Research Article

Comparative status of glycogen phosphorylase BB, myoglobin, and CK-MB for early diagnosis of acute myocardial infarction

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ABSTRACT

Background: Early and correct diagnosis of acute myocardial infarction (AMI) is of utmost importance to enable the immediate and intensified treatment which consequently reduces the mortality due to AMI. Under this condition, cardiac markers are used to evaluate heart functions. Glycogen phosphorylase BB (GPBB) is new marker invented to diagnose AMI within 4 h of onset of chest pain. **Objective:** The objective of the study is to compare the sensitivity and specificity of GPBB with myoglobin (MB) and creatine kinase MB (CKMB) within 4 h after the onset of chest pain. **Materials and Methods:** This study includes 150 AMI patients and 100 normal healthy individuals as controls. In all the cases and controls, serum GPBB and MB were measured by enzyme-linked immunosorbent assay, whereas CK-MB was measured by diagnostic kit supplied by ERBA. **Results:** The sensitivity and specificity of GPBB were greater than MB and CKMB within 4 h after the onset of chest pain. **Conclusion:** GPBB was the most sensitive and specific cardiac marker compared to MB and CKMB in AMI patients during the first 4 h after the onset of chest pain. Hence, GPBB can be used for the early diagnosis of AMI.

KEY WORDS: Glycogen Phosphorylase BB; Acute Myocardial Infarction; Myoglobin; Creatine Kinase Myoglobin

INTRODUCTION

Chest pain is one of the most common complaints among patients presenting to cardiology or emergency department.[1,2] Coronary artery disease is one of the cardiac diseases leading to acute myocardial infarction (AMI), angina, sudden death, and many other complications. The complications of acute myocardial infarction are maximum in the first few hours and decrease with passage of time.[3] Early accurate diagnosis and treatment of AMI can reduce the mortality and morbidity.

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The majority of deaths due to AMI occur during the first 4 h, if AMI cases are diagnosed and treated effectively during the first hour (so-called golden hour), the mortality can be reduced from 9% to 3%, but if delayed for 3-4 h, mortality can be 5 times higher.[4]

Diagnosis of an acute coronary syndrome like AMI is based on the assessment of risk factors, careful and rapid assessment of electrocardiogram (ECG) and measurement of cardiac enzymes.[1,5] At present, creatine kinase-MB isoenzyme (CKMB), MB and cardiac troponins T and I (cTnI & cTnT) are used in the diagnosis of AMI.[6] However, these cardiac markers are also not satisfactory for the early diagnosis of AMI after the onset of chest pain. MB is an early and sensitive marker of cardiac cell damage but lacks specificity.[7] CKMB begins to increase between 3 and 5 h after the onset of myocardial infarction.[8] CK-MB though more specific for cardiac injury, lacks early sensitivity.[6]

Glycogen phosphorylase (GP) is bound to glycogen in sarcoplasmic reticulum and catalyzes the first step of glycogenolysis after activation, which involves the separation of glucose-1-phosphate from glycogen.[9] It has three major isoenzymes: BB (brain), MM (muscle), and LL (liver). GPBB is also found in heart muscle, including human myocardium.[10] During myocardial ischemia, activation of GPBB results in an increase in glycogen degradation. Thus, GPBB which is connected to glycogen in a macromolecular complex that is structurally bound to sarcoplasmic reticulum believes to release from glycogen and then enters the bloodstream via the T-tubulus system within 1-4 ho of onset of AMI.[11-13] Hence, this study has been aimed to compare the sensitivity and specificity of GPBB with those of MB and CKMB within 4 h after the onset of chest pain.

MATERIALS AND METHODS

This study has been conducted in the Department of Biochemistry and Cardiology, G.R. Medical College and J.A. Group of Hospitals, Gwalior. The study included 250 subjects of age group 35-75 years. Out of them, 100 were normal healthy age-matched controls and 150 of them were patients of AMI admitted to the Cardiology Department of J.A. Group of Hospitals. Each patient undergone clinical and laboratory evaluation, which included the detailed clinical history, clinical examination, ECG, chest X-ray, routine blood investigations and cardiac biomarkers (CK-MB and cTnT [card test]) as a part of routine assessment and diagnosis of AMI was made after review of all the above information by a cardiologist.

Inclusion Criteria

The patients arriving to the cardiology department within 4 h of onset of chest pain.

Exclusion Criteria

The patients arriving to hospital after 4 h of onset of chest pain, those with diabetes mellitus, chronic muscle disease, renal disease, liver disease, recent surgery, implanted pacemaker, autoimmune disease, and arthritis.

This study has been approved by the Institutional Ethical Clearance Committee and written informed consent was obtained from all the study participants.

About 5 ml of venous blood sample was taken from AMI cases (within 4 h of chest pain) and controls under all aseptic precautions. Serum was separated and kept at −20°C until the analysis was performed. Levels of MB were measured by enzyme immunoassay using life diagnostics kit, whereas CKMB was measured by the diagnostic kit supplied by ERBA. Normal reference levels of MB and CKMB were accepted as 12-92 ng/ml and <25 U/L, respectively. Levels of GPBB were measured by enzyme-linked immunosorbent assay using QAYEE-BIO for life sciences kit. Normal reference level of GPBB was accepted as 7-18.47 ng/ml (established according to the values observed in control subjects with the help of StatsDirect 3).

Statistical Analysis

Data are presented as mean ± standard deviation values. The statistical differences between cases and controls were determined by student independent sample *t*-test. Data analyses were performed with the Statistical Package for the Social Sciences, version 21.0 (SPSS, Chicago, Illinois, USA). Sensitivity, specificity, positive and negative predictive values (PPV and NPV) were calculated, and receiver operating characteristic (ROC) curve analysis was performed with the help of StatsDirect 3.

RESULTS

A total of 250 subjects were included in this study. Of these, 150 were cases of AMI and rest 100 were controls. Table 1 and Figure 1 show the mean levels of cardiac markers in AMI cases and controls. The mean levels of cardiac markers GPBB, MB and CKMB activity were higher in AMI cases when compared to that of controls and were statistically significant at $P < 0.001$. Table 2 shows sensitivity, specificity, PPV and NPV of GPBB which were greater than MB and CKMB. Table 3 shows area under the curve (AUC) of GPBB, MB, and CKMB. The AUC of GPBB was greater than MB and CKMB. Figures 2-4 show ROC curve analysis of GPBB, MB, and CKMB, respectively.

DISCUSSION

Myocardial ischemia results from the reduction of coronary flow to such an extent that supply of oxygen to the myocardium does not meet the oxygen demand of myocardial tissue. When this ischemia is prolonged and irreversible, then myocardial cell death and necrosis occur which is defined as myocardial infarction.[14] AMI is the major cause of mortality and long-term morbidity in the modern world. Early and correct

Table 1: Mean levels of cardiac markers in AMI cases and controls

Parameters	Mean±SD	
	Controls	AMI cases
GPBB (ng/ml)	11.79±2.82	61.59±33.85**
MB (ng/ml)	62.79±26.38	184.77±65.92**
CKMB (U/L)	19.21±5.71	27.64±13.34**

**Highly significant (P<0.001). GPBB: Glycogen phosphorylase BB, MB: Myoglobin, CKMB: Creatine kinase MB, AMI: Acute myocardial infarction, SD: Standard deviation

Table 2: Sensitivity, specificity, PPV and NPV of cardiac markers within 4 h of onset of AMI

Parameters	Cut off	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
GPBB	≥19	96.00	98.00	98.63	94.23
MB	≥92	90.66	85.00	90.07	85.86
CKMB	≥25	34.00	86.00	78.46	46.49

GPBB: Glycogen phosphorylase BB, MB: Myoglobin, CKMB: Creatine kinase MB, AMI: Acute myocardial infarction, PPV: Positive predictive value, NPV: Negative predictive value

Table 3: The ROC curve analysis of cardiac markers within 4 h of onset of AMI

Parameters	AUC	Standard error	*P* value	CI	
				Lower limit	Upper limit
GPBB	0.995	0.002	0.000	0.989	0.999
MB	0.963	0.009	0.000	0.944	0.982
CKMB	0.697	0.032	0.000	0.633	0.762

GPBB: Glycogen phosphorylase BB, MB: Myoglobin, CKMB: Creatine kinase MB, AMI: Acute myocardial infarction, ROC: Receiver operating characteristic, AUC: Area under the curve, CI: Confidence interval

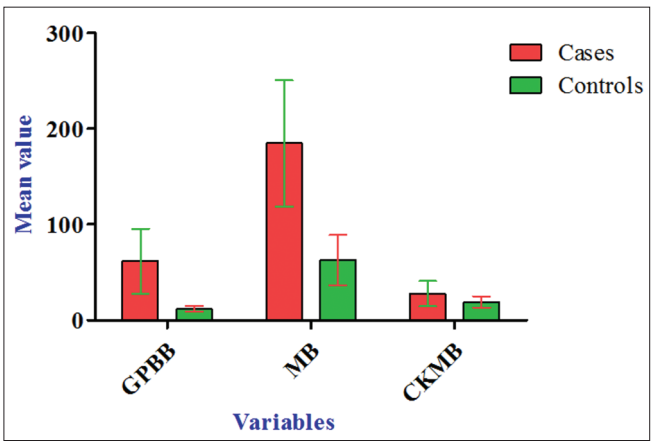

Figure 1: Status of cardiac markers in acute myocardial infarction cases and controls

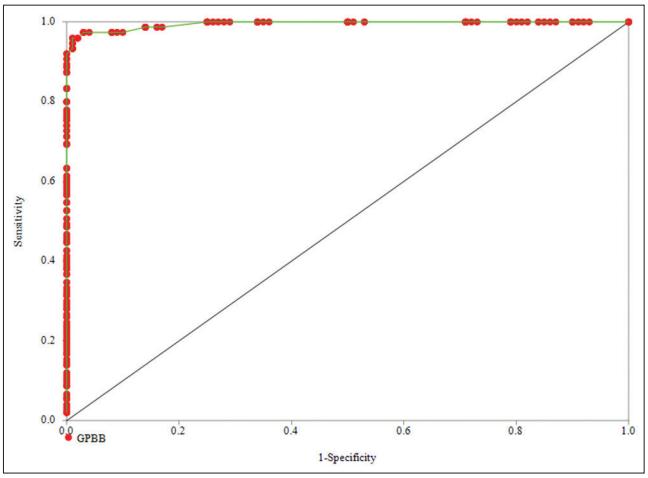

Figure 2: The receiver operating characteristic curve analysis of glycogen phosphorylase BB within 4 h of onset of acute myocardial infarction

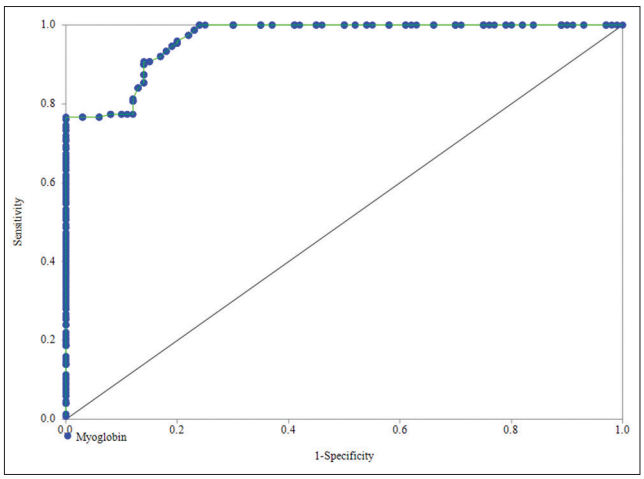

Figure 3: The receiver operating characteristic curve analysis of myoglobin within 4 h of onset of acute myocardial infarction

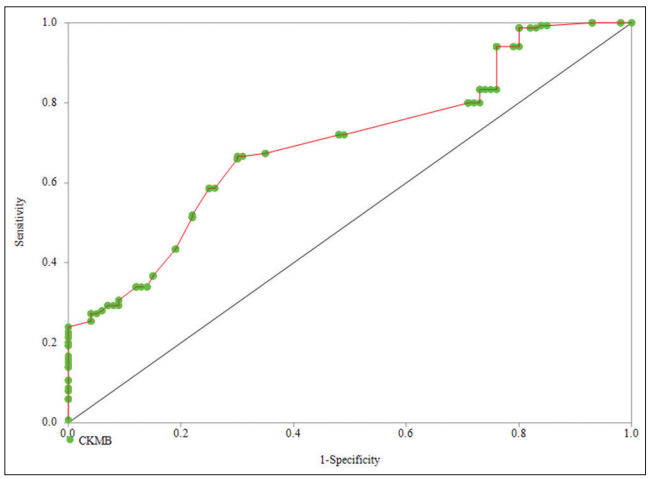

Figure 4: The receiver operating characteristic curve analysis of creatine kinase MB within 4 h of onset of acute myocardial infarction

diagnosis is of utmost importance to enable the immediate and intensified treatment which consequently reduces the mortality.[15]

Although CKMB, MB, and cardiac troponin starts to rise early after AMI, lack sensitivity and specificity. Now, several

alternative markers - for example, ischemia modified albumin,[16] heart fatty acid binding protein.[17] and GPBB[10] - have been analyzed for the clinical diagnosis of myocardial ischemia within the first 1-3 h after the onset of chest pain. GPBB is bound to glycogen in sarcoplasmic reticulum and catalyzes the first step of glycogenolysis after activation, which involves the separation of glucose-1-phosphate from glycogen.[11] During myocardial ischemia, activation of GPBB results in an increase in glycogen degradation. GPBB isoenzyme is released into bloodstream via the T-tubules system with the peak value within the first 4 h after the onset of chest pain.[11,18] The early release of GPBB into the blood is a common result of the combination with of escalated glycogenolysis and increased permeability of cell membranes which is typical for myocardial ischemia and necrosis.[12,13,19]

In this study, we found that GPBB was the most sensitive and specific biomarker to detect myocardial infarction when compared to MB and CKMB at the first 4 h (Table 2). This finding is in agreement with Rabitzsch et al.[20] and Cubranic et al.[21] who also reported the highest sensitivity of GPBB in the early hours of chest pain. MB which appears in the blood early after AMI lacks specificity because it also increases in other muscular disorders and cannot be distinguished from that released from heart.[6] Moreover, the sensitivity and specificity of MB in our study found to be less than GPBB (Table 2). CKMB though increased in AMI within 4 h of chest pain, had low sensitivity and specificity (Table 2) as compared to GPBB and MB.

ROC curve analysis showed GPBB had the highest area under curve followed by MB and CKMB (Table 3). The better diagnostic value of GPBB compared to MB and CKMB may be due to early release from the injured myocardium.

LIMITATIONS

In this study, cTnT was estimated qualitatively and qualitative estimation detects cTnT levels above a certain level only. Another limitation of the present study is results are based on single-center only.

CONCLUSION

GPBB was the most sensitive and specific cardiac marker compared to other tested cardiac markers MB and CKMB in AMI patients during the first 4 h after the onset of chest pain. Hence, GPBB can be used for the diagnosis of AMI within 4 h of chest pain.

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