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ACUTE MYOCARDIAL INFARCTION;
SIGNIFICANCE OF 1ST SET OF CK-MB IN DIAGNOSIS

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ABSTRACT... Objective: To assess the reliability of the first set of CK-MB in establishing diagnosis of acute myocardial infarction in different subgroups of the patients according to their time of presentation after symptom onset. **Material and methods:** Prospective observational study was carried out in Armed Forces Institute of Cardiology/National Institute of Heart Diseases (AFIC/NIHD) Rawalpindi, from April to September 2005. We studied 300 consecutive cases presenting with typical electrocardiographic changes of acute ST Elevation Myocardial Infarction to the Emergency & Reception department of AFIC/NIHD (confirmed later on as acute STEMI with raised serial serum cardiac enzymes levels). We documented values of CK-MB at the time of presentation in different subgroups of the patients according to duration of symptom onset. **Results:** This study was predominantly male dominated (approximately 78%), with a mean age of 58 +11 years. Majority of patients i.e.216 (72%) presented within first 6 hours of onset of symptoms, 60 (20%) within 6-12 hrs, 6 (2%) within 12-24 hrs and 18 (6%) after 24 hrs of onset of symptoms. Overall serum cardiac enzymes sent at the time of presentation revealed that 126 (42%) patients had normal CK-MB (<24U/L) and another 66 (22%) had a minimal rise in CK-MB (25-49 U/L). Only 108 (36%) patients 3 had serum CK-MB levels more than double the normal value. Amongst the patients presenting within the first 6 hours of onset of symptoms, 104 (48%) had normal CK-MB values, 48 (22%) had a minimal rise (<49 U/L) and only 64 (30%) had a significant rise in CK-MB levels i.e. more than double the normal values or more than 5% of CK value. Out of 60 patients who presented within 6-12 hours of onset of symptoms, 54(90%) had more than double the normal value of CK-MB and 6(10%) had mild rise in CK-MB. All the patients (100%) who presented within 12-24 hours of onset of symptoms i.e. 6(2%) and more than 24 hours 18(6%) had significant rise in CK-MB. **Conclusion:** This study shows that the first set of CK-MB alone has very little value in diagnosing acute myocardial infarction especially in the patients who presented within 6 hours of onset of symptoms. Reliability of CK-MB in diagnosing acute myocardial infarction greatly improves to the maximum in those patients who present more than six hours after symptom onset.

Key words: CK-MB, Acute STEMI, Symptoms duration

INTRODUCTION

In practice, the patient's symptoms are frequently atypical for coronary artery disease, and only 40% to 60% of patients with acute myocardial infarction (AMI) have diagnostic electrocardiographic abnormalities[1,2]. Hence cardiac-specific serum markers are often the final arbiter by which AMI is diagnosed or excluded because of these limitations. Currently no cardiac-specific serum

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marker meets all the criteria for an "ideal" marker of AMI. No test is both highly sensitive and highly specific for acute infarction within 6 hours following the onset of chest pain, the time frame of interest to most emergency physicians in making diagnostic and therapeutic decisions. The diagnosis of AMI can not be excluded on the basis of a single cardiac marker value obtained within a few hours after symptom onset. The total CK level is far too insensitive and nonspecific a test to be used to diagnose AMI. It retains its value, however, as a screening test, and serum of patients with abnormal total CK values should undergo a CK-MB mass assay. Elevation in CK-MB is a vital component of ultimate diagnosis of AMI. The test is highly specific, however, and an abnormal value (particularly when it exceeds 5% of the total CK value) at any time in a patient with chest pain is highly suggestive of an AMI. The facility to do measurement of CK-MB fraction for ultimate diagnosis of chest pain is now freely available in most of our hospitals.

The objective of this study was to assess the reliability of the first set of CKMB in diagnosing acute MI in a patient presenting at varying time intervals after symptoms onset to the emergency departments in our set up.

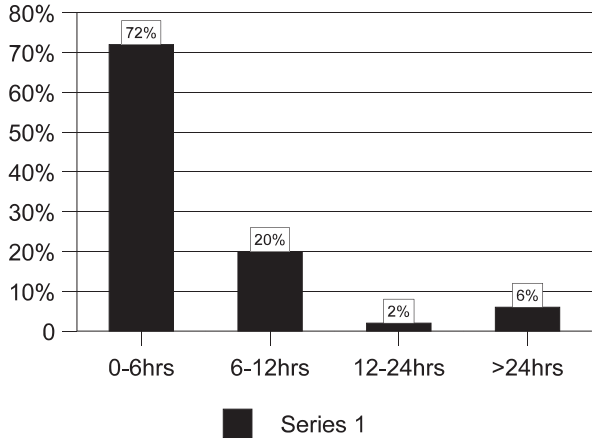
MATERIAL AND METHODS

The 300 consecutive cases presenting to the emergency reception of AFIC/NIHD with typical electrocardiographic changes of acute ST Elevation Myocardial Infarction were studied. We recorded particulars, duration of symptoms and the values of serum CK-MB at the time of presentation in different subgroups of the patients according to their time of presentation after symptom onset. The cases were followed for 24 hours after admission to confirm acute STEMI with rise in serial cardiac enzymes levels.

RESULTS

Amongst the 300 patients studied, 234(78%) were male with a mean age of 58 +11 years. The ages ranged between 42 to 82 years. Majority of patients i.e.36 (72%) presented within first 6 hours of onset of symptoms, 60 (20%) within 6-12 hrs, 6 (2%) within 12-24 hrs and 18 (6%) after 24 hrs of onset of symptoms as shown in figure 1.

Fig-1. Duration of onset of symptoms



Overall serum cardiac enzymes sent at the time of presentation revealed that 126 (42%) patients had normal CK-MB (<24U/L) and another 66 (22%) had a minimal rise in CKMB (25-49 U/L). Only 108 (36%) patients had serum CK-MB levels more than double the normal value or more than 5% of CK value as shown in figure 2.

Fig-2. CK-MB level in acute STEMI

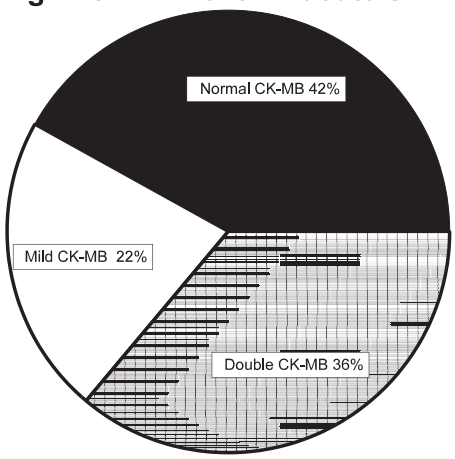
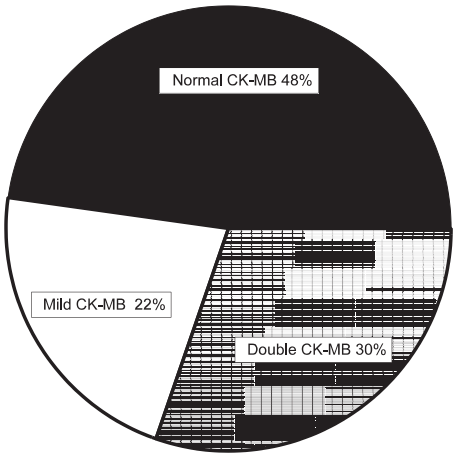


Fig-3. CK-MB during six hours presentation



DISCUSSION

Prompt and accurate diagnosis of patients presenting to the emergency department with chest pain is one of the greatest challenges that emergency physicians regularly face. Myocardial cell death can be recognized by the appearance in the blood of different proteins released into the circulation from the damaged myocytes: myoglobin, cardiac troponin T and I, CK, LDH, as well as many others[3]. Myocardial infarction is diagnosed when blood levels of sensitive and specific biomarkers such as cardiac troponin or CKMB are increased in the clinical setting of acute myocardial ischemia[4]. The classic criteria's for the diagnosis of acute myocardial infarction especially in our set up are clinical history, characteristic electrocardiographic findings and diagnostic elevation in the serum creatine kinase MB fraction (CK-MB). At times, these are difficult to apply in the emergency setting. Emergency physicians must have some understanding of the limitations posed by the biokinetic properties of cardiac markers before employing the tests to make patient management decisions.

Creatine kinase (CK) is found not only in cardiac muscle, but also in skeletal muscle, brain, and kidney, and in lesser amounts in the lung and the gastrointestinal tract[3]. Because the molecule is too large to enter the capillaries, CK is transported from cardiac muscle by the cardiac lymphatic system to eventually be released into the serum. Because of this lymphatic transport, there is an inevitable delay between release from the tissue and increases in serum concentration. Increases in serum CK are characteristically detectable within 3 to 8 hours of MI. The enzyme peaks at 12 to 24 hours after injury, and values typically return to baseline within 3 to 4 days[5]. Although wide ranges of diagnostic accuracy have been reported, the more reliable studies of total CK values obtained at the time of emergency department presentation show sensitivity of only about 40% and specificity of about 80%[5, 6]. When only total CK values obtained at 4 to 12 hours after chest pain onset are considered, the sensitivity increases to about 50% but does not rise much further with longer symptom durations[6]. The peak value of total CK has limited ability to predict the size of the infarction[7].

Among patients with an AMI, diagnostic elevations in CK-MB are seen in about one half of patients at 3 hours following the onset of chest pain[6,8].The sensitivity of a single CK-MB determination in diagnosing AMI depends heavily on the time elapsed since chest pain onset. Measured within 4 hours from the time of symptom onset, the sensitivity of CK-MB is poor, as low as 25% in some studies and about 50% in most[8-12]. When measured at 4 hours after symptom onset, test sensitivity rises to the range of 40% to 76%, and as the time from symptom onset approaches 4 to 12 hours, the sensitivity further increases to 60% to 100%. The conclusion that these entire studies share is that although the sensitivity of CK-MB improves significantly over time, it is extremely unreliable within 4 hours of symptom onset and at no point is a single determination sensitive enough to allow an AMI to be excluded which is the same conclusion drawn from our study. The specificity of CK-MB is greater than 85% and has achieved 100% in some studies[8-12]. False-positive test results can be seen in many of the same conditions that cause elevation in total CK values. Myocardial cells are by far the most abundant potential sources of CK-MB, and the appearance of CK-MB in the serum is therefore highly suggestive of MI. Skeletal muscle does contain small amounts of CK-MB, however, an abnormal CK-MB elevations can be seen in trauma,

muscular dystrophies, myositis, rhabdomyolysis, and extremely vigorous exercise[5]. Specificity is improved by requiring that the CK-MB value not only be elevated, but that it be at least 5% of the total CK value[5]. Emergency physicians must take the limitations of the CK-MB assay into account when making clinical decisions based on results of this cardiac-specific marker. Although abnormal elevations at any time following the onset of chest pain strongly suggest an AMI, at no time does a normal value reliably exclude an acute coronary event. The utility of a single CK-MB result in the emergency department probably rests primarily in determining the most appropriate setting for the patient to undergo further evaluation. Patients with positive test results are very likely to have an ultimate diagnosis of AMI and should generally be admitted to the coronary care unit. Patients with unremarkable ECGs, in whom there is a low clinical suspicion for AMI and normal initial CK-MB values, can be appropriately admitted to a less intensive care setting or emergency department observation unit, where an AMI can be formally excluded based on the results of serial CK-MB tests or other testing.

CONCLUSION

Patients presenting to the emergency department with chest pain or other symptoms suggestive of acute cardiac ischemia, the diagnosis of AMI can not be excluded on the basis of a single cardiac marker value obtained within a few hours after symptom onset. At no time should results of serum markers outweigh ECG findings or clinical assessment of the patient's risk and stability.

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