Biochemistry & Pharmacology: Open Access

Adak, Biochem Pharmacol 2012, 1:4
DOI: 10.4172/2167-0501.1000e120

Editorial Open Access

Clinically Relevant Biomarkers for Myocardial Infarction

Manoranjan Adak*

National Medical College and Teaching Hospital, Tribhuvan University, Nepal

Editorial

Myocardial ischaemic outcome from the reduction of coronary flow of oxygen to the myocardium does not meet the oxygen demand of myocardial tissue. The prolonged and irreversible effect of ischemia is a leading cause for myocardial cell death. Over the past 50 years, it has become clear that the cascade of thrombotic events following atherosclerotic plaque rupture causes occlusion of the coronary artery, interrupting blood supply and oxygen to myocardium thus resulting in infarction [1]. Coronary atherosclerosis results in 1.5 million reported cases of acute Myocardial Infarction (MI) annually in the United States, accounting for approximately 500,000 deaths and it remains the foremost cause of death in the USA [2]. Early treatments of myocardial ischaemia to prevent necrosis with treatments such as fibrinolysis, coronary artery bypass grafting and percutaneous coronary intervention have improved effect [3]. Unless medical involvement is immediate, prolonged ischemia of the myocardium results in a major cardiac arrest. The goals of the early treatment of MI include dissolving the obstructing clot, restoring blood-flow of the occluded coronary artery, and salvaging as much myocardium as possible [4].

Myocardial infarction is a burning problem throughout globe because mortality and morbidity rate increases significantly. Timely diagnosis allows clinicians to risk stratify their patients and select appropriate treatment. The diagnosis of MI is based on clinical symptoms, Electrocardiographic (ECG) changes and characteristic pattern of changes in some serum enzymes such as Creatine Kinase (CK), Creatine Kinase isoenzyme MB (CKMB), Lactate Dehydrogenase isoenzyme-1 (LD-1) and cardiac specific proteins like troponins [5]. Since the clinical symptoms are not very reliable, ECG is the most widely used method of the diagnosis of myocardial infarction. However, many times ECG shows inconclusive pattern [6]. In such a situation the importance of serum biochemical markers of myocardial injury arises to confirm the diagnosis of myocardial injury.

Accurate and timely biochemical marker testing for aiding the diagnosis of myocardial infarction (MI) has been important for the appropriate disposition and treatment of patients for the past several decades. Creatine kinase (CK) muscle, brain (CK-MB) mass, and myoglobin measurements were the standard up to the mid-1990s [7]. CK-MB starts to increase 4–8 hrs after coronary artery occlusion and returns to base line within 2–3 days [8]. However, its use is limited by its presence in skeletal muscle and normal serum and by sensitivity of the assay to interference, causing some to question its utility [9]. Myoglobin is another cytoplasmic protein found in cardiac and skeletal, but not smooth muscle. It is released even earlier within 1–2 hrs of acute myocardial infarction and peaks within 5–6 hrs [8]. Unfortunately, any injury to skeletal muscle also causes elevated levels of myoglobin, reducing specificity. Fatty Acid-Binding Proteins (FABPs) are small (15-kDa) cytoplasmic proteins expressed in all tissues with active fatty acid metabolism. Among the nine proteins, heart-specific FABP (H-FABP) is found in heart but also kidney, brain, skeletal muscle, and placenta [10]. Following acute myocardial infarction, H-FABP can be detected within 20 min and peaks at 4 hrs, considerably faster even than CK/CK-MB in the same patient group [11]. The most specific and sensitive cardiac proteins released after acute myocardial infarction are cardiac troponins I and T. Both troponins I and T are released slowly, peaking 18 hrs after myocardial infarction, and remain elevated for 7–10 days [8]. This slow release is likely the result of their relatively inaccessible cellular location compared with CK-MB, myoglobin, and H-FABP. In addition, the absent or extremely low normal circulating levels of troponin provide the greatest dynamic range of any of the currently available biomarkers [12]. Although there is no doubt troponins have revolutionized the detection and management of patients with MI [13], they do have disadvantages. The slow release of troponin delays diagnosis and the initiation of specific treatments that could salvage heart tissue in those in whom it is raised. Similarly, patients in whom it is absent and who are ultimately reassured and discharged are admitted to the hospital unnecessarily. It is therefore widely accepted that there is a need for new biomarkers that can diagnose MI earlier during its natural history and/or that have a short plasma half-life, allowing use in diagnosis and quantification of reinfarction. Other novel biomarkers, glycogen phosphorylase-BB (GP-BB)], along with markers of neurohormonal activation [NT-pro-brain natriuretic peptide (NT-proBNP)], haemostatic activity (D-dimer), and vascular inflammation [high sensitivity C-Reactive Protein (hsCRP), Myeloperoxidase (MPO), Matrix Metalloproteinase-9 (MMP-9), Pregnancy Associated Plasma Protein-A (PAPP-A), and soluble CD40 Ligand (sCD40L) are also reported [14].

Recent studies have shown that some miRNAs are present in the systemic circulation and they are new sensitive biomarkers for MI [15]. MicroRNAs (miRNAs) are 22 nucleotides long non-coding RNAs which inhibit mRNA translation or induce its degradation; each miRNA can target several mRNAs and each mRNA can be the target of different miRNAs, therefore their effects can be very complex [16]. Many miRNAs exhibit a tissue-specific distribution and they appear to play a key role in cell function both under physiological and pathological conditions; indeed, marked changes in the tissue level of some miRNAs have been found in myocardial infarction [17,18].

The ideal biomarker of cardiac injury should be cardiac specific and released rapidly after myocardial injury in direct proportion to the extent of damage. Several biomarkers of acute myocardial infarction have been described in the literature, but only a few, none of which are ideal, have found their way into routine clinical practice. A multimarker approach incorporating biomarkers and clinical scores will increase the prognostic accuracy. However, it is important to note that only troponin has been used to direct therapeutic intervention and none of the new prognostic biomarkers have been tested and proven to alter

***Corresponding author:** Manoranjan Adak, National Medical College and Teaching Hospital, Tribhuvan university, Nepal, Tel: 977-9815226878; Fax: 977-51-532261; E-Mail: manoranjanadak@rediffmail.com, itsmradak@gmail.com

Received April 25, 2012; **Accepted** April 28, 2012; **Published** April 30, 2012

Citation: Adak M (2012) Clinically Relevant Biomarkers for Myocardial Infarction. Biochem Pharmacol 1:e120. doi:10.4172/2167-0501.1000e120

outcome of therapeutic intervention. Novel biomarkers have improved prediction of outcome in acute myocardial infarction, but none has been demonstrated to alter the outcome of a particular therapy or management strategy.

References

1. DeWood MA, Spores J, Notske R, Mouser LT, Burroughs R, et al. (1980) Prevalence of total coronary occlusion during the early hours of transmural myocardial infarction. N Engl J Med 303: 897-902.
2. Thygesen K, Alpert JS, White HD; Joint ESC/ACCF/AHA/WHF Task Force for the Redefinition of Myocardial Infarction (2007) Universal definition of myocardial infarction. J Am Coll Cardiol 50: 2173-2195.
3. Tunstall-Pedoe H, Vanuzzo D, Hobbs M, Mahonen M, Cepaitis Z, et al. (2000) Estimation of contribution of changes in coronary care to improving survival, event rates, and coronary heart disease mortality across the WHO MONICA Project populations. Lancet 355: 688-700.
4. Sweeney JP, Schwartz GG (1996) Applying the results of large clinical trials in the management of acute myocardial infarction. West J Med 164: 238-248.
5. Chan D, Ng LL (2010) Biomarkers in acute myocardial infarction. BMC Med 8: 34.
6. Menown IB, Mackenzie G, Adgey AA (2000) Optimizing the initial 12-lead electrocardiographic diagnosis of acute myocardial infarction. Eur Heart J 21: 275-283.
7. Nigam PK (2007) Biochemical markers of myocardial infarction. Ind J Clin Biochem 22: 10-17.
8. Apple FS, Wu AH, Mair J, Ravkilde J, Panteghini M, et al. (2005) Future biomarkers for detection of ischemia and risk stratification in acute coronary syndrome. Clin Chem 51: 810-824.
9. Saenger AK, Jaffe AS (2008) Requiem for a heavyweight: the demise of creatine kinase-MB. Circulation 118: 2200-2206.
10. Pelsers MM, Hermens WT, Glatz JF (2005) Fatty acid-binding proteins as plasma markers of tissue injury. Clin Chim Acta 352: 15-35.
11. Wunderlich MT, Hanhoff T, Goertler M, Spener F, Glatz JF, et al. (2005) Release of brain-type and heart-type fatty acid-binding proteins in serum after acute ischaemic stroke. J Neurol 252: 718-724.
12. French JK, White HD (2004) Clinical implications of the new definition of myocardial infarction. Heart 90: 99-106.
13. Antman EM, Tanasijevic MJ, Thompson B, Schactman M, McCabe CH, et al. (1996) Cardiac-specific troponin I levels to predict the risk of mortality in patients with acute coronary syndromes. N Engl J Med 335: 1342-1349.
14. McCann CJ, Glover BM, Menown IB, Moore MJ, McEneny J, et al. (2008) Novel biomarkers in early diagnosis of acute myocardial infarction compared with cardiac troponin T. Eur Heart J 29: 2843-2850.
15. D'Alessandra Y, Devanna P, Limana F, Straino S, Di Carlo A, et al. (2010) Circulating microRNAs are new and sensitive biomarkers of myocardial infarction. Eur Heart J 31: 2765-2773.
16. Bartel DP (2004) MicroRNAs: genomics, biogenesis, mechanism, and function. Cell 116: 281-297.
17. Shan ZX, Lin QX, Fu YH, Deng CY, Zhou ZL, et al. (2009) Upregulated expression of miR-1/miR-206 in a rat model of myocardial infarction. Biochem Biophys Res Commun 381: 597-601.
18. Dong S, Cheng Y, Yang J, Li J, Liu X, et al. (2009) MicroRNA expression signature and the role of microRNA-21 in the early phase of acute myocardial infarction. J Biol Chem 284: 29514-29525.