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Journal of Advanced Scientific Research

Available online through http://www.sciensage.info

ISSN
0976-9595
Research Article

COMPARATIVE STUDY OF GLYCOGEN PHOSPHORYLASE BB AND CREATINE KINASE MB AT FIRST HOUR AFTER OF ACUTE MYOCARDIAL INFARCTION

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ABSTRACT

Acute myocardial infarction (AMI) results from the intervention of blood supply to the heart, due to this heart cells to die. It is the leading cause of mortality and morbidity in present days. Chest pain is the most common symptom in majority of the patients with AMI. Cardiac markers are released during chest pain. So there is an emerging need to detect for early, specific cardiac markers. Glycogen phosphorylase BB (GPBB) is potential marker of chest pain and myocardial infarction. Objective of the study was to compare the sensitivity and specificity of GPBB and CKMB at 1st hour after of acute myocardial infarction. Blood samples from 80 AMI patients and 50 age and sex matched healthy controls were collected and analyzed for cardiac enzymes CK-MB (by automated analyzer) and GPBB (by ELISA reader). GPBB had released after 1 hour and higher peak value after 3 h of chest pain in AMI patients. The receiver operating characteristic curves was significantly greater for GPBB when compare with CKMB in AMI patients. GPBB is considerably sensitive and specific at the first hour of admission in AMI patients. It is elevated in all of the AMI patients.

Keywords: Acute Myocardial Infarction, Chest pain, Glycogen Phosphorylase BB, Creatine kinase MB

1. INTRODUCTION

Acute myocardial infarction is the "loss of heart function due to insufficient blood flow to the heart compared to its need. It is caused by obstructive changes in the circulation to the heart [1]. It is the biggest health problem throughout world [2]. AMI is one of the most common diseases among the developing countries [3]. A large number of people die every year due to this grave disease [4]. Diabetes Mellitus, Hypertension, Smoking, Age and Gender have been found as powerful risk factors of AMI. It has also been observed that infarction increases as the age of the patients increases. Another study shows that patients less than the age of 40 is 10% of all the cases [5-6]. A study shows that the incidence of this disease was more frequent among the patients of age group 50-59 years [7]. There are many symptoms but the most common is chest pain, which may travel into the shoulder, arm, back, neck or jaw. This type of pain always starts from the center or left side of the chest and remains for few minutes. The onset of symptoms in acute myocardial infarction is usually gradual, over several minutes and rarely instantaneous [8-10]. The majority of passing due to AMI occur during the first 4 h, if these 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 [11]. There are many cardiac markers like LDH, AST, CKMB, TnT, TnI but not satisfactory for the early diagnosis of AMI after the onset of chest pain. CKMB begins to increase between 3 and 5 h after the onset of myocardial infarction it is more specific for cardiac injury, lacks early sensitivity [12-13]. Another new marker Glycogen phosphorylase BB has been discussed in recent year as a potentially useful biomarker in the early detection of ischemia [14]. It is a glycogenolytic enzyme that plays an essential role in the regulation of carbohydrate metabolism. It catalyzes the first step of glycogenolysis, in which glycogen is converted to glucose-1-phosphate [15]. Three different isoenzymes of glycogen phosphorylase (GP) exist; GPMM (present in muscles), GPLL (liver) and GPBB (brain and heart muscles). Glycogen phosphorylase-BB appears to be released into the circulation 1-4 h after myocardial injury [16-17]. Data regarding the diagnostic usefulness of GPBB for early diagnosis of AMI is very limited. Hence, we planned this study with the aim to assess the diagnostic accuracy of GPBB and CKMB in AMI patients admitted to cardiology department of G.R. Medical College, Gwalior. In addition, we compared the

sensitivity and specificity of GPBB with those of CKMB at 1h, 3h and 6h of chest pain.

2. METHODOLOGY

The study has been carried out in the Department of Biochemistry and Cardiology, G.R. Medical College and J.A. Group of Hospitals, Gwalior. In this study we included 130 subjects of age group 30-70 years. Out of them, 50 were normal healthy age-matched controls and 80 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. 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 (at 1hr, 3hr and 6hr of chest pain) and controls under all aseptic precautions. Serum was separated and kept at -20°C until the analysis was performed. Levels of GPBB were measured by enzyme-linked immunosorbent assay using QAYEE-BIO for life sciences kit whereas CKMB was measured by the diagnostic kit supplied by ERBA. Data are presented as mean ± standard deviation values. The statistical differences between cases and controls were determined by student independent sample *t*-test. Sensitivity, specificity, positive and negative predictive values (PPV and NPV) was performed with the Statistical Package for the Social Sciences, version 21.0 (SPSS, Chicago, Illinois, USA).

3. RESULTS

A total of 130 subjects were included in this study. Of these, 80 were cases of AMI and rest 50 controls.

Table 1: Mean values of CKMB and GPBB in patients and controls

Groups		CKMB	GPBB
Controls (50)		19.55±5.43	13.78±3.88
AMI Patients (80)	At 1 hour	19.57±3.24^{NS}	47.36±18.90**
	At 3 hour	22.93±8.10*	82.08±23.67**
	At 6 hour	78.70±12.09**	63.65±14.67**

Table 1 show the mean levels of cardiac markers in AMI cases and controls. The mean levels of cardiac markers GPBB and CKMB were higher in AMI cases when compared to controls and were statistically significant at $P < 0.001$. Table 2 shows sensitivity, specificity, PPV and NPV of GPBB which were greater than CKMB at 1hr, 3hr and 6hr.

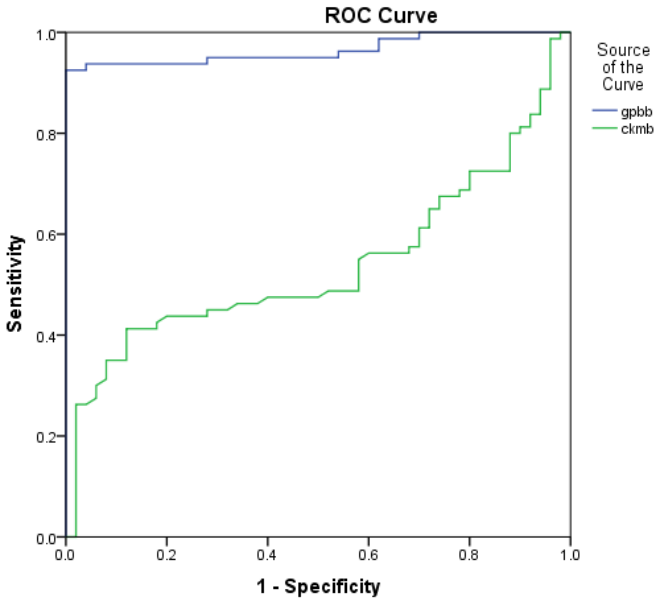

Fig. 1: Receiver operating characteristics curve analysisfor GPBB and CKMB level within 1 hour in acute myocardial infarction

Table 2: Sensitivity, Specificity, PPV and NPV of cardiac markers at 1st, 3rd and 6th hour after onset of AMI patient

Parameters	Hours	Cutoff value	Sensitivity	Specificity	PPV	NPV
GPBB	At 1 hour	≥19	93%	94%	96.15%	90.38%
	At 3 hour	≥19	100%	94%	96.39%	100%
	At 6 hour	≥19	97.5%	94%	96.3%	95.92%
CKMB	At 1 hour	≥25	2.5%	64%	10%	29.09%
	At 3 hour	≥25	23.75%	64%	51.35%	34.41%
	At 6 hour	≥25	88.75%	64%	79.78%	78.05%

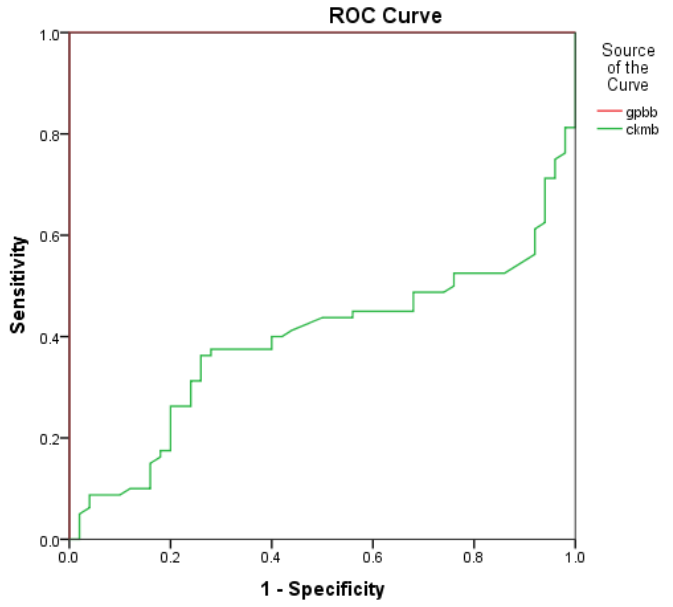

Fig. 2: Receiver operating characteristics curve analysis for GPBB and CKMB level within 3 hour in acute myocardial infarction

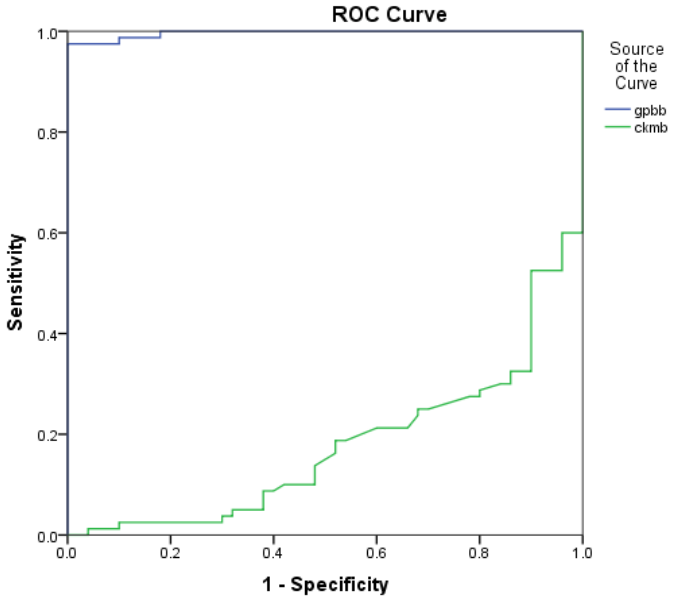

Fig. 3: Receiver operating characteristics curve analysis for GPBB and CKMB level within 6 hour in acute myocardial infarction

4. DISCUSSION

Acute Myocardial Infarction (AMI) occurs during the period when circulation to a region of the heart is obstructed and necrosis ensues. AMI is characterized by severe pain (angina pectoris), frequently associated with pallor, perspiration, nausea, shortness of breath, and dizziness. A precursor state of AMI is myocardial ischemia, in which obstruction of a coronary artery leads to severe oxygen deprivation of the myocardium prior to necrosis [18]. Acute Myocardial Infarction more commonly known as a heart attack is a medical emergency, the leading cause of death for both men and women all over the world. It is due to death of heart muscle from the sudden blockage of a coronary artery by a blood clot or coronary thrombosis [19].

Early and correct diagnosis is of utmost importance to enable the immediate and intensified treatment which consequently reduces the mortality [20]. Cardiac troponins, CK-MB and myoglobin are the commonly used cardiac markers that are used for the detection of AMI [21]. Though these markers are start to rise after the onset of AMI, lacks sensitivity and specificity. In addition to this, another early marker of cardiomyocyte damage, GPBB has been introduced in patients with ACS. Glycogen phosphorylase is a key enzyme taking part in glycogenolysis. Three isoenzymes exist, known as BB (brain andheart), MM (muscle) and LL (liver), that have different functionand immunologic properties [22, 23]. The GP-BB is associated with glycogen in the sarcoplasmic reticulum (mainly in cardiomyocytes) and catalyzes the initial step of glycogenolysis, i.e. release of glucose-1-phosphate from glycogen. Glycogen phosphorylase from damaged myocardial cells may indicate initiation of glycogenolysis resulting from acute myocardial ischaemia. Low oxygen level in the myocardium induces glycogenolysis leading to loss of plasma membrane integrity and extracellular leak of soluble intracellular proteins. This process is accompanied by a rapid increase in serum GP-BB level in patients with an acute MI, prior to the rise of other biomarkers such as creatinine kinase, CK-MB, myoglobin and troponin T [17].

In the present study, we have evaluated the cardiac markers viz. GPBB and CKMB in AMI patients at 1h, 3h and 6 h of acute chest pain. GPBB was significantly increased in AMI patients at 1h, 3h and 6h of chest pain compared to controls. Though the level of GPBB was increased during early hours, it starts to decrease from 6 h onwards. These increased levels of GPBB during early hours of AMI is due to escalated glycogenolysis and increased permeability of cell membranes which is typical for myocardial ischemia and necrosis [24]. Similarly, we found the increased levels of CKMB in AMI patients at 3 h and 6 h of chest pain as compared to the controls. There was greater increase in the level of CKMB at 6 h of cheat pain than 3 h of chest pain in AMI patients as compared to controls. However, we did not find any

significant difference in the level of CKMB in AMI patients at 1 h of chest pain when compared to control subjects. This is because CKMB appears in blood 3-5 hours after an AMI. Though CKMB begins to increase between 3 and 5 hours after the onset of AMI and reaches to peaking at 16 to 20 hours, it is not perfectly specific to cardiac injury as it increases during massive musculoskeletal disease [25, 26].

The sensitivity and specificity of GPBB were 93% and 94% at 1 hour, 100% and 94% at 3 hour and 97.5% and 94% at 6 hours of chest pain. The greatest sensitivity and specificity of GPBB were observed at 3 hours of chest pain. The sensitivity and specificity of CKMB were 2.5% (almost nil) and 64% at 1 hour, 23.75% and 64% at 3 hour and 88.75% and 64% at 6 hour of chest pain. Indeed, the sensitivity and specificity of GPBB were greater than the CKMB during early hours of chest pain (*i.e.* at 1 hour, 3 hour and 6 hour). Though CKMB has greatest sensitivity and specificity at 6 hour of chest pain, it was lower as compared to GPBB, indicating that GPBB is the better cardiac marker than CKMB for early diagnosis of AMI. Mair et al., showed that among all biomarkers tested on admission, including CK-MB, CK-MB mass, myoglobin, troponin T and GP-BB, only the latter was significantly increased in the majority of patients with unstable angina [27]. Peetz et al. reported that the GP-BB was more sensitive and specific than myoglobin and CK-MB mass (95.5-100% *vs* 85-95% and 71.4-91.3%, respectively) when measured within initial 6 h [28]**.** GP-BB may be considered as a marker of ischaemia or infarction and not only established necrosis [29]**.** Similarly, Cubranic et al. concluded that GPBB may contribute to early diagnosis of ischemic heart disease, with sensitivity of 0.97 and specificity of 0.81 in patients with AMI admitted within 3 hours of onset of the symptoms [30]. Recently in the year 2018, Singh et al reported greater sensitivity and specificity of GPBB in patients of AMI within 4 h after the onset of chest pain [31]. Our results showed that the GPBB may be considered a really useful early biomarker of myocardial infarction. Hence the GPBB will consider as a marker of early biomarker for AMI diagnosis.

5. CONCLUSION

In conclusion, GPBB can be used as an early biomarker for the diagnosis of AMI since it starts to release in blood circulation within 1 hour of AMI due to hypoxia. Moreover, it has got high sensitivity, specificity, positive predictive value and negative predictive value within 1 hour of AMI. This study is continued to prove the sensitivity of glycogen phosphorylase BB in early or 1 hour of AMI in large number of samples.

Compliance with ethical standards

This study was approved by the Institutional Ethical Committee, Gajra Raja Medical College, Gwalior (M.P.). Informed written consent was obtained from all the patients.

Funding

There was no financial support.

Conflict of interest

No Conflict of Interest.

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