Original Article

Importance of evaluation of cardiac markers in myocardial infarction

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Abstract

Myocardial ischemia results from 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 the myocardial cell death and necrosis occurs which is defined as myocardial infarction. Oxygen deprivation due to prolonged ischemia leads to a cascade in metabolism in myocardial tissues beginning from anaerobic glycolysis, inhibition of ATP-dependent transport process in cell membrane, electrolyte shift, cellular edema and finally loss of cell membrane integrity. Due to increased glycolysis there is increased lactate concentration. This decreases the intracellular pH, resulting in release and activation of lysosomal proteolytic enzymes and thereby disintegrating intracellular structure and structurally bound proteins. The release and appearance of these ischemia affected biomolecules in blood stream is an outcome of these metabolic changes. Elevated enzyme activity associated with disease is generally assumed to reflect activity of enzyme released from injured tissue. In most of the conditions, the same enzymes with which an injured organ is richly endowed are those exhibiting elevated activity in serum following organ injury. Time course of depletion of enzyme activity from a damaged organ parallels time course of increase of activity of same enzyme in serum following insult. Early and accurate identification of myocardial necrosis in patients experiencing symptoms suggestive of myocardial infarction is a common and important clinical challenge. Since the clinical symptoms are not very reliable, ECG is the most widely used method of diagnosis of myocardial infarction. But many a times ECG shows inconclusive pattern in such a situation the importance of serum biochemical markers of myocardial injury.

Keywords: Acute Myocardial Infarction (AMI), Creatine Phosphokinase Isoenzyme MB (CPK-MB), Lactate Dehydrogenase (LDH), Serum Glutamate Oxaloacetate Transaminase (SGOT).

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INTRODUCTION

Acute myocardial infarction (AMI) continues to be a major cause of morbidity and mortality worldwide.[1,2] It remains a leading cause of death in India and represents an enormous cost to health care system.[3] Myocardial infarction (MI) as a pathological concept was recognized in beginning of 20th century. At autopsy, vegetation due to endocarditis on aortic valve was found to have blocked the orifice of right coronary artery.[3] Myocardial cell death can be recognized by the appearance in the blood of different ischemia affected biomolecules released into the circulation from the damaged myocytes. Serum Creatinine Phophokinaseisoenzyme (CPK-MB), serum glutamate oxaloacetate transaminase (SGOT), Lactate dehydrogenase (LDH) determinations have become established criteria in laboratory diagnosis of acute myocardial infarction.[4] CPK isoenzyme, SGOT and LDH determination are of immense value in assessment of patient with coronary artery disease and provides increased specificity for diagnosis of MI.[5] Ruling out of AMI requires serial collection and testing of blood for cardiac markers.[6] Myocardial infarction is diagnosed when blood levels of sensitive and specific biomarkers are increased in the clinical settings of acute myocardial ischemia. With this background, the present study was planned under the following aims and objectives:

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1. To estimate serum CPK-MB as a sensitive indicator of acute myocardial infarction in patients with chest pain.
2. To compare serum LDH and serum SGOT in acute myocardial infarction patients.
3. To co-relate the serial activity of serum LDH and serum SGOT with those of serum CPK-MB in acute myocardial infarction patients.

MATERIAL AND METHODS

The major use of cardiac biomarkers is the detection of myocardial infarction (MI). The rationale of using the measurement of a protein in blood for this purpose is straightforward. The myocyte is the major cell in the heart, and the heart's purpose is to pump blood. Because myocytes essentially cannot be regenerated, if heart cells die, then cardiac function has a high probability of being impaired. When cell dies, proteins inside the cell will be released, with proteins in the cytoplasm leaving the cell more rapidly than ones in membranes or fixed cell elements. The present study was a case control type of study. Convenient purposive sampling was done to obtain the sample of cases and controls. The study comprised of 100 clinically established cases of myocardial infarction admitted in intensive care unit (ICU), and medicine wards of hospital. The control group consists of 100 normal healthy males and females admitted in the same hospital.

Collection of blood samples

About 5ml of blood sample was collected by venepuncture, without application of tourniquet, with all aseptic precautions in plain bulb and allowed to clot. The first sample was collected 6hrs. after the onset of chest pain, second sample after 24hrs. and third sample after 48 hrs of chest pain. After 30min of every collection, the serum was separated by centrifuging at 3000rpm for 5min. Standard procedures for immediate serum analysis was carried out for CPK-MB, LDH and SGOT. Data obtained from the cases and controls was entered in microsoft excel. The analysis was done with help of SPSS software. Mean and standard deviation (SD) were calculated and compared by applying Z –test. Significanct p-values were considered as those less than 0.05.

RESULTS

In the present study serum CPK-MB, serum LDH and serum SGOT were estimated in 100 patients diagnosed as myocardial infarction 100 normal healthy males and females were studied as controls. After acute MI, CK-MB appears in blood within approximately 4-8 hrs, peaks at 12-24 hrs and persists throughout initial 72 hrs period. (Pal 2002)[7] Given these kinetics, measurement of CK-MB every 12 hrs is an adequate and cost -effective method for diagnosis of AMI. (Adams *et al* 1993)[8]**.** Accordingly, the blood samples to know CPKMB values of pateints of MI (i.e. cases) were collected at 6, 24 and 48 hours. CPKMB values of controls were also determined. Figure 1 ahead represents theserum CPKMB values in controls and in cases at 6 hours, 24 hours and 48 hours.

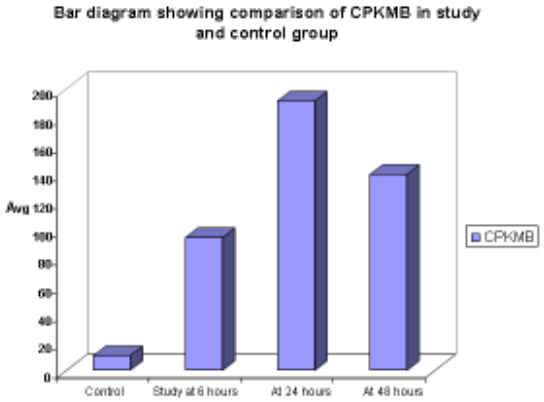

Figure 1: Serum CPKMB values of controls and cases

Mean of CPKMB in the cases and controls were statistically compared to know the difference if any, using test of significance in the form of Z test. This is represented ahead in table 1.

Table 1: Comparison of CPKMB in patients and control group:

Group	CPKMB Mean ± SD (n=50)	Z Value	P Value
Control	10.88 ± 5.68	-	-
Study At 6 hours	94.83 ± 33.13	17.66	<0.0001
At 24 hours	191.70 ± 58.50	21.75	<0.0001
At48 hours	139.59 ± 39.75	22.67	<0.0001

P < 0.001highly significant

Thus serum CPK-MB levels were raised and reached the peak at around 24 hrs. and then started declining. These findings are consistent with Adams *et al* 1993, Wagner *et al* 1973, Singh *et al* 2007, Nigam 2007[8,9,1,10] In an extensive study of isoenzymes of CPK i.e. CK-MB normal values of CK-MB were put forward as 2% of total CPK and rise above 4% indicate AMI and values below 4% rule out AMI. (Varat *et al* 1975)[11]**.** Analysis of 66 patients of AMI at 12 and 24 hrs after onset of symptoms not only detected all patients, but also provided a considerable margin for error in keying the sampling intervals to estimated time of onset of infarction. (Irvin *et al*)[12]**.** Many physicians use peak CK-MB as a qualitative impression as to the size of myocardial infarction. (Wu *et al* 1999).[6] Infarct size as assessed by CK-MB closely correlates with the volume of the infarction, the ejection fraction, incidence of ventricular arrhythmias and prognosis. (Adams *et al* 1993)[8] Advantage of CK isoenzymes (CK-MB) over LDH in addition to its greater

specificity relate to its most rapid release from injured tissues, more rapid clearance from plasma and recent availability of sensitive and convenient assays for CK isoenzyme.(Robert 1984)[13] Serum LDH also shows a change in MI pateints. The same was measured in the cases. The graphical representation of the same is shown in figure 2 ahead.

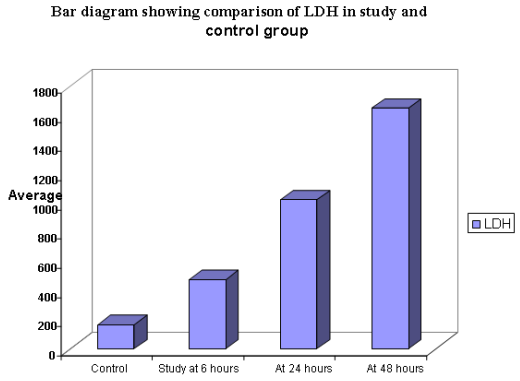

Figure 2: LDH in controls and cases

Mean of values of LDH in control group was compared with that of the cases at 6 hours, 24 hours and 48 hours. Tabular presenattion of this is shown in table 2.

Table 2: Comparison of LDH in patients and control group

Group	LDH Mean ± SD (n=50)	Z Value	P Value
Control	166.26 ± 36.64	-	-
Study At 6 hours	474.30 ± 125.84	16.62	<0.0001
At 24 hours	1021.2 ± 106.06	53.87	<0.0001
At 48 hours	1647.35± 136.68	74.01	<0.0001

P < 0.001 – Highly Significant

LDH showed a significant rise when compared with the controls. The findings are consistent with Nigam 2007, Braunwald 1998, Straus *et al* 1980, Wroblewski *et al* 1956.[10,14,15,16] West *et al* in their study in 1966 observed that the LDH values tend to remain elevated longer than those of other enzymes (i.e. SGOT, CPK-MB). Peak serum LDH are observed between the second and fourth day after infarction, may reach up to 8 times the normal and slowly decline over a period of 5-14 days.[17] Braunwald had also confirmed that serum LDH rises between 24-48hrs and remains elevated for as long as 7-14 days[14]**.** Adams *et al* from their research in 1993 also mentioned that a good correlation has been found between LDH and anatomic estimates of infarct size. It is possible that the release ratios of LDH are less affected by reperfusion and estimates of infarct size by these markers thus are superior to those based on CK and CPK-MB in patients treated with thrombolytic agents.[8] Robert in 1984 and Nigam in 2007 had observed that as a test for diagnosis of MI, LDH is highly effective and despite slower release of LDH with peak values reached at 48 to 72hrs, LDH has a diagnostic advantage in late comers, since plasma values remain elevated for 10 to 14 days.[13,10] Soble *et al* in a clinical study found that, true positive LDH elevation occurred in 86% of 282 patients with MI diagnosed clinically and in all 39 patients with myocardial infarction proven at autopsy.[4] Roe *et al* concluded that although CK-MB fraction is most specific isoenzyme for detection of myocardial injury, LDH can provide additional information regarding patients' clinical course. (1972)[18] Serum SGOT levels became significantly elevated approx. 6hrs. after the onset of chest pain, rising to a peak at about 24hrs after onset of pain. The levels then returned towards normal, reaching the normal range on 3rd to 6th day.[19] SGOT levels in the present study are depicted in figure 3 ahead.

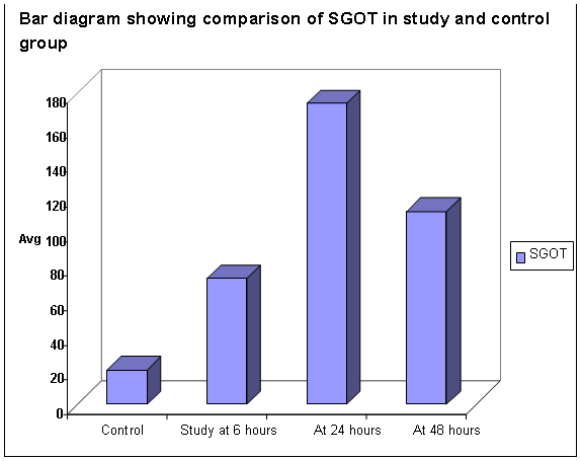

Figure 3: SGOT levels in controls and cases

Myocardial injury results in a decrease of activity of SGOT in the injured heart muscle and is reflected by a proportionate increase in the activity of serum. Peak SGOT activity is roughly proportionate to the amount of myocardial cell damage found at autopsy. Higher the SGOT activity larger the infarct, for ex. SGOT peak from a 0.5gm infarct was 64 units and for an 18gm infarct 500 units.[20,21] In the present study, SGOT values of controls and that of cases at 6 hours, 24 hours and 48 hours were analysed to obtain the mean. The mean values were compared to note the difference statistically. It is represented in table 3.

Table 3: Comparison of SGOT in patients and control group

Group	SGOT Mean ± SD (n=50)	Z Value	P Value
Control	19.8 ± 9.28	-	-
Study at 6 hours	72.81 ± 30.71	11.68	<0.0001
At 24 hours	173.90 ± 56.03	19.19	<0.0001
At 48 hours	111.49 ± 42.48	14.91	<0.0001

P < 0.001 highly significant

The present study findings are consistent with Soble *et al* 1972, West *et al* 1966, Kattus *et al* 1956, Nigam 2007.[4,22,10] Chinskyet el in their study in 1959observed that Serum SGOT levels became significantly elevated approx. 6hrs. after the onset of chest pain, rising to a peak at about 24hrs after onset of pain. The levels then returned towards normal, reaching the normal range on 3rd to 6th day.[23] In another study by La Due *et al*, serum SGOT activity in 16 patients with acute transmural myocardial infarction rose to levels 2-20 times normal within 24hrs and returned to normal range within 3 to 4 days thereafter without exceptions.[24] In yet another study, SGOT activity was followed for 2-10 days in 300 acute MI patients. SGOT activity rose 1.5 to 20 times normal within the first 12-48hrs after infarction in 297 of these patients.[20] The three biomarkers i.e. CPKMB, LDH and SGOT were also compared to know the activity in the study group. The findings are shown in figure 4.

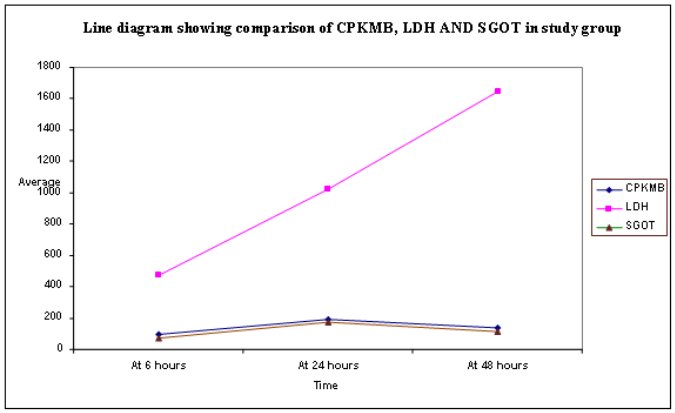

Figure 4: Comparison of CPKMB, LDH and SGOT

Thus CPKMB and SGOT both showed a peak at 24 hours and then the levels decreased. But for LDH there was a rise till 48 hours. The trends in the fall in serum enzymes are so because of the much higher rate of clearance of CPK-MB and SGOT from the circulation than that of LDH which is indicated by their disappearance constants which are about ten times higher than that of LDH. In a study group which included 55 patients with elevated total enzymes (CPK-MB**,** LDH, and SGOT) it was proven that CPK-MB was both sensitive (present in 96%) and specific (absent in 100%).[25] In a study conducted on 25 uncomplicated cases of acute myocardial infarction, the activities of enzymes CPK-MB, LDH and SGOT was found to be higher in "Q" wave myocardial infarction as compared to the "non-Q" wave and controls. (Singh *et al* 2002)[1] These findings are comparable with cases of the present study. Thus it was observed that CPK-MB activity is the earliest to rise in AMI while serum LDH the last. Serum LDH activity is also late to fall than those of other two enzymes. The explanation for this type of trends in rise and fall of the serum enzymes is found in two different studies by La Due and Witteveen *et al*.[20] Increased levels in serum of these cardiac enzymes after MI results from release of these enzymes from damaged heart muscle cells in excess of that which the body can destroy or excrete.

CONCLUSION

The present study brings out the usefulness of prompt and serial estimations of three enzymes CPK-MB, LDH and SGOT in diagnosis, timing severity as regards to complications and mortality and prognosis of an acute myocardial infarction in correlation with other clinical and investigative data.

REFERENCES

1. Alkasingh, Sheila Uthappa, V. Govindaraju, T. Venkatesh. Serum markers for early diagnosis of Non-'Q'wave and 'Q'wave myocardial infarction. IJCB 2002; 17(1): 25-28.
2. Kristian Thygesen, Joseph S. Alpert, Harvey D. White. Universal definition of myocardial infarction. Circulation 2007; 116: 2634 – 2653.
3. Santosh B Shinde, Anil Tendulkar, Neela D Patil. Relevant cardiac biochemical markers. BHJ 2004; 46: 399-407.
4. P. K. Nigam.Biochemical markers of myocardial injury. IJCB 2007; 22(1): 10-17.
5. Sobel B. E, Shell W. E. Serum enzyme determinations in the diagnosis and assessment of myocardial infarction. Circulation 1972; 45: 471-482.
6. L.H.Opic. Metabolic response during impending myocardialinfarction. Circulation 1972; 45: 483-490.
7. Wu A.H. B, Apple F.S, et al. National academy of clinical biochemistry standards of laboratory practice: Recommendations for the use of cardiac markers in coronary artery diseases. ClinChem 1999; 45(7): 1104-1121.
8. Shymali Pal. Estimation of CKMB from RIQAS control serum at 37 degree Celsius. IJCB 2002; 17 (2): 88-90.
9. Adams J. E, Abendschein D. S, Jaffe A.S. Biochemical markers of myocardial injury. Circulation 1993; 88, 2: 750-763.
10. Wagner G.S, Roc C.R, et al. The importance of identification of the myocardial- specific isoenzyme of creatine phosphokinase (MB form) in the diagnosis of acute myocardial infarction. Circulation 1973; 47: 263 – 269.
11. Varat M.A, Mercer D.W. Cardiac specific creatine phosphokinase isoenzyme in the diagnosis of acute myocardial infarction.Circulation 1975; 51: 855-859.
12. Irvin R.J, Cobb F.R, Roe C.R. Acute myocardial infarction and MB creatinephosphokinase.Arch Intern Med 1980; 140: 329-334.
13. Roberts R. The two out of three criteria for the diagnosis of infarction. Chest 1984; 86/ 4: 511- 513.
14. Antman EM, Braunwald E. Myocardial Infarction. In: Fauci S.A, Martin J. B, Braunwald E, et al eds.

Harrison's principles of internal medicine 14thed Singapore: Mc Graw – Hill book-Co, 1998: 1352-1363.
15. Strauss H.D, Roberts R. Plasma MB creatine kinase activity and other conventional enzymes. Arch Intern Med 1980; 14: 336-339.
16. Wroblewski F, Ruegsegger P, La Due J.S. Serum lactic dehydrogenase activity in acute transmural myocardial infarction. Science 1956; 132: 1122-1123.
17. West M, Eshchar J, Zimmerman H. J. Serum enzymology in the diagnosis of myocardial infarction and related cardiovascular conditions. M.C.N.A 1966; 50: 171-191.
18. Roe C.R, Limbird L. E. Combined isoenzyme analysis in the diagnosis of myocardial injury: Application of electrophoretic methods for the detection and quantitation of the creatine phosphokinase MB isoenzyme. J. Lab. Clin. Med. 1972; 80(4): 577-589.
19. Chinsky M. Shmagranoff G. L, et al. Serum transaminase activity. J.Laband Clinical Med.1956; 47(1): 108-117.
20. John S La Due. Laboratory aids in diagnosis of myocardial infarction. J.A.M.A 1957; 165(14): 1776-1781.
21. Chapman BL. Relation of cardiac complications to SGOT levels in AMI. BHJ 1972; 34(9): 890-6.
22. West M, Eshchar J, Zimmerman H. J. Serum enzymology in the diagnosis of myocardial infarction and related cardiovascular conditions. M.C.N.A 1966; 50: 171-191.
23. Chinsky M. Shmagranoff G. L, et al. Serum transaminase activity. J.Laband Clinical Med.1956; 47(1): 108-117.
24. La Due J.S, Wroblewski F, Karmen A. Serum glutamic oxaloacetic transaminase activity in human acute transmural myocardial infarction. Science 1954; 120: 497-499.
25. Roark S. F, Wagner G.S, et al. Diagnosis of acute myocardial infarction in a communityhospital.Circulation 1976; 53(6): 965-969.

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