Original Article

Role of Heart Type Fatty Acid Binding Protein (H-Fabp) As Cardiac Bio Marker in Ischemic Heart Disease

Imran Mehboob Baig*, Arjumand**, Abdul Shakoor Memon*, M. Asadullah***

*Department of Physiology & **Department of Pathology Basic Medical Sciences Institute, Jinnah Postgraduate Medical Center, *** Department of Pharmacology, Hamdard College of Medicine & Dentistry Karachi, Pakistan*

Introduction: Cardiovascular diseases constitute significant morbidity and mortality worldwide. Heart-type fatty acid binding protein (H-FABP) is a small intracellular protein which is abundant in the myocardium and rapidly released within 1-3 hours from damaged cardiomyocytes and may be the earliest available plasma marker of acute myocardial injury.

Material and Method: A cross sectional study was conducted at the department of physiology, BMSI, JPMC from 2010 to 2012. During this period 60 patients suspected with Ischemic heart disease were included, out of which 37 were male and 23 were female. Levels of cardiac markers troponin T and H-FABP were measured in the serum of all patients and the results were compared.

Result: Total numbers of 60 individuals were included in study out of which 61.66% (37) were males and 38.33% were females. H-FABP shows a positive result within one hour of onset of symptoms with a mean value of 22.8 ng/ml while Troponin T shows a negative result with a mean value of 0.28 ng/ml. While after 1 hour of onset of symptoms both H-FABP and Troponin T are showing positive results by having a value >6 ng/ml and >1.5 ng/ml respectively.

Conclusion: Point-of-care assays of H-FABP in patients presenting within one hours of symptom onset may lead to an earlier diagnosis of Ischemic Heart Disease.

Key words: Ischemic heart disease, H-FABP, Troponin T, Myocardial injury

Introduction

Cardiovascular disease is a global public health problem which contributes to about 30% of global mortality and 10% of all of the global diseases. Around 80% of total deaths that are occurring due to global diseases in developing countries are due to cardiovascular diseases[1,2]. The most common cause of Cardio Vascular Disease morbidity and mortality is ischemic heart disease (IHD)[3].

Myocardial ischemia, a major cause of myocardial injury and necrosis, is initiated whenever the coronary arterial flow cannot supply sufficient oxygen to the myocardium [4]. Most common cause of myocardial ischemia is atherosclerotic coronary artery disease.

Myocardial ischemia is developed whenever there is an imbalance between myocardial oxygen supply and myocardial oxygen consumption. The presence of atherosclerotic plaque within the vessel wall may lead to this imbalance when myocardial oxygen demands increase such as during exertion [5]. There are five main manifestations of Ischemic heart disease, namely stable angina pectoris, unstable angina pectoris, MI, heart failure and sudden death. The phrase 'acute coronary syndromes' includes unstable angina, non-ST-elevation MI, ST-elevation MI and sudden cardiac death [6].

ECG alone is often insufficient for the diagnosis of acute coronary syndrome or acute myocardial infarction, since ST-segment deviation may be observed in other conditions So the electrocardiography (ECG) and measurement of cardiac troponins are the current diagnostic cornerstones and complement the clinical assessment [7,8].

Recent available cardiac biomarkers Troponin is considerably more sensitive and specific for heart damage than total creatine kinase (CK) or its isoform,

Correspondence: Dr. Imran Mehboob Baig
E-mail: dr_aim1@hotmail.com

CK-MB [9]. Unfortunately, troponin is elevated only 6–9 hours after onset of ischemia [7,8]. So cardiac troponins, CK-MB and myoglobin, which are routinely used in the diagnosis of IHD, are not elevated in the initial hours, precluding their usefulness in the early diagnosis [10].

The diagnosis of acute myocardial infarction consequently requires prolonged monitoring over a period of 6 to 12 hours and serial blood sampling. A delay in confirming a diagnosis of acute myocardial infarction may increase the risk of complications [7,8]. Cardiac troponins, the preferred biochemical marker for IHD frequently, show a delayed appearance in serum so patients with suspected IHD have normal cardiac troponin T levels on admission. Therefore there is still a need for reliable early markers [11]. A biomarker that reliably detects myocardial ischemia in the absence of necrosis would be useful for initial identification of unstable angina patients and for differentiating patients with chest pain of an etiology other than coronary ischemia [12].

There are data documenting the diagnostic utility of H-FABP as an early marker of myocardial infarction (MI) and as a marker of reperfusion after ST-segment elevation MI [13,14]. Recent studies in laboratories and the emergency department have shown that heart-type fatty acid-binding protein (H-FABP), a more recently developed cardiac biomarker, is able to detect myocardial damage as soon as one hour after onset of ischemia and, therefore, is regarded the earliest plasma marker available [15,16].

Heart Type Fatty Acid Binding Protein (H-Fabp)

Heart-type fatty acid binding protein (H-FABP) is a small intracellular protein consisting of 132 amino acid residues and weighing 14.5kDa. It is water soluble and abundant in the cytoplasm [17].

H-FABP is abundant in the myocardium and rapidly released from cardiomyocytes into the circulation after the onset of cell damage [18].

The reasons for using H-FABP in early diagnosis of ACS are high myocardial content, presence in mainly cytosol, low molecular weight, relative tissue specificity, and early (within two hours) appearance in plasma and urine after AMI onset [19]. An elevated H-FABP identified patients at risk for death and major cardiac events even when troponins and CK-MB are not elevated [20].

Recent research also suggests that human heart-type fatty-acid-binding protein (H-FABP) appears in plasma 1–3 h after cardiac damage, and may be the earliest available plasma marker of acute myocardial injury. It may have better diagnostic accuracy than other cardiac markers in the early stages after the onset of symptoms [21,22].

Materials and Methods

During analysis of a cross sectional study conducted at the department of physiology BMSI, JPMC Karachi from 2010 to 2012 ; 60 patients suspected with Ischemic heart disease were included. 37 (61.66%) were male and 23 (38.33%) were females. They were between the age group of 30-65 years.

Levels of cardiac markers troponin T and H-FABP were measured at the 1st, 2nd and 4th hours by Enzyme linked-Immuno-Sorbent Assay (ELISA) test-specific antibody system kits and the results were compared. Normal reference levels for troponin T and H-FABP were accepted in the range of 0.0–0.1 ng/ml and 0–6ng/ml respectively.

Results

Troponin T and H-FABP findings with time of onset of symptoms in patients with ischemic chest pain			
Time Of Onset Of Symptoms	No.	Troponin T Mean	H - FABP Mean
Male			
> 2 hours	7	1.59	33.6
1 - 2 hours	11	1.46	29.6
Within 1 hour	19	0.28	14.9
Female			
> 2 hours	5	1.48	33.2
1 - 2 hours	7	1.46	29.4
Within 1 hour	11	0.28	13.9
Total			
> 2 hours	12	1.53	33.5
1 - 2 hours	18	1.46	29.5
Within 1 hour	30	0.28	22.8

Table is showing comparison of H-FABP with Troponin T with respect to the time sample collection after the onset of chest pain of cardiac origin. It shows that H-FABP shows a positive result within one hour of onset of symptoms with a mean value of 22.8 ng/ml

while Troponin T shows a negative result with a mean value of 0.28 ng/ml. While after 1 hour of onset of symptoms both H-FABP and Troponin T are showing positive results by having a value >6 ng/ml and >1.5 ng/ml respectively.

Discussion

Chest pain is one of the most common complaints among patients admitted to emergency departments. It may be the initial and sole complaint of Ischemic heart disease (IHD) [10]. The biochemical markers myoglobin, creatine kinase-MB isoenzyme (CK-MB), and cardiac troponins are currently used in the diagnosis of AMI. These cardiac markers are not satisfactory for detecting AMI in the early phase, especially within 3-6 h of the onset of AMI [23]. The major limitation of standard cardiac troponin assays is their low sensitivity at the time of a patient's presentation, owing to a delayed increase in circulating levels of cardiac troponins [8]. Another consequence of the use of troponin is that its measurement can not distinct between unstable angina and myocardial infarction [24].

Heart-type fatty acid binding protein (H-FABP) is a small intracellular protein weighing 14.5kDa and found abundantly in the cytoplasm [17]. Heart type fatty acid binding protein (H- FABP) is the most widely distributed FABP. It is found in heart, skeletal and smooth muscle, mammary epithelial cells, aorta, distal tubules of the kidney, lung, brain, placenta and ovary [25]. According to Glatz *et al* (1997) H-FABP is released within two hours of symptom onset, reaches its peak concentration within 4–6 hours and returns to its normal basal levels by 20 hours [26].

The aim of this study is to determine the efficacy of H-FABP compared to troponin T in the early diagnosis of ACS, and to assess its cardio sensitivity and specificity in normal healthy individuals and patients suffering from acute coronary syndrome (ACS). We have demonstrated the sensitivity and specificity of H-FABP for the detection of early phase (at the first hour of myocardial injury) of Ischemic heart disease, and compared it to the routinely used marker, troponin T. Our data indicates that for IHD detection, serum H-FABP shows a significantly higher diagnostic sensitivity and specificity than troponin T, especially soon after (within 1-2 hr) the onset of symptoms. Same is shown in the study of Pasuoglu *et al.,* 2007 [27] which showed 71.1% (61) individuals with elevated H-FABP levels.

Data of our study is completely supported by Umat Cavus *et al*., 2006 [19] where at the first hour of myocardial injury, H-FABP had shown superiority to

that of troponin T by showing a positive result (H-FABP level of >6ng/ml in patients) while troponin T showed a negative result. This trend changed at the fourth hour of myocardial injury where H-FABP sensitivity and specificity became equal to CK-MB and troponin T.

Conclusion:

Point-of-care assays of H-FABP in patients presenting within one hours of symptom onset may lead to an earlier diagnosis of IHD. Its use in IHD appears feasible. It also has the advantage in bedside testing and rapid test results.

References

1. World Health Organization. Reducing Risks, Promoting Healthy Life. WHO Report 2002. Geneva: WHO, 2002
2. World Health Organization. World Health Statistics 2008. Geneva: WHO, 2008.
3. Ezzati M. 2004. Comparative Quantification of Health Risks: Global and Regional Burden of Disease Attributable to Selected Major Risk Factors. Geneva: World Health Organization.
4. Wu AHB, ed. Cardiac markers, 2nd ed. Totowa, NJ: Humana Press, 2003:467pp.
5. Crea F, Gaspardone A. New look to an old symptom: angina pectoris. Circulation 1997;96:3766–3773.
6. Shanthi Mendis, Kristian Thygesen, Kari Kuulasmaa, Simona Giampaoli, Markku Mähoänen, Kathleen Ngu Blackett, Liu Lisheng. Writing group on behalf of the participating experts of the WHO consultation for revision of WHO definition of myocardial infarction. International Journal of Epidemiology 2010;1–8
7. Anderson JL, Adams CD, Antman EM, Bridges CR, Califf RM: ACC/AHA 2007 guidelines for the management of patients with unstable angina/non-ST-Elevation myocardial infarction: J Am Coll Cardiol 2007, 50:e1-e157.
8. Bassand JP, Hamm CW, Ardissino D, et al. Guidelines for the diagnosis and treatment of non-ST-segment elevation acute coronary syndromes. Eur Heart J 2007, 28:1598-1660.
9. Thygesen K, Alpert JS, White HD, et al. Universal definition of myocardial in farction. Circulation 2007;116:2634-53.
10. Alhadi HA, Fox KA. Do we need additional markers of myocyte necrosis: the potential value of heart fatty-acid-binding protein. Q J Med 2004; 97:187–98.
11. Hamm CW. Acute coronary syndromes: The diagnostic role of troponins. Tromb Res 2001;103:S63–S69.
12. Hassan M.E. Azzazy, Maurice M.A.L. Pelsers, and Robert H. Christenson. Unbound Free Fatty Acids and Heart-Type Fatty Acid Binding Protein: Diagnostic Assays and Clinical Applications. Clinical Chemistry 52:1 19–29 (2006)
13. de Groot MJ, Muijtjens AM, Simoons ML, Hermens WT, Glatz JF. Assessment of coronary reperfusion in patients with myocardial infarction using fatty acid binding protein concentrations in plasma. Heart. 2001;85:278–285.
14. Seino Y, Ogata K, Takano T, Ishii J, Hishida H, Morita H, Takeshita H, Takagi Y, Sugiyama H, Tanaka T, Kitaura Y. Use of a whole blood rapid panel test for heart-type fatty acid-binding protein in patients with acute chest pain: comparison with rapid troponin T and myoglobin tests. Am J Med. 2003;115:185–190.
15. Glatz JF, van der Vusse GJ, Simoons ML, et al. Fatty acid-binding protein and the early detection of acute myocardial infarction. Clin Chim Acta 1998; 272:87–92.

16. Pelsers MM, Hermens WT, Glatz JF: Fatty acid-binding proteins as plasma markers of tissue injury. Clin Chim Acta 2005, 352:15-35.
17. Glatz J. F. C. and Van der Vusse G. J. (1996) Cellular fatty acid-binding proteins: their function and physiological significance. Prog. Lipid Res. 35: 243–282
18. Furuhashi M, et al. Serum ratio of heart-type fatty acid-binding protein to myoglobin. A novel marker of cardiac damage and volume overload in hemodialysis patients. Nephron Clin Pract 2003;93:C69–C74. [PubMed: 12616033]
19. Umut Cavus, MD; Figen Coskun, MD; Bunyamin Yavuz, MD; Orcun Ciftci, MD; Levent Sahiner, MD; Hakan Aksoy, MD; Ali Deniz, MD; Engin Ozakın, MD; Kudret Aytemir, MD, Prof, FESC; Lale Tokgozoglu, MD, Prof, FESC, FACC; and Giray Kabakci, MD, Prof, FESC Ankara, Turkey. Heart-Type, Fatty-Acid Binding Protein Can Be a Diagnostic Marker in Acute Coronary Syndromes. Journal of the National Medical Association vol. 98, NO. 7, JULY 2006 1067
20. Michelle O'Donoghue, James A. de Lemos, David A. Morrow, abina A. Murphy, Jacqueline L. Buros, Christopher P. Cannon and Marc S. Sabatine. Prognostic Utility of Heart-Type Fatty Acid Binding Protein in Patients With Acute Coronary Syndromes. Circulation 2006;114;550-557
21. Alhadi HA, Fox KA. Do we need additional markers of myocyte necrosis: the potential value of heart fatty-acid-binding protein. Q J Med 2004; 97:187–98.
22. Chan CP, Wan TS, Watkins KL, et al. Rapid analysis of fatty acid-binding proteins with immunosensors and immunotests for early monitoring of tissue injury. Biosens Bioelectron 2005; 20:2566–80.
23. Watanabe T, Ohkubo Y, Matsuoka H, Kimura H, Sakai Y, Ohkaru Y et al. Development of simple whole blood panel test for detection of human heart-type fatty acid-binding protein. Clin Biochem 2001; 3: 257-63.
24. Van de Werf F, Ardissino D, Betriu A, Cokkinos DV, Falk E, Fox KA, et al. Management of acute myocardial infarction in patients presenting with ST-segment elevation. The Task Force on the Management of Acute Myocardial Infarction of the European Society of Cardiology. Eur Heart J 2003;24(1):28-66.
25. Zimmerman AW, Veerkamp JH. New insights into the structure and function of fatty acid-binding proteins. Cell Mol Life Sci 2002;59:1096–1116.
26. Glatz JF, Van der Vusse GJ, Maessen JG, et al. Fatty acid-binding protein as marker of muscle injury: experimental finding and clinical application. Acta Anaesthesiol Scand Suppl. 1997;111:292-294.
27. Hatice PASAOGLU, Ebru OFLUOGLU, Mustafa N. ILHAN, Atiye ÇENGEL, Murat ÖZDEMIR, Emre DURAKOGLUGIL, Murat ERDEN. The Role of Heart-Type Fatty Acid-Binding Protein (H-FABP) in Acute Myocardial Infarction (AMI) Compared to Conventional Cardiac Biochemical Markers. Turk J Med Sci 2007; 37 (2): 61-67