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CO-RELATION BETWEEN LACTATE DEHYDROGENASE AND CREATINE KINASE-MB IN ACUTE MYOCARDIAL INFARCTION

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ABSTRACT. The aim of our study was to know the most potent cardiac marker from SGOT, LDH and CK-MB and to evaluate the sensitivity and specificity of that marker in diagnosis of myocardial infarction. For this purpose we were selected 30 patients of acute myocardial infarction from different hospitals of solapur city. Blood samples from 30 healthy volunteers were collected and referred as controls. In acute myocardial infarction (AMI) patients the activity of SGOT and LDH were found significantly higher ($p < 0.01$) as compared to controls. The values were 71.82 ± 12.26 IU/L (control = 35.48 ± 4.43 IU/L) and 239.79 ± 27.57 IU/L (control = 170.39 ± 16.82 IU/L) respectively for SGOT and LDH. But, as both of above markers are also found to be increased in many other clinical conditions, they are non-specific for diagnosis of acute myocardial infarction. Thus, are useful only along with CK-MB to know severity of myocardial infarction . On other hand, CK-MB also found to be elevated at significant level ($p < 0.01$). The values were 22.88 ± 3.39 U/L (control = 11.04 ± 2.03 U/L). CK-MB is present in large proportion in myocardium and also it is only specific for myocardial tissue. Thus, it is not found to be elevated in any other clinical conditions. Similarly, CK-MB gets elevated in serum more early as compared to other markers in myocardial infarction hence, it has been considered as the 'Gold Standard' for confirmation of acute myocardial infarction.

Key Words: Myocardial infarction, lactate dehydrogenase, creatine kinase-MB, myocardium.

INTRODUCTION

Myocardial infarction (MI) or acute myocardial infarction (AMI), commonly known as a heart attack, results from the interruption of blood supply to a part of the heart, causing heart cells to die. This is most commonly due to occlusion (blockage) of a coronary artery following the rupture of a vulnerable atherosclerotic plaque which is an unstable collection of lipids (cholesterol and fatty acids) and white blood cells (especially macrophages) in the wall of an artery. The resulting ischemia (restriction in blood supply) and ensuing oxygen shortage, if left untreated for a sufficient period of time, can cause damage or death (infarction) of heart muscle tissue (myocardium).(Nigam,2007 ; Rashmi Raghuvanshi et.al.,2007 ; WHO,1979 ; Antman E et al.2000) Diagnosis of acute myocardial infarction is based on clinical features, presence of risk factors, electrocardiographic change and levels of cardiac biomarkers in the serum. Some patients with myocardial infarction have atypical signs and symptoms. Classical symptoms of acute myocardial infarction include sudden chest pain (typically radiating to the left arm or left side of the neck), shortness of breath, nausea, vomiting, palpitations, sweating, and anxiety (often described as a sense of impending doom). Women may experience fewer typical symptoms than men, most commonly shortness of breath, weakness, a feeling of indigestion and fatigue. Some have little or no chest discomfort and the electrocardiographic changes may not indicate the diagnosis. In such cases cardiac biomarkers are a useful diagnostic tool, especially 4 to 6 hour after the onset of signs and symptoms of myocardial infarction. In patients with possible acute myocardial infarction who have atypical signs and symptoms and inconclusive electrocardiographic findings, measurements of serum levels of cardiac biomarkers are used to assist in the diagnosis and appropriate

triage. Clinically, measurement of the serum level of one or more specific cardiac biomarker is used to determine the extent of myocardial damage and to assess a patients prognosis. Historically, creatine kinase- MB (CK-MB) , lactate dehydrogenase (LDH) and transaminases especially SGOT have been used for routine clinical management.(Philip Ludbrook et.al.,1975 ; Peter Guzy,1977)

These cardiac markers are highly sensitive and exhibit good specificity. Their diagnostic use may depend on factors like timing and conditions of sample collection, sample processing etc. Early diagnosis of acute myocardial infarction is very useful to prevent severe and irreversible damage to myocardium. (Hitesh Shah and Haridas N,2003)

MATERIALS AND METHODS

5 ml of venous blood were collected in a plain bulb from 30 patients of AMI for the study from various hospitals in the solapur city. The sample were collected after arrival of patient in hospital. The blood samples for the controls (n = 30) were collected from the volunteers. The obtained blood was centrifuged at 3000 rpm for 15 minutes. The serum were collected and used for assay. As erythrocytes contains high amount of LDH , hemolysis should be avoided. The biochemical parameters and methods to be used for their estimations were as follows:

Creatine kinase – MB: It was assayed by immunological UV method. The immunoinhibition of M sub-units of CK-MM and CK-MB, with an specific antibody allows the determination of the B sub-unit of CK-MB. CK-B activity corresponding to half of CK-MB is measured by the increasing rate of absorbance resulting from NADH formation. This rate is measured at 340 nm.(Burtis C and Ashwood E,1994)

SGOT: Reitmann and Frankel method was used. 100 µl serum was added to 500 µl of buffered substrate and incubated for one hrs . After one hrs 500 µl of DNPH was added. After 10 minutes 5.0 ml of 0.4 N NaOH was added. Colour formed in 20 minutes and read at 540 nm. (Bergmeyer H, 1986)

Lactate Dehydrogenase (LDH): 100 µl of serum was added to 1.0 ml buffered substrate. Then 100 µl NADH was added. After incubation of 15 minutes 1.0 ml DNPH added. After 20 minutes 10 ml 0.4 N NaOH was added. In control tube 1.0 ml each of buffered substrate and DNPH, 200 µl of buffer was taken and after 20 minutes 10 ml 0.4 N NaOH was added. The liberated pyruvate was read at 540 nm.(Rao B and Deshpande V,2007)

RESULTS AND 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 occurs which is defined as myocardial infarction. (Golam K. alam and David B,2002)

Oxygen deprivation due to prolonged ischemia leads to a cascade changes in the metabolism in the myocardial tissues beginning from anaerobic glycolysis, inhibition of ATP-dependent transport process in cell membrane, electrolyte shift, cellular edema and to finally loss of cell membrane integrity. Due to increased glycolysis lactate concentration decreases the intracellular p^H , resulting in release and activation of lysosomal proteolytic enzymes and thereby disintegrating intracellular structures and structurally bound proteins. The release and appearance of these ischemia affected biomolecules in the blood stream is an outcome of these metabolic changes. (McCullough D et.al1992 ; Kent Lewandrowski et.al.2002)

The diagnosis of acute myocardial infarction (AMI) has traditionally been based on the characteristic clinical history, electrocardiographic abnormalities and increased serum concentrations of cardiac marker enzymes. ECG is the most widely used method of the diagnosis of myocardial infarction. But many times ECG shows inconclusive pattern. Thus, the measurements of serum enzymes as a reflection of damage to myocardial muscle cells still play an important role in the diagnosis of AMI. The most commonly used biomarkers are serum glutamate oxaloacetate transaminase (SGOT), creatine kinase-MB (CK-MB) and lactate dehydrogenase (LDH).(Behar S. et.at,1977 ; Rude R et.al.1983 ; Drexel H et.al.,1983 ; Chan K et.al.,1986 ; Patel N and Graham J, 1999 ; Mauro Panteghini, 2004) We had estimated the activities of above enzymes in acute myocardial infarction with respect to control.

According to our estimation, serum glutamate oxaloacetate transaminase (SGOT) activity in controls were 35.48 ± 4.43 IU/L while same in patients of myocardial infarction were found to be 71.82 ± 12.26 IU/L. Thus, there was nearly 2.0 times increase in SGOT activity in acute myocardial infarction as compared to controls ($p < 0.01$). **(Table-I)**

The activity of lactate dehydrogenase (LDH) in controls were 170.39 ± 16.82 IU/L while in patients of

myocardial infarction were 239.79 ± 27.57 IU/L. Thus, there was nearly 1.4 times increase in LDH activity in acute myocardial infarction as compared to controls ($p < 0.01$). **(Table-I)**

The activity of creatine kinase-MB (CK-MB) in controls were 11.04 ± 2.03 U/L while in patients of myocardial infarction were 22.88 ± 3.39 U/L. Thus, there was nearly 2.1 times increase in CK-MB activity in acute myocardial infarction as compared to controls ($p < 0.01$). **(Table-I)**

Table- I : Showing comparative values of enzyme activities in controls and in test (AMI patients) :

Enzyme Activity	Control (N = 30)	AMI Patients (N = 30)	P Value Compared To Normals
CK-MB activity in U/L	11.04 ± 2.03	22.88 ± 3.39	$p < 0.01$
SGOT activity in IU/L	35.48 ± 4.43	71.82 ± 12.26	$p < 0.01$
LDH activity in IU/L	170.39 ± 16.82	239.79 ± 27.57	$p < 0.01$

The levels of serum glutamate oxaloacetate transaminase activity begin to rise 3-8 hours after the onset of the myocardial injury with peak levels on an average at 24 hours and finally it returns to normal levels in 3-6 days. It was considered as a very good marker of cardiac injury as it was found to be normal in pulmonary embolism, acute abdominal conditions and other heart conditions such as angina and pericarditis. But later on, its use becomes limited due to its elevation in trauma to skeletal muscles, bone and liver diseases. Thus, this may have chances of false positive results. (Varley H and Gowenlock A,1984 ; Baron D et.al. 1956; Kachmar J, 1976)

An increase in serum lactate dehydrogenase (LDH) activity is found following myocardial infarction beginning within 6 – 12 hours and reaching a maximum at about 48 hours and it remains elevated for 4-14 days before coming down to normal levels. The prolonged elevation makes it a good marker for those patients admitted to the hospital after several days of myocardial infarction. However, its use is discouraged due to its non-specificity as its increased levels are found in progressive muscular dystrophy, myoglobinuria, leukemia, pernicious anemia, megaloblastic and hemolytic anemia, renal disease and in generalized carcinoma. On other hand as erythrocytes contain large amount of lactate dehydrogenase, any slight hemolysis causes large elevation in serum enzyme activity of lactate dehydrogenase thus predicting false positive results. (Fogh A and Strensen,1982 ; Lee T and Goldman L, 1986) Serum creatine kinase activity increases following myocardial infarction beginning within 6 hours and peaking on an average at 24 hours and returning to normal within 2-3 days. The area under the peak and the slope of the initial rise are proportional to the size of the infarction. However, its presence in large amounts in skeletal muscle and increased levels found in muscular dystrophy, hypothyroidism, hypothermia, alcoholism, cerebrovascular accidents and a variety of myopathies make it unsuitable as a marker of myocardial injury. However, creatine kinase has three isoenzymes namely CKBB, CKMB and CKMM each consisting of two subunits named according to main tissue of occurrence : B (brain) and M (skeletal muscles). Myocardium contains 40% CKMB and 60% CKMM where as skeletal muscles contain about 97% CKMM, 2-3% CKMB and traces of CKBB. Being highest in proportion in myocardium CKMB has been used as the biochemical marker in patients with suspected acute myocardial infarction (AMI). Serum CK-MB kinetics gives useful information regarding the extent and timing of myocardial injury. It begins to increase between 3-5 hours after the onset of infarction and peaking at 16-20 hours. Excluding acute myocardial infarction , other diseases never causes elevation in the serum CK-MB activity. Thus, it has been considered as the 'Gold Standard' for confirmation of acute myocardial infarction. (Seckinger D et.al,1983 ; Roberts R,1988; Collison P et.al.,1992; Lott J et.al.1995)

CONCLUSION

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 occurs which is defined as myocardial infarction. Among the diagnostic tests available to detect heart muscle damage are an electrocardiogram (ECG), echocardiography, cardiac MRI and various blood tests. The most often used blood cardiac markers are the creatine kinase-MB (CK-MB), serum glutamate oxaloacetate transaminase, lactate dehydrogenase and the troponin levels. However, assay of troponin is

costly. The other cardiac markers like serum glutamate oxaloacetate transaminase (SGOT) and lactate dehydrogenase (LDH) are non-specific as they are elevated in other diseases also. Thus, being highest in proportion in myocardium CK-MB has been used as the biochemical marker in patients with suspected acute myocardial infarction (AMI). Serum CK-MB kinetics gives useful information regarding the extent and timing of myocardial injury. It begins to increase between 5-6 hours after the onset of infarction and peaking at 22-24 hours. Excluding acute myocardial infarction , other diseases never causes elevation in the serum CK-MB activity. Thus, it has been considered as the 'Gold Standard' for confirmation of acute myocardial infarction.

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