HYGEIA
Vol.1, No.1
March-Aug, 09

Short review

Cardiac Biomarkers

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Abstract

Cardiac biomarkers are protein molecules released into the bloodstream from heart muscle damaged by a blocked artery and, these enzymes are measured to have a general idea of how much muscle damage has been done. They were known as cardiac enzymes, but the recently discovered and most accurate biomarker troponin is not an enzyme. Cardiac enzymes are used to determine a heart attack as opposed to a bad episode of angina[1,2]. New biomarkers are available, which are more specific and have a higher sensitivity in the diagnosis of acute coronary syndromes.

Key words: Cardiac biomarkers, Creatine kinase, Troponin

Introduction

Historically, creatine kinase (CK) and lactate dehydrogenase have been used for routine clinical management. However, these biomarkers are not without problem. The biomarkers show a characteristic rise and fall pattern after a heart attack. It may take four hours or more after the onset of symptoms for the test to become abnormal and upto 24 hours for the level to peak. Blood tests are taken from the patient several times.

Creatine kinase: Determination of serum levels of creatine kinase (CK) and its isoenzymes have long been used for the diagnosis of myocardial infarction. CK is an enzyme present in many parts of the body and can be fractionated into three isoenzymes, viz, MM, MB and BB.[4,5,6]

Creatine kinase MB isoenzyme: The physiological role of CK is to maintain an adequate store of high energy phosphorylated creatine, which is used to restore ATP levels depleted during muscle contraction. CK is composed of 2 subunits, each with a molecular weight of 43 K Da. The three isoenzymes result from the pairing of two different subunits (B for brain and M for muscle). CK- MM predominates in the skeletal muscle and CK-MB is most prevalent in heart muscle. After myocardial infarction (MI), elevated CK-MB levels appear within 3- 8 hours, peaking within 9-30 hours and levels return to normal after 48- 72 hours.

Although CK-MB has been the gold standard for detecting myocardial necrosis, is does have several limitations and is not an ideal marker. The limitations include, it is not an early marker, chances of false diagnosis of AMI and lack of cardiac specificity. Several determinations of CK-MB enhance its efficiency for the diagnosis of AMI and for assessing reperfusion following thrombolytic therapy.[7,8,9]

Myoglobin : This is a relatively small (17.8 K Da) heme protein that transports oxygen within the muscle cells and constitutes about 2% of muscle protein in both the skeletal and cardiac muscles. Because of its low molecular weight, myoglobin is rapidly released into the circulation and is the first marker to exhibit raising levels after an AMI. Elevated levels appear in circulation after 0.5-2 hours.

However, elevated levels may also be related to various skeletal muscle traumas and renal failure and are not specific for cardiac muscle injury. Several determinations improve the specificity. Despite the lack of cardiac specificity, myoglobin appears the best fir for the role of an early marker for AMI. As in the case of other cardiac biomarkers, myoglobin also serves as a useful marker for the successful reperfusion following thrombolytic therapy.[10]

Cardiac troponin (C Tn 1) : Troponin is a complex consisting of three single chain polypeptides : troponin -1, which prevents muscle contraction in the absence of calcium, troponin T, which connects the troponin complex to tropomysin and troponin C, which binds calcium. Together with tropomysin and under the influence of calcium, troponin regulates muscle contraction. After MI, elevated levels of cardiac muscle specific isoform C Tn 1 levels appear within 3-6 hours. Levels peak within 14-20 hours and return to normal after 5-7 days. Like CK-MK, it does not meet the criteria for an early marker. Several

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determinations of C Tn 1 are necessary, which is also useful for assessing reperfusion following thrombolysis. The most important characteristic of C Tn 1 is its apparent absolute cardiac specificity. Among patients with acute coronary syndromes, C Tn 1 levels have been reported to provide prognostic information useful for the early identification of patients with an elevated risk of unstable angina progressing to AMI and death.[11,12,13,14,15]

B- type natriuretic petide (BNP) : This is secreted primarily by the ventricular myocardium in response to wall stress, including volume expansion and pressure overload. Multiple studies have demonstrated that BNP may also be a useful prognostic indicator in acute coronary syndrome.[16,17]

C- reactive protein (CRP) : This is a non specific marker of inflammation and is considered to be directly involved in coronary plaque atherogenesis. Current data indicate that CRP is a useful prognostic indicator in patients with acute coronary syndrome. In combination with Tn I and BNP, CRP may be a useful adjunct.[18]

Myeloperoxidase (MYO) : This is a leucocyte enzyme that generates reactant oxidant species and has been linked to prothrombotic oxidized lipid production, plaque instability, lipid laden soft plaque creation and vasoconstriction from nitrous oxide depletion. Studies have shown that elevated MPO levels independently predicted increased risk of major adverse cardiac events including myocardial infarction, reinfarction, need for revascularization or death at 30 days to 6 months. It may be a useful early marker based on its ability to detect plaque vulnerability that preceeds acute coronary syndrome. Further validation studies are needed to determine its specificity, sensitivity, positive predictive value and negative predictive value.[19,20]

Ischemia modified albumin (IMA): Current cardiac biomarkers are markers of cell death that occurs in a cute myocardial infarction. A novel marker, IMA is produced when circulating serum albumin contacts ischemic heart tissues. IMA can be measured by the Albumin Cobalt Binding (ACB) assay that is based on IMA's ability to bind to cobalt. Based on investigations of myocardial ischemia induced by balloon inflation during percutaneous coronary intervention, IMA levels raise within minutes of transient ischemia, peaks within six hours and can remain elevated for as long as 12 hours.[21,22,23,24,25]

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