the improved performance of newer diagnostic technologies. Current criteria for the diagnosis of AMI using the joint ESC/ACC consensus definition are shown in Table 1

Table 1

Cardiology Definition of Acute, Evolving, or Recent Myocardial Infarction²

1. Typical rise and gradual fall (troponin) or more rapid rise and fall (creatinine kinaseMB) of biochemical markers with at least one of the following:

- Ischemic symptoms
- Development of pathologic Q waves on electrocardiogram
- Electrocardiographic changes indicative of ischemia (ST segment elevation or depression)
- Coronary artery intervention (e.g., coronary angioplasty)

2. Pathologic (morphologic) findings of an acute myocardial infarction

3. High sensitivity and specificity in blood samples
4. Rapid release into the blood following myocardial injury
5. Favorable kinetics permitting detection of acute coronary syndromes and myocardial necrosis in days after the person seeks care
6. Correlation between blood level of marker and extent of myocardial injury and prognosis
7. Commercial assays available that are rapid, simple, and automated
8. Role defined for marker in diagnosis and management that is based on findings of clinical studies in peer-reviewed literature

Table 2: Biochemical findings of study population

Variable (critical value)	Less than	More than
CK-MB (25 U/L)	45 (64.3%)	25 (35.7%)
CTnT (0.01 ng/ml)	21 (30%)	49 (70%)
CTnI (0.2 ng/ml)	8 (11.4%)	62 (88.6%)

The status of significant correlation and sensitivity of these biomarkers are given in tables 3 and 4 respectively.

Table 3: Correlation of CK-MB, CTnT and CTnI values

Correlation of	Statistically	p value
CK-MB and CTnT	Highly significant	<0.01
CK-MB and CTnI	Significant	<0.05
CTnT and CTnI	Highly significant	<0.01

Table 4: Diagnostic Sensitivity of CK-MB, CTnT and CTnI

Sensitivity of	Status
CK-MB Vs. CTnT	100%
CK-MB Vs. CTnI	40%
CTnT Vs. CK-MB	51%
CTnT Vs. CTnI	79%
CTnI Vs. CK-MB	100%
CTnI Vs. CTnT	100%

Table 1: General and clinical characteristics of study population

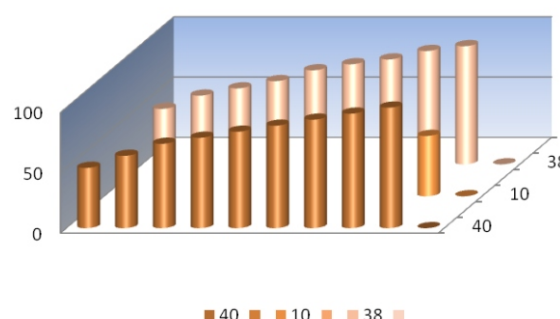
Variable	Number	Range	Mean \pm SD
Total number	100	---	---
Male	58 (82.9%)	---	---
Female	12 (17.1%)	---	---
Age (years)			
Duration of chest pain			
Within 4 hours	29 (41.4%)	28-70	53.7 \pm 10.3
After 4 hours	41 (58.6%)	---	---
Smokers	47 (67.14%)	---	---
Past history of			---
Hypertension (HTN)	27 (38.57%)	---	--
Diabetes mellitus (DM)	6 (8.57%)		
HTN & DM	10 (14.28%)		
Nil	27 (38.57%)		
Family history of			
HTN, DM & IHD	40 (57.14%)	---	--

Table—2

Features of an "Ideal" Blood-Based Cardiac Marker

1. High concentration in the myocardium
2. Absence from nonmyocardial tissue

SENSITIVITY OF CK--MB cTnT cTnI



MATERIAL AND METHODS

This cross-sectional study was conducted at Emergency department of Cardiology of GGS Medical College, Faridkot from session 2012---13. The study population consisted of 54 patients & 46 as controls. Diagnosed cases of AMI from both sexes, with clinical history of typical chest pain for more than 30 minutes with evidence of acute changes of myocardial infarction on ECG were included. All the patients/relatives ratified the informed consent form. The patients with history of previous myocardial infarction, chronic renal failure, muscle injury, surgery, muscle disease etc. were excluded.

Ten ml of venous blood was drawn at the time of admission. After centrifugation, the serum was preserved at -20 °C. The serum was analyzed for CTnI by solid-phase, chemiluminescent immunometric assay⁸, with Immulite supplied by DPC (Siemens). The CTnT was analyzed by electrochemiluminescence immunoassay (ECLIA) based upon sandwich principle⁹ with Elecsys 2010 analyzer supplied by Roche. The serum was also analyzed for CK-MB Biotech ELISA model¹⁰

DISCUSSION

Approximately 20 - 23% of patients presenting at emergency cardiology cases with chest pain have coronary disease¹¹. This cross-sectional study was conducted to evaluate the "Diagnostic significance of CTnI, CTnT and CK-MB in acute myocardial infarction (AMI).

There was a highly significant correlation between reference concentrations of CK-MB (42.8% and CTnT (65.40%) (P value= 0.00). This observation complements the study of Mohler et al (1998)¹². According to their study 62% cases showed increased CK-MB concentration and 90% had increased CTnT levels within 4 hours of admission (P value= 0.067). The observation made by Majeed et al (2002)¹³ that CTnT is an early indicator of AMI and is superior to CK-MB in diagnosis of AMI also complements this study.

There was a significant correlation between reference concentrations of CK-MB (42.8%) and CTnI (65.40%) (P value= 0.04) in this study. The CTnI was positive in 74.6% cases of this study with the mean duration of chest pain of 5.18 hours. This observation is in accordance with the observation made by Chiu et al (1999)¹⁴ with a positive value of 80.8% cases when the blood was taken and analyzed in the interval 4 - 8 hours after the onset of chest pain. The sensitivity of CTnI as 74.6% for detection of AMI mentioned by Apple et al (1999)¹⁵ may be due to the time difference (0 to 6 hours after presentation to emergency room) and higher limit value of 1.5ng/ml. The value of CK-MB mentioned by Apple et al (1999)¹⁵ and Chiu et al (1999)¹⁴ differ from the observation made in this study (77.5% and 96.2% Vs 35.7%). This disparity in observation is due to the fact that CK-MB in this study was analyzed by automated analyzer method, which inhibits the CK-M sub unit without affecting the activity of CK-B subunit. The activity measured by this method and multiplied with a factor of 2

reflects the activity of CK-MB. Both the above mentioned studies measured CK-MB mass by sandwich-type ELISA immunoassay using anti-CK-MB and anti-CM-MM monoclonal antibodies with the upper reference limit of (7.5ng/ml & 5ng/ml) which is a better detection value. Serum cardiac marker should have high sensitivity and high specificity so that the diagnosis of MI is not missed. The present study found a statistically highly significant increase in cardiac troponin-I levels in subjects with MI at the time of admission to the cardiac ICU when compared to CK-MB, cardiac troponin-I showed a high diagnostic efficiency of 97%, with a very sensitivity (96%) and specificity (98%) and positive predictive value (96%).

There was a highly significant correlation between reference concentrations of CTnT and CTnI (P value= 0.01) in this study. This observation is in accordance with the observation made by Chiu et al (1999)¹⁴ with a positive value of CTnI in 80.8% cases.

CONCLUSION

It is concluded that CTnT is the preferred, more precise, dependable and cost effective serum markers to rule out AMI as compared to CTnI and CK-MB.

Recommendations: It is high need of the hour that whatever we could achieve is just the starting a chapter. I would be satisfied if this small attempt can be the starting of a new wave of diagnosis

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