ROLE OF CREATINE KINASE MB AND LACTATE DEHYDROGENASE IN CARDIAC FUNCTION – A REVIEW

Jagdish Kakadiya*, Nehal Shah

Department of Pharmacology, Dharmaj Degree Pharmacy College, Petlad-Khambhat Road, Dharmaj, Dist: Anand, Gujarat, India.

ADDRESS FOR CORRESPONDENCE

Mr. Jagdish L. Kakadiya

Dharmaj degree pharmacy college,

Amrapali Township, Petlad-Khambhat road,

Dharmaj, Dist: Anand-388430,

Gujarat, India.

jagdishkakadiya@gmail.com

CREATINE KINASE MB

CK-MB mass has been reported to be useful for the diagnosis of myocardial infarction, re-infarction, and the sizing of infarction.

For optimal diagnostic usefulness, a cardiac marker should be specific for cardiac tissue, should be rapidly released into the bloodstream with a direct proportional relationship between the extent of myocardial injury and the measured level of the marker, and should persist in blood for a sufficient length of time to provide a convenient diagnostic time window [1].

Creatine kinase (CK) is a dimeric enzyme found primarily in brain and muscle tissue. There are 3 isoforms of creatine kinase: BB, MM, and MB. BB is found primarily in the brain. Skeletal muscles primarily contain the MM isoform, with traces of MB (estimates of 1-4% of CK activity). Cardiac muscles also contain primarily the MM isoform, but higher amounts of MB, typically around 20% of CK activity [2]. Serum from healthy individuals typically contains the MM isoform and a small amount of the MB isoform. CK-MB can be released into the bloodstream by a number of actions, including skeletal muscle injury and myocardial damage. The rise in CK-MB in the bloodstream occurs between 4-6 hours following a myocardial infarction (MI).

The concentration peaks after approximately 24 hours and returns to baseline after 36-72 hours. As the level of CK-MB is not cardiac specific, the results of a single test are not indicative of a myocardial infarction (MI). Typically an MI is diagnosed based on the pattern of CK-MB analyses taken at 3 hour intervals for a 6 to 9 hour period or at 6 to 8 hour intervals for a 24 hour period.

CK-MB is known to exist in two forms: CK-MB2, the gene product, and CK-MB1, which is modified upon release into the bloodstream. Carboxypeptidase cleavage of the C-terminal Lysine residue of the M subunit transforms CK-MB2 into CK-MB1. In healthy individuals, CK-MB2 is in equilibrium with the modified CK-MB1 subform at a ratio of approximately 1:1. In the early hours of myocardial infarction, the abrupt release of CK-MB2 from myocardium produces an upward shift in the serum CK-MB2/CK-MB1 ratio, usually before total CK-MB (CK-MB2 +

CK-MB1) exceeds normal levels. While assays for serum levels of total CK-MB have long been used to aid in the diagnosis of myocardial infarction, determinations of the serum CK-MB2/CK-MB1 ratio are also proving useful.

Although the cardiac-specific troponins, troponin I (cTnI) and troponin T (cTnT) are now considered the biochemical markers of choice in the evaluation of acute coronary syndromes (ACS) including STelevation myocardial infarction, non-ST-elevation myocardial infarction, and unstable angina, CK-MB can also be used as a secondary marker to aid in the diagnosis of myocardial infarction and measuring the degree of myocardial necrosis. Since low levels of CK-MB can be detected in the blood of healthy persons, any CK-MB value above the 95th percentile may be indicative of some degree of myocardial necrosis [1]. Each institution should establish its own reference range for its patient population, and this range should be used to determine an appropriate limit indicative of acute myocardial infarction (AMI). The European Society of Cardiology / American College of Cardiology consensus document notes that in the clinical setting of a reinfarction, CK-MB may be more useful for monitoring for MI than cardiac troponin I (cTnI) or cardiac troponin T (cTnT) because CK-MB remains increased for only 2-4 days following an MI, in contrast to up to 5 days for cTnI or 10 days for cTnT [3, 4, 5, 6, 7]. Clinical studies have also demonstrated a close relationship between the extent of injury to the myocardium (infarct size) following MI and increased serum CK-MB mass concentrations. Similarly, significant correlations have been observed between CK-MB estimated infarct sizing and left ventricular echocardiography [8]. Other conditions involving skeletal muscle damage like accidents, blunt trauma, severe burns, and extreme exercise or myopathic disorders such as myocarditis that are not secondary to ischemic coronary artery disease can also lead to skeletal muscle or myocardial injury and have the potential to cause elevations in the blood concentrations of CK-MB. These conditions should be considered when interpreting results and the CK-MB level should be used in conjunction with clinical symptoms, signs, patient history, and ECG changes [1, 9].

LACTIC DEHYDROGENASE:

This enzyme catalyzes the reversible reaction between pyruvic and lactic acids. LDH is present in nearly all types of metabolizing cells, but different cells have different forms of the enzyme which can be distinguished. The enzyme is especially concentrated in the heart, liver, red blood cells, kidneys, muscles, brain, and lungs. The total LDH can be further separated into five components or fractions labeled by number: LDH-1, LDH-2, LDH-3, LDH-4, and LDH-5. Each of these fractions, called isoenzymes, is used mainly by a different set of cells or tissues in the body. The LDH isoenzymes test assists in differentiating heart attack, anemia, lung injury, or liver disease from other conditions that may cause the same symptoms. LDH-1 is found mainly in the heart. LDH-2 is primarily associated with the system in the body that defends against infection. LDH-3 is found in the lungs and other tissues, LDH-4 in the kidney, placenta, and pancreas, and LDH-5 in liver and skeletal muscle. Normally, levels of LDH-2 are higher than those of the other isoenzymes.

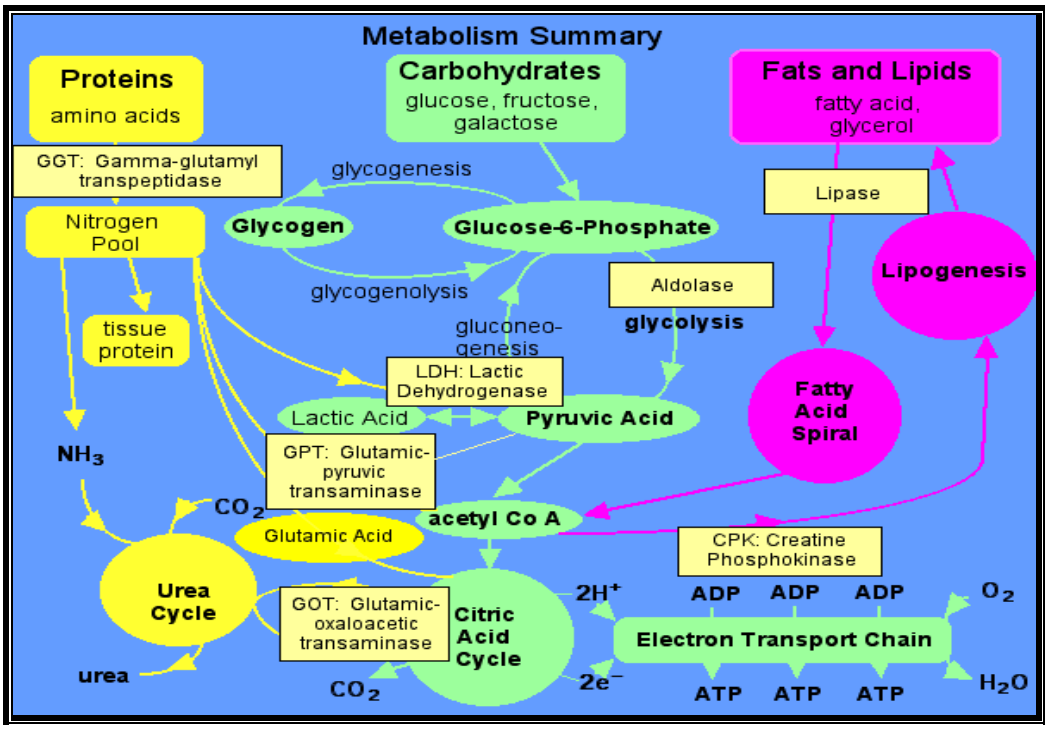

Figure 1 Metabolism Summary

Certain diseases have classic patterns of elevated LDH isoenzyme levels. For example, an LDH-1 level higher than that of LDH-2 is indicative of a heart attack or injury; elevations of

LDH-2 and LDH-3 indicate lung injury or disease; elevations of LDH-4 and LDH-5 indicate liver or muscle disease or both. A rise of all LDH isoenzymes at the same time is diagnostic of injury to multiple organs.

One of the most important diagnostic uses for the LDH isoenzymes test is in the differential diagnosis of myocardial infarction or heart attack. The total LDH level rises within 24-48 hours after a heart attack, peaks in two to three days, and returns to normal in approximately five to ten days. This pattern is a useful tool for a delayed diagnosis of heart attack. The LDH-1 isoenzyme level, however, is more sensitive and specific than the total LDH. Normally, the level of LDH-2 is higher than the level of LDH-1. An LDH-1 level higher than that of LDH-2, a phenomenon known as "flipped LDH," is strongly indicative of a heart attack.

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