A STUDY ON THE ROLE OF HEART TYPE FATTY ACID BINDING PROTEIN IN ACUTE MYOCARDIAL INFARCTION

submitted to

The Tamil Nadu Dr.M.G.R.Medical University

M.D. DEGREE EXAMINATION

BRANCH – I (GENERAL MEDICINE)

KILPAUK MEDICAL COLLEGE

THE TAMIL NADU DR.M.G.R. MEDICAL UNIVERSITY

CHENNAI

APRIL 2011

BONAFIDE CERTIFICATE

This is to certify that **"A STUDY ON THE ROLE OF HEART TYPE FATTY ACID BINDING PROTEIN IN ACUTE MYOCARDIAL INFARCTION "** is a bonafide work done by **Dr. Shama Prakash.K,** post graduate student, Department of General Medicine, Kilpauk Medical College, Chennai-10, under my guidance and supervision in partial fulfillment of regulations of **The Tamilnadu Dr.M.G.R.Medical University** for the award of **M.D.Degree Branch I (General Medicine)** during the academic period from May 2008 to April 2011.

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INTRODUCTION

Coronary heart disease which was earlier more common in developed countries is now common in developing countries including India.[1] Asian Indians have much higher incidence of coronary artery disease (CAD) as compared to all other ethnic groups.CAD among Asian Indians has been found to be more severe, diffuse and associated with serious complications and increasing mortality at a younger age and its incidence has dramatically increased in recent years.[2]

Acute myocardial infarction (AMI) is the rapid development of myocardial necrosis caused by a critical imbalance between oxygen supply and demand of the myocardium. Studies have shown that effective salvage of the ischaemic myocardium following a sudden or ongoing interruption of coronary blood flow requires immediate initiation of therapy.[3]Diagnosis in the early stages of AMI is sometimes difficult because the initial ECG may not reveal any changes indicative of myocardial ischaemia [4] and also due to the delayed release of serum cardiac biomarkers such as CK-MB and Troponins. Hence detection of a rapidly appearing serum biomarker for myocardial damage would facilitate a more appropriate diagnostic and therapeutic approach in patients with chest pain who are suspected to have AMI. Although myoglobin is considered as an useful marker for early diagnosis of AMI [5] it has been reported to be less specific.[6]

Heart type fatty acid binding protein (H-FABP) has been proposed as an early cardiac biomarker for the diagnosis of AMI using animal models [7,8,9] and clinical samples.[10,11,12,13]H-FABP is able to detect myocardial damage as soon as one hour after the onset of ischaemia and therefore is regarded as the earliest plasma biomarker available to diagnose AMI.[14] A bedside test for H-FABP providing results within 15 minutes is available and it can reduce the diagnostic uncertainty in those suspected to have AMI who present in early hours.[15] But not much data is available regarding the utility of H-FABP in Indian population.

Hence in this study the role of Heart type fatty acid binding protein in the diagnosis of acute myocardial infarction, particularly in the initial hours after symptom onset, is studied and compared with the established biomarkers CK-MB and Troponin.

AIM OF THE STUDY

1. To study the role of heart type fatty acid binding protein in the diagnosis of acute myocardial infarction.
2. To compare the heart type fatty acid binding protein with the standard cardiac biomarkers CK-MB and Troponin.

REVIEW OF LITERATURE

HISTORICAL REVIEW:

William Harvey proposed that blood circulates because of the force of the heart (1616).[16,17] On July 21, 1768, William Heberden presented "Some Account of a Disorder of the Breast" to the Royal College of Physicians, London: "But there is a disorder of the breast marked with strong and peculiar symptoms, considerable for the kind of danger belonging to it, and not extremely rare. The seat of it, and sense of strangling and anxiety with which it is attended, may make it not improperly be called angina pectoris."[16,18] His classic account marks the beginning of our appreciation of coronary artery disease. Edward Jenner and Caleb Parry were the first to suspect a coronary oetiology, which Parry published in 1799. Nevertheless, a coronary cause of angina pectoris was not readily accepted until the late 19th century.[19] Karl Huber suggested that atheroma could cut off the blood supply and lead to myocardial fibrosis (1882).[18] Adam Hammer was the first to report the premortem diagnosis of myocardial infarction (1878).

By the late 19th century, angina pectoris was linked with coronary artery disease, although there was confusion between angina pectoris and myocardial infarction. Coronary disease was thought to be uncommon at that time. In 1901, Osler called the anterior branch the "artery of sudden death" later stating that "the tragedies of life are largely arterial." The concept that coronary thrombosis was always fatal was finally dispelled by

James Herrick (1912).[20,21] Herrick was the first to grasp the variable course of myocardial infarction. The three-lead electrocardiogram was used by Herrick and Smith to diagnose experimental infarction (1918) and in humans by Pardee (1920).[22] Precordial leads, introduced by Frank Wilson in the 1930s, furthered the diagnosis. By the 1930s, myocardial infarction was a familiar diagnosis felt to be increasing in frequency. The clinical-pathologic correlations of atherosclerosis and thrombosis with infarction were greatly strengthened by the 1940 postmortem coronary injection studies of Blumgart, Schlesinger, and Davis. Autoradiographic postmortem studies by Fulton in Glasgow (1976) and DeWood's coronary arteriographic studies (1980) finally proved that a thrombus was the primary event. The "vulnerable plaque" hypothesis (1966) has gained widespread support as the cause of acute coronary disease and sudden death. Inflammation, ignited by risk factors underlies "atherothrombosis," and plaque disruption is now realized to be multifocal.[23]

EPIDEMIOLOGY:

The 20th century saw unparalleled increase in life expectancy and major shift in the causes of illness and death throughout the world.[24] During this transition , cardiovascular diseases (CVD) became the most common cause of death worldwide. A century ago CVD accounted for less than 10 percent of all deaths. Today it accounts for approximately 30 percent of

deaths worldwide including nearly 40 percent in high income countries and about 28 percent in low and middle income countries.[25] .

One sixth of the world's population lives in India and India is experiencing an alarming increase in heart disease.CVD accounted for 32% of all the deaths in 2000 [26]and the WHO estimates that 60% of the world's cardiac patients will be Indians by 2010. As expected, CVD mortality rates tend to be higher in urban than the rural areas and CVD is much more prevalent among the upper and middle classes.[27,28] CAD appears to be dominant form of CVD in India. From the 1960's to the 1990's the CAD prevalence increased two fold in rural India and three-fold in urban India. The prevalence is even higher in South India.[29]

ANATOMY OF CORONARY CIRCULATION[30]

Blood supply to the heart comes from the right and left coronary arteries.

Right Coronary Artery (RCA)

It arises from right aortic sinus and descends in the right atrioventricular groove curving posteriorly at the right cardiac border to reach the crux.

The branches of right coronary artery are,

A. Conus artery is the first branch of RCA, arising within few millimeters of origin of RCA. It passes anteriorly and upwards over the RV outflow tract towards left anterior descending artery.

B. Sino atrial node artery is second branch of RCA. In about 38% of patients, it may arise from left circumflex artery. It sends branches to sinus node and usually also to right atrium or both atrium.

C. Acute marginal branches arise from mid portion of RCA. There are one or more medium sized branches which supply anterior wall of RV.

D. Posterior descending artery is the next important branch of RCA. When RCA is dominant (in 85% of the patients), the posterior descending artery originates at or shortly before the crux and passes forward in the posterior interventricular groove, giving rise to number of small inferior septal branches, which supply the lower portion of interventricular septum.After giving rise to posterior descending artery, dominant RCA continues beyond the crux and passes upwards in the distal portion of left atrioventricular groove, where it gives rise to posterior left ventricular branches. 15% of patients do not have RCA dominance. About half of these patients have left circumflex artery dominance. Other half of patients without RCA dominance have balanced circulation - RCA gives rise to posterior descending artery and left circumflex artery gives rise to posterior left ventricular branches.

Left Coronary Artery

Left main coronary artery arises from the upper portion of the left aortic sinus. It passes behind the right ventricular outflow tract, extending for 0-10 mm and then bifurcates into left anterior descending artery and left circumflex artery.

A. Left anterior descending artery (LAD) passes down the anterior inter-ventricular groove towards the cardiac apex. Its major branches are septal and diagonal branches. Septal branches arise from left anterior descending at approximately 90 degree angle and pass into interventricular septum. Diagonal branches pass over the anterolateral aspect of the heart.

B. Left circumflex artery (LCA) originates at the bifurcation of left main coronary artery and passes down the left atrioventricular groove. The left circumflex artery usually gives off one to three obtuse marginal branches as it passes down the atrioventricular groove. These are the principal branches of the left circumflex artery , since they supply the free wall of the left ventricle along its lateral aspect.Beyond the origin of obtuse marginal branches, the distal left circumflex artery tends to be small. The left circumflex artery also gives rise to 1 or 2 left atrial circumflex branches, which supply the lateral and posterior aspects of the left atrium.

Coronary Venous System

Coronary veins return blood from the myocardial capillaries to the RA.

A. The great cardiac vein lies in the anterior interventricular sulcus, it drains the base of the heart and drains into the coronary sinus. It receives tributaries from the anterior interventricular septum, the wall of the both ventricles and the left atrium.

B. The middle cardiac vein drains into the coronary sinus and receives tributaries from the posterior interventricular septum and ventricular walls.

C. 3-12 anterior cardiac veins drain the wall of the right ventricle and empties directly into the right atrium.

D. The coronary sinus is formed as a continuation of the great cardiac vein, is 2-5 cm long, it receives veins from the posterior left ventricle and the left atrium. It drains directly into the right atrium.

RISK FACTORS FOR CORONARY ARTERY DISEASE [31]

1. Established Evidence

Advanced Age, Physical inactivity, Obesity, Smoking[32,33,34], Hypertension[34], Diabetes Mellitus [35,36], Increased LDLc [34]and Decreased HDLc.

2. Emerging Risk Factors

a) Inflammatory markers: CRP , Serum Amyloid A.

b) Procoagulant markers: Homocysteine [37] , Plasminogen activator inhibitor type 1 (PAI) [38], Lipoprotein (a). [38]

c) Process markers: Fibrinogen [39], D dimer ,Coronary artery calcification.

d) Genetic factors: Tumor necrosis factors , Transforming growth factors , IL-1 , CD 14 , Adhesion molecules etc.

RISK FACTORS FOR ASIAN INDIANS [29]

A. Non modifiable: Male age > 35 years, Female age > 45 years, Family history of premature CAD (at age <55 years).

B. Modifiable –Non lipids: Hypertension, Smoking / tobacco abuse, Diabetes mellitus / insulin resistance syndrome, Obesity / BMI > 22, Homocysteine > 10 micro mol/L, High PAI – 1.

C. Modifiable-Lipids:Total Cholesterol >150 mg%,

Triglycerides > 150mg%, LDLc > 100 mg%, Apo (A) < 100 mg%,

HDLc Males < 40 mg% , HDLc Females < 50 mg%, TC/HDLc > 4.5, LDLc/HDLc > 3.5, Apo (A)/Apo (B) < 1.2,

Lipid Tetrad= LP(a)*TG*LDLc%HDLc > 20,000

ACUTE MYOCARDIAL INFARCTION:

The WHO criteria for the diagnosis of AMI includes:

1. History of ischaemic type of chest discomfort.
2. Evolutionary changes on serially obtained ECG tracings.

3. Typical rise and fall in serum cardiac markers.

Diagnosis of AMI requires at least two of the three criteria.[40] But recently myocardial infarction has been redefined.

REVISED DEFINITION OF MI [41]

Criteria for acute, evolving or recent MI

Either one of the following criteria satisfies the diagnosis for an acute, evolving or recent MI:

(1) Typical rise and/or fall of biochemical markers of myocardial necrosis with at least one of the following:

a) Ischaemic symptoms.

b) Development of pathologic Q waves in the ECG.

c) ECG changes indicative of ischaemia (ST elevation or depression).

d) Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality.

(2) Pathological findings of an acute MI.

Criteria for Healing or Healed MI

Any one of the following criteria satisfies the diagnosis for healing or healed MI:

1) Development of new pathologic Q waves on serial ECGs. The patient may or may not remember previous symptoms. Biochemical markers of myocardial necrosis may have normalized, depending on the length of time that has passed since the infarction developed.

2) Pathological findings of a healed or healing infarction.

Hence in the diagnosis of Acute MI the role of cardiac biomarkers has gained more significance.

CAUSES OF AMI

Almost all MIs result from coronary atherosclerosis, generally with superimposed coronary thrombosis.

CAUSES OF MI WITHOUT CORONARY ATHEROSCLEROSIS [42]

Coronary artery disease other than atherosclerosis

Arteritis

Leutic, Granulomatous (Takayasu disease), Polyarteritis nodosa, Mucocutaneous lymph node (Kawasaki) syndrome, Disseminated lupus erythematosus, Rheumatoid arthritis, Ankylosing spondylitis.

Trauma to coronary arteries

Laceration, Thrombosis, Iatrogenic, Radiation etc.

Coronary mural thickening with metabolic disease or Intimal Proliferative disease

Mucopolysaccharidoses (Hurler disease), Homocysteinuria, Fabry's disease, Amyloidosis, Juvenile intimal sclerosis (idiopathic arterial calcification of infancy), Intimal hyperplasia associated with contraceptive steroids or with the postpartum period, Pseudoxanthoma elasticum, Coronary fibrosis caused by radiation therapy.

Luminal narrowing by other mechanisms

Spasm of Coronary arteries (Prinzmetal angina with normal Coronary arteries), Spasm after nitroglycerin withdrawal, Dissection of the aorta, Dissection of the Coronary artery.

Emboli to Coronary arteries

Infective endocarditis, Nonbacterial thrombotic endocarditis, Prolapse of the mitral valve, Mural thrombus from LA, LV or pulmonary veins, Prosthetic valve emboli, Cardiac myxoma, Emboli associated with cardiopulmonary bypass surgery and coronary arteriography, Paradoxical emboli, Papillary fibroelastoma of the aortic valve ("fixed embolus"), Thrombi from intracardiac catheters or guidewires.

Congenital coronary artery anomalies

Anomalous origin of left coronary from pulmonary artery, Left coronary artery from anterior sinus of valsalva, Coronary artery aneurysms, Coronary arteriovenous and arteriocameral fistulas.

Myocardial oxygen demand-supply disproportion

Aortic stenosis, Incomplete differentiation of the aortic valve, Aortic insufficiency, Carbon monoxide poisoning, Thyrotoxicosis, Takotsubo cardiomyopathy, Prolonged hypotension.

Hematological (in situ thrombosis)

Polycythaemia Vera, Thrombocytosis, Disseminated intravascular coagulation, Hypercoagulability etc.

Miscellaneous

Cocaine abuse, Myocardial contusion, Myocardial infarction with normal coronary arteries, Complication of cardiac catheterization.

PATHOLOGY AND PATHOPHYSIOLOGY OF MI [43,44]

Almost all myocardial infarctions result from coronary atherosclerosis, generally with superimposed coronary thrombus. During natural evolution of atherosclerotic plaque, an abrupt and catastrophic transition may occur, characterised by plaque rupture and exposure of substance that promotes platelet activation and thrombin generation. The resultant thrombus interrupts the blood flow to cause myocardial infarction. The plaques which are more likely to rupture are one with thick lipid core and thin fibrous cap. The process of plaque rupture is likely to be multifactorial. Stress induced by intraluminal pressure, coronary vasomotor tone and disruption of nutrient vessels combine to produce plaque rupture at margins of fibrous cap. Such rupture leads to sudden occlusion of the vessel due to aggregation of RBCs, Platelets, macrophages and leads subsequently to thrombus formation. There is further vasoconstriction due to Thromboxane A2, a powerful vasoconstrictor liberated from the platelets. If due to natural fibrinolytic substances in the body a partial or complete lysis of the clot occurs, the patient develops unstable angina or non Q wave MI or NSTEMI due to partial restoration of blood flow. However if no such fibrinolytic activity occurs, the patient develops STEMI or Q wave MI.

Left Ventricular Systolic Function

Upon interruption of flow the affected myocardium loses its ability to shorten and perform contractile work. Four abnormal contraction patterns are seen in sequence as follows,

1) Dys-synchrony: Dissociation in the time course of contraction of adjacent segments.
2) Hypokinesis: Reduction in extent of shortening.
3) Akinesis: Cessation of shortening.
4) Dyskinesis: Paradoxical expansion.[45,46]

Initially, the non-infarcted area shows hyperkinesia. This is thought to be due to compensatory mechanisms and subsides by about 2 weeks after infarction. If sufficient quantity of myocardium is affected, LV pump function becomes depressed - cardiac output, stroke volume and blood pressure decreases and the end systolic volume increases. In fact, the degree to which the end systolic volume increases is the most powerful indicator of mortality of acute myocardial infarction. When 15% of LV is involved, ejection fraction may be depressed.Clinical heart failure occurs when thearea of abnormal contraction exceeds 25%, whereas cardiogenic shock occurs with loss of 40% of LV myocardium.

Left Ventricular diastolic function

Left ventricular diastolic properties are altered in infarcted and ischaemic myocardium, leading initially to an increase but later to a reduction in left ventricular compliance. The magnitude of the diastolic abnormality appears to be related to the size of the infarct.

Ventricular remodelling

As a consequence of MI, changes occur in the LV size, shape and thickness involving both the infarcted and non-infarcted segments and are collectively referred to as ventricular remodelling , a process that in turn can influence ventricular function and prognosis of the patient .[47] Infarct expansion plays an important role in ventricular remodelling.Remodelling is also caused by dilatation of viable portion of ventricles, commencing immediately and progressing for months or years thereafter.[48]

CLINICAL MANIFESTATIONS OF AMI

Precipitating factors:

1) Unusually heavy exercise in fatigued or emotionally stressed or habitually inactive patients. [49]
2) Non cardiac surgical procedure.
3) Hypotension and increased myocardial oxygen demands secondary to aortic stenosis, fever, tachycardia and agitation.

4) Other less common factors includes respiratory infection, hypoxaemia of any cause, pulmonary embolism, hypoglycaemia, administration of ergot preparation, use of Cocaine, sympathomimetics, allergy etc.

Circadian Periodicity

Peak incidence of myocardial infarction is between 6 A.M. and 12 noon. Early morning hours are associated with rise in plasma catecholamines and cortisol and increase in platelet aggregability.

Prodromal symptoms

Usually characterized by malaise, exhaustion and chest discomfort.

Nature of pain

It is variable in intensity. In most patients it is severe and in some instances it is intolerable. The pain is prolonged often lasting for more than 30 minutes and frequently for hours. The discomfort is described as constricting, crushing or compressing, often the patients complain of sensation of a heavy weight or squeezing in the chest, sometimes it may be characterized as stabbing. The pain is usually retrosternal in location, spreading frequently to both the sides of anterior chest. Often pain radiates down the ulnar aspect of left arm, producing tingling sensation in the left wrist, hand and finger. In some patients, pain of AMI, may begin in the epigastrium and simulate a variety of acute abdominal disorders. In other patients discomfort of AMI radiates to shoulder, upper extremities, neck, jaw and interscapular region. In some patients, particularly elderly, it is

manifested clinically not by chest pain but rather by symptoms of acute LVF, chest tightness, extreme weakness and fatigue or frank syncope[50]. Pain of myocardial infarction represents ongoing ischaemia.

Other Symptoms

Nausea and vomiting may occur. These symptoms occur more commonly in patients with inferior wall MI. Occasionally, patients complain of diarrhoea or a violent urge to evacuate the bowels during the acute phase.Other symptoms include feeling of profound weakness, dizziness, palpitations, cold perspiration and sense of impending doom.

Atypical presentations

These include heart failure, atypical location of pain, CNS manifestations resembling those of stroke ,apprehension and nervousness, sudden mania or psychosis, syncope, overwhelming weakness, acute indigestion and peripheral embolization. Silent MI is common in diabetics, hypertensives, women and elderly patients.

PHYSICAL EXAMINATION

Patients with AMI often appear anxious and in considerable distress. In patient with LVF and sympathetic stimulation, cold perspiration and skin pallor may be evident. In patients with cardiogenic shock the skin is cold and clammy with cyanosis and marked facial pallor.

Heart rate, Blood pressure and JVP

Heart rate may vary from bradycardia to a rapid or irregular tachycardia.Ventricular premature beats are common. Majority of the patients are normotensives. Slight hypertensive response is seen in first few hours secondary to sympathetic response to pain. Patients with cardiogenic shock have systolic BP< 90mmHg and evidence of end organ hypoperfusion. More than half of the patients with inferior wall MI have excessive parasympathetic stimulation with hypotension, bradycardia or both. About half of the patients with anterior wall MI showing sympathetic stimulation have hypertension, tachycardia or both[51]. Usually the JVP fails to show any abnormality in AMI. But associated right ventricular infarction often results in raised JVP.

Cardiac examination

Despite severe symptoms and extensive myocardial damage, the findings on examination may be unremarkable. In the presence of LV systolic dysfunction, an outward movement of LV may be palpated and early diastole coincides with S_3. On auscultation the S_1 is muffled or inaudible immediately after MI and the intensity increases during convalescence. Soft S_1 may also indicate prolonged PR intervals. In the presence of LBBB, there will be paradoxical splitting of S_2. S_3 is usually heard in patients with large infarction, common in transmural anterior wall

than in inferior wall or non transmural MI. An S_4 is almost universally heard in patients with acute MI in sinus rhythm. Systolic murmur, transient or persistent can be heard due to papillary muscle dysfunction or LV dilatation or tricuspid regurgitation. Moist rales are audible in patients who develop LVF or reduction in LV compliance in AMI. In 1967, Killip and Kimball proposed a prognostic classification based on presence and severity of rales[52].

Class I - Free from rales and S_3

Class II - Rales in <50% of lung fields with or without S_3

Class III - Rales >50% of lung fields with S_3 .Frequently have pulmonary oedema.

Class IV - Cardiogenic shock with systolic pressure < 90 mm Hg and evidence of peripheral vasoconstriction, cyanosis, mental confusion, oliguria.

Mortality rate in these classes were as follows: Class I - 0 to 5 % , Class II- 10 to 15 %, Class III - 35 to 45 % and Class IV - 85 to 95 % .

DIAGNOSIS OF AMI

It is based on ECG, Cardiac biomarkers and Imaging. The revised definition has given greater importance to biomarkers.

Cardiac Biomarkers

Necrosis compromises the integrity of the sarcolemmal membrane and intracellular macromolecules (serum cardiac biomarkers) begin to diffuse into the cardiac interstitium and ultimately into the microvasculature and lymphatics in the region of the infarct .[53] The rate of appearance of these macromolecules in the peripheral circulation depends upon several factors including intracellular location, molecular weight, local blood and lymphatic flow and the rate of elimination from the blood.

Characteristics of an ideal biomarker are:

1. For optimal specificity it should be present in high concentration in the myocardium and be absent in non myocardial tissue and serum.
2. For optimal sensitivity it should be rapidly released into the blood after myocardial injury (which is based on the molecular size and the intracellular location of the molecule) and there should be stoichiometric relationship between the plasma level of the marker and extent of myocardial injury.
3. The marker should persist for an appropriate length of time to provide a convenient time window.
4. The assay methodology should be inexpensive and easy to perform.

No single biomarker satisfying the ideal criteria exists. Wu et al [54] recommended that two biochemical markers should be used for routine AMI diagnosis; an early marker (reliably increased in the blood within 6 hours of

onset of symptoms) and a definitive marker (increased in the blood after 6 to 9 hours and remaining abnormal for several days)

CONVENTIONAL BIOMARKERS

ASPARTATE AMINOTRANSFERASE (AST/SGOT)

The levels of serum AST 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. Initially it was considered as a very good marker of cardiac injury but later on, its use became limited due to its elevation in trauma to skeletal muscles and liver diseases. [55]

LACTATE DEHYDROGENASE (LDH)

An increase in serum LDH activity is found following myocardial infarction beginning within 6 - 12 hours and reaching a maximum at about 48 hours. 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 several days after MI. RBC's are rich in LDH and hence, haemolysis may give falsely elevated results. Its use is discouraged due to its non-specificity as increased levels are found in progressive muscular dystrophy, myoglobinuria, leukaemia, pernicious anaemia, megaloblastic and haemolytic diseases [56].

MYOGLOBIN

Myoglobin is a haem protein that is present in the cytoplasm of cardiac and skeletal muscle cells; its function is to transport intracellular

oxygen. It is elevated in 2 - 3 hours after myocardial injury. The advantage of this marker is the high negative predictive value of serum myoglobin for excluding early infarction. This has encouraged its use along with more specific markers such as CK-MB and cardiac troponins to improve the diagnosis of AMI. The disadvantage is that, myoglobin is found both in skeletal and cardiac muscles, so its specificity is compromised in the presence of skeletal muscle damage [57].

CREATININE KINASE (CK)AND ITS ISOENZYME MB (CK-MB)

Serum CK activity increases following MI beginning within 6 hours and peaking on an average at 24 hours and returning to normal within 2-3 days. 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 [58] makes it unsuitable as a marker of myocardial injury.

CK has three isoenzymes namely CK-BB, CK-MB and CK-MM. Myocardium contains 40% CK-MB and 60% CK-MM along with traces of mitochondrial CK (macro CK type II) whereas skeletal muscles contain about 97% CK-MM, 2-3% CK-MB and traces of CK-BB and mitochondrial macro type II. Being highest in proportion in the myocardium CK-MB has been used as a biochemical marker in patients with suspected 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. It has been considered as the 'Gold Standard' for confirmation of AMI [59]. However, the techniques used (electrophoresis and immunoinhibition) to quantitate CK-MB catalytic activity were not sensitive enough for early use, being relatively non-specific and long turn-around time restricted its use primarily for confirming MI at 24 hours post injury [60]. The CK-MB mass assay has a diagnostic sensitivity of 50% at 3 hours. and 80% at 6 hours. It has been found that CK-MB mass slope calculated from serial blood samples collected 0-12 hours after the onset is a rapid and accurate diagnostic approach to categorize the patients with suspected AMI [61]. Despite all these advantages of CK-MB mass assay, it has two main limitations: (1) it is not perfectly specific to cardiac injury, with increases occurring also during massive musculoskeletal injury and (2) the early release pattern limits its use for the late MI diagnosis. But it has a definite place for the diagnosis of reinfarction and has prognostic value in patients with unstable angina. The ratio of the CK-MB / total CK(>2.5) has also been proposed for the diagnosis of MI by some authors [62] but it has been discouraged by others due to certain limitations [63] as in following instances: (1) when high levels of total CK are present because of skeletal muscle injury (a large quantity of CK-MB must be released from the myocardium to satisfy criteria); (2) when chronic skeletal muscle injury releases large amounts of CK-MB; and (3) when total CK measurements are within the normal reference range for the

laboratory and CK-MB is elevated (possibly indicating that a microinfarction has occurred). Patients with minimally elevated CK-MB and normal CK have a prognosis that is generally worse than that for patients with suspected MI but no CK-MB elevation.CK-MB isoforms (subtypes) are also considered as sensitive markers for early diagnosis of MI . There is only one CK-MB isoform within tissue but after release into the circulation CK-MB is chemically modified resulting in two bands on traditional high voltage electrophoresis : one tissue subtype MB2 and the other the modified subtype MB1. The ratio of MB1/MB2 provides the basis for a positive MB subtype result. However, CK-MB isoforms offer no advantage over CK-MB mass as an early marker of MI [64] and CK-MB mass measurement is more practical to perform in the laboratory and easily automated than the measurement of CK-MB isoforms with available methods.

CARDIAC TROPONINS

These are regulatory proteins found in the skeletal and cardiac muscles. The 3 subunits that have been identified include cardiac troponin I (cTnI), cardiac troponin T (cTnT) and cardiac troponin C (cTnC)[65]. The complex regulates the calcium-modulated interaction between actin and myosin on the thin filament. Each troponin subunit is encoded by a separate gene, whereas TnI and TnT exist as specific skeletal and cardiac muscle isoforms. The function of cTnI is to inhibit actinomyosin ATPase activity.

The cTnC interacts tightly with cTnI, reversing the inhibitory effect. Most intracellular cTnI and cTnT is bound to the myofibrils in the cardiac myocyte. However, a small percentage exists in a cytosolic pool[57]. These cardiac troponins appear in the blood as early as 3 - 4 hours after the acute episode and remain elevated for 4 - 14 days [66]. The maximal amount of free cTnI was released shortly after the injury due to breakdown of the myofibrillary complex in damaged myocytes; cytosolic troponins reach the blood stream quickly resulting in a rapid peak of serum troponin which is observed during the first few hours [67]. This is followed by the release of structurally bound troponin resulting in a second peak lasting for several days. An increase in the concentration of serum cardiac troponins reflects myocardial damage but does not indicate mechanism [65]. Both cTnT and cTnI are almost equally good markers and it is difficult to say which is better because both have some positive and negative points. cTnI is 100% cardiospecific and as opposed to cTnT it is not elevated in chronic renal disease, trauma and skeletal muscle disease[68]. The overall diagnostic specificity and efficiency of cTnI is better than cTnT and it is proved to be the most sensitive marker in detecting myocardial necrosis following percutaneous intervention . However, the third generation cTnT assays don't allow the skeletal TnT interference. Both cTns undergo post translational modifications such as phosphorylation, oxidation, reduction, proteolysis and form complex with other troponins. cTnI is more prone to these

modifications and these modifications may prevent some antibodies used in the assay system from binding to the molecules and thereby diminishing the signal. There are some discrepancies in the standardization of cTnI assays. The same sample tested with assays from different manufacturers may give several fold difference in the results whereas cTnT assay is manufactured by only one manufacturer . The life-time of cTnT in blood (5-14 days) is some what more than that of cTnI (4-10 days).The disadvantages of cardiac troponins is its elevation in patients with myocarditis and in such conditions where cardiac damage might not be expected such as stroke, pulmonary embolism, pulmonary hypertension and severe renal dysfunction.

NEWER BIOMARKERS

Heart type fatty acid binding protein (H-FABP)

Brain Natriuretic Peptide (BNP): BNP is synthesized and stored in atrial and ventricular myocytes, although plasma BNP originates mainly from the left ventricle. The plasma concentration is related to the magnitude of the atrial or ventricular overload. The increase in the circulating concentrations of BNP was found soon after AMI as shown by Morita et al [69], whereas Morrison et al [70] have shown that the increased value of BNP helps in differentiating cardiac and pulmonary causes of dyspnoea. Disorders associated with right ventricular dysfunction, such as primary pulmonary hypertension, and pulmonary embolism are also associated with increased plasma BNP concentration.

Glycogen Phosphorylase BB: GPBB is in the form of sarcoplasmic reticulum glycogenolysis complex. It is released within 2 - 4 h after the onset of myocardial damage and returns to the reference range within 1 - 2 days after MI. The release of GPBB in parallel with myoglobin or heart-type fatty acid binding protein indicates irreversible myocardial damage [71]. At the time of tissue hypoxia glycogen is broken down, GPBB is converted to a soluble form and becomes free to move in the cytoplasm. During ischaemic conditions, rapid increase in glycogenolysis and simultaneously increase in plasma membrane permeability occurs, which favours early release of GPBB. Thus GPBB serves as an accurate marker for the detection of ischaemic myocardial damage but is yet to be confirmed with high-quality GPBB assays.

Adiponectin: Adiponectin is a 247 amino-acid peptide hormone, which circulates at a relatively high concentrations in the blood stream, accounting for 0.05% of total serum proteins and is inversely associated with obesity, insulin resistance, type 2 diabetes mellitus and cardio- vascular diseases (CVD)[72].

Xanthine Oxidase: Xanthine oxidase produces oxygen free radicals which oxidize cellular proteins and membranes resulting in myocardial cellular injury [73]. The elevated levels of xanthine oxidase activity in the blood of patients with myocardial infarction is the main advantage of this marker.

But the disadvantage of this marker is that it is also found elevated in non-cardiac conditions like liver disorders[74].

Pregnancy Associated Plasma Protein A (PAPP-A): Bayes-Genis et al showed the presence of PAPP-A in unstable plaques from patients who died suddenly of cardiac causes [75]. PAPP-A was abundantly expressed in plaque cells and extracellular matrix of ruptured unstable plaques, but not in stable plaques. Circulating PAPP-A levels were significantly elevated in patients with unstable angina or acute myocardial infarction than in patients with stable angina.

Carbonic anhydrase III: The tissue distribution of carbonic anhydrase III is limited to skeletal muscles and its assay is used in combination with that of myoglobin. It has been suggested that an increase in the myoglobin:carbonic anhydrase III ratio is diagnostic of myocardial injury[76]. Currently available assays for carbonic anhydrase are relatively time consuming, limiting the clinical use of the myoglobin:carbonic anhydrase III ratio.

Myosin light chains: A small amount (<1%) of MLC is found in the muscle cell as a cytosolic precursor of myosin synthesis. This unbound free fraction is released into the circulation rapidly after myocardial injury and its molecular size enables it to be filtered by the glomerulus. Assays developed so far tend to be for MLC 1, as MLC 2 is very labile. However, MLC 2 has the potential for greater cardiac specificity [77].After myocardial

injury, MLC 1 appears in the circulation 3–6 h after the onset of pain, due to the release of the unbound cytosolic fraction. Peak values occur after about 4 days, and elevated plasma concentrations persist for 10–14 days, reflecting continuing release from infarcted myofilaments.

Ischaemia modified albumin (IMA): Under normal physiological conditions, transition metals bind to the N-terminus of the albumin molecule. Ischaemia causes a structural modification to the N-terminus of the protein possibly as a result of exposure to reactive oxygen species. This alters the ability of the protein to bind to metals such as cobalt. The albumin–cobalt binding test is a rapid spectrophotometric procedure, which can be easily automated, to provide a measure of serum IMA [78]. Serum IMA can differentiate myocardial ischaemic patients from non-ischaemic individuals, but is a poor discriminator between ischaemic patients with and without MI.

Markers of inflammation

Atherosclerosis is associated with an inflammatory process, and markers of inflammation are being investigated as potential tools for cardiovascular risk prediction. Markers of inflammation such as C-reactive protein, Interleukins (IL-18,IL-6), Myeloperoxidase, Whole blood Choline, CD-154, Urocortin have also been suggested as predictors of cardiovascular risk and studies are ongoing regarding their usefulness.

Electrocardiographic findings

During initial stage of acute phase of MI, total occlusion of the infarct artery produces ST segment elevation. Most patients initially presenting with ST elevation evolve Q waves on the ECG and are ultimately diagnosed as having sustained a Q wave MI. A small proportion may sustain only a non Q wave MI. When the obstructing thrombus is not totally occlusive or obstruction is transient or if a rich collateral network is present, no ST elevation is seen. Such patients are diagnosed as either unstable angina (Biomarkers negative) or a non ST elevation MI (Biomarkers positive). Among patients presenting with ST segment elevation, if a serum marker is detected and no Q wave develops, the diagnosis of non Q wave MI is ultimately made. Serial standard 12-lead ECGs remain a potent and extremely clinically useful method for the detection and localization of MI.

IMAGING

2D Echocardiography, Doppler Echocardiography, Computed Tomography, Cardiac Magnetic Resonance and Nuclear Imaging like Radionuclide Angiography, Perfusion Imaging, Infarct Avid Scintigraphy, Positron Emission Tomography have also been used to evaluate Myocardial Infarction[79].

MANAGEMENT OF AMI

General measures include: Establishing an IV line, Obtaining initial blood samples for cardiac enzymes level, complete blood count, electrolytes and

lipid profile, Monitoring vital signs and Pulse oxymetry to measure oxygen saturation.

Oxygen therapy: 2-4 litre /min via nasal prongs is indicated in most patients with AMI because mild hypoxaemia is common. In stable patients without hypoxaemia it is usually discontinued after six hours.

Anti Ischaemic Treatment: Nitrates: Given sublingually or buccal spray (0.3 – 0.6 mg).If the pain persists after 3 doses given 5 min apart, IV Nitroglycerine 5 – 10 micro gram per minute is advised.

Beta Blockers: Metoprolol 5 mg IV over (1 -2 min) repeated after 5 min for total dose of 15mg, followed by 25-50 mg orally 6th hourly or Esmolol 0.1mg / kg / min IV.

Control of Pain: Morphine: 2-5mg IV. May be repeated if necessary.

Oral anti platelet Therapy: Aspirin-Initial dose of 162 – 325 mg non-coated formulation, followed by 75-160 mg per day. Clopidogrel- Loading dose 300mg, followed by 75 mg per day.

Anticoagulant Therapy

Heparins: (UFH) Bolus 60-70units /kg (Max 5000 units) IV, followed by infusion 12-15 units /kg/hour.

Deltaparin: 120 IU / kg SC, 12th hourly.

Enoxaparin: 1mg /kg SC 12th hourly.

In case of STEMI, patients should be considered for reperfusion therapy with thrombolytic agents like,

a. Tissue plasminogen activator (tPA): 15mg bolus followed by 50 mg IV over first 30 min, followed by 35mg over next 60 min.
b. Streptokinase (SK) 1.5 million units IV over 1 hour.
c. Tenecteplase (TNK) 0.53 mg / kg over 10 seconds as a bolus.
d. Reteplase (rPA) given as double bolus regimen. 10 million units bolus over 2-3 min, followed by 10 million units bolus 30 minutes later. Patients can also be taken for Primary PCI.

Activity: After bed rest for the first 12 hours, if no complications, sitting is advised within 24 hours, walking within the room by 2-3 days. After 3 days patients can increase walking progressively .

Diet: For first 4 -12 hours nil orally or clear liquids by mouth.

Afterwards, diet should provide 30 % calories from fat; carbohydrates should make up 50 -55 % of total calories. Food should be enriched with high potassium, magnesium and fibre but low in sodium.

Bowel: A bedside commode rather than a bed pan, a diet rich fibre and routine use of stool softeners is adviced.

Sedation: Diazepam 5mg or lorazepam 1mg or alprazolam 0.5 – 1 mg can be given at bedtime.

Beta Adrenoreceptor Blockers: Benefits immediately to relieve pain, to reduce the infarct size, to improve myocardial oxygen supply, to decrease the incidence of serious ventricular arrhythmias.

Angiotensin Converting Enzyme Inhibitors: Benefits by reducing the ventricular remodelling after MI and by the reduction of the risk of CCF.

It should be prescribed within 24 hours of MI. Angiotensin receptor blockers may be useful in patients with depressed LV function or with clinical heart failure who are intolerant to ACE Inhibitors.

COMPLICATIONS OF AMI

A. Mechanical Complications: Ventricular septal rupture , Mitral regurgitation , Cardiac rupture, Pseudoaneurysm , Ventricular aneurysm .

B. Ischaemic Complications: Infarct extension, Inhospital reinfarction, Post infarction angina.

C. Embolic Complications.

D. Inflammatory Complications:

Early pericarditis, Late pericarditis (Dressler`s syndrome).

E. Cardiogenic Shock

F.Arrhythmias:Ventricular premature beats , Accelerated idioventricular rhythm, Ventricular tachycardia , Ventricular fibrillation , Supraventricular arrhythmias , Junctional rhythm , Sinus bradycardia , Asystole.

G. Atrioventricular and Intraventricular Conduction Blocks

HEART TYPE FATTY ACID BINDING PROTEIN

The fatty-acid-binding proteins (FABP) are a family of cytosolic proteins that shows a large degree of structural homology. Discovered by Ockner in 1972 in studies on the intestinal absorption of fatty acids [80], they are called FABPs because they exhibit a high affinity for the non-covalent binding of fatty acids. These proteins are widely distributed and are present in the fatty acid metabolizing tissues of many mammals. There are several types and all have low molecular mass (12–15kDa), but they differ markedly in tissue distribution, concentration within the tissue, isoelectric point, binding capacity, and binding specificity [81].The FABPs are relatively tissue-specific, and are designated by a letter that refers to their tissue of origin, e.g. L-FABP, H-FABP, I-FABP, referring to liver, heart and intestinal FABPs respectively; tissue-specific FABPs have also been reported in the muscle, adipose tissue, kidney, brain and nerve cells. Tissue-specific FABPs such as L-FABP and I-FABP have been used to detect pathologies in these tissues using specific antibodies raised against these proteins [82]. Different FABPs share between 30–80% amino acid sequence homology.

Heart-FABP is a small (15 kDa) soluble non-enzyme protein. It is composed of 132 amino acids [83]. It is one of the most abundant proteins in the heart and comprises 5–15% of the total cytosolic protein pool in the aqueous cytoplasm. The gene is located on chromosome 1 [84]. H-FABP

binds two molecules of fatty acids and is involved with the delivery of fatty acyl coenzyme A for oxidation with the generation of energy in the mitochondria. Myocardial ischaemia results in a significantly higher level of fatty acids in the plasma and the myocardial tissue, which can be harmful to the heart [85]. The presence of H-FABP may serve a protective function for the myocardial cells against the oxidation of these fatty acids while still having these substances readily available for the metabolic needs of the cell. During ischaemia (e.g. AMI), H-FABP leaks out of myocardial tissue and the concentration increases in the plasma [86]. The leakage of H-FABP from the myocardium may make the myocardium more vulnerable to the harmful effects of fatty acids during reperfusion and may account for some of the complications seen during reperfusion, e.g. arrhythmias. Some reports have suggested another protective role for H-FABP, as scavengers of free radicals that are present in the heart during ischaemia [87].

The different FABPs from heart, liver and intestine share between 20–35% amino acid sequences homology and heart, nerve, and adipose tissue FABPs share 60–80% amino acid sequence homology. Antibodies raised against heart, liver or intestinal FABPs in the earlier studies may thus have up to 5% cross-reactivity with each other and have a detection limit of around 1ng/ml. The newer assays have a much improved sensitivity and can detect H-FABP in concentrations as low as 0.25 ng/ml; the cross-reactivity with other tissue FABPs is <0.005% [88].

The rationale for the use of H-FABP as a marker for the early diagnosis of myocardial injury is based on the following features: (i) the presence of this soluble protein in the myocardium in high concentration (ii) virtual confinement to the cytoplasmic space (iii) small molecular size (iv) relative tissue specificity, with a relative distribution of H-FABP outside the heart similar to that of CK-MB[89] and (v) early release into the plasma and urine (within 2h) after onset of myocardial injury. H-FABP bears a considerable resemblance to myoglobin in terms of size, location within the cell, release and clearance kinetics. However, when compared to myoglobin, H-FABP concentration in the heart muscle is greater than that in skeletal muscles, and its normal baseline concentration is several fold lower than that of myoglobin. These advantages make H-FABP potentially a more suitable cardiac marker than myoglobin .[90,91,92]

Measurement of H-FABP and normal range

The method of measurement is based on sandwich ELISA) using two monoclonal antibodies specific for H-FABP [93]. The normal ranges reported for H-FABP in plasma and serum are assay and method dependent. Tanaka et al. (1991) has reported the normal range for H-FABP to be 0.0–2.8μg/l; [10] Wodzig et al. (1997) reported 0.3–5μg/l as the normal limit; [88] and Tsuji et al. (1993) used 3μg/l (normal range 0–0.6μg/l).[12] H-FABP is not likely to be found in the blood stream under normal conditions.

Plasma H-FABP and acute myocardial infarction

H-FABP was introduced by Glatz in 1988 as a potential novel biochemical marker for the early diagnosis of AMI.[94] This assumption was soon confirmed in several studies.[10,11,95] Under normal conditions H-FABP is not present in plasma or interstitial fluid, but is released into the blood upon cellular injury. The cytoplasmic to vascular concentration of H-FABP is of the order of 200000:1. This makes the plasma estimation of H-FABP suitable for the early detection and quantification of myocardial tissue injury. The H-FABP is released into the plasma within 2 hours after symptom onset and is reported to peak at about 4–6 hours and return to normal base line value in 20 hours. Within the period of 30–210 minutes after symptom onset, H-FABP has >80% sensitivity for the diagnosis of AMI.[11] Within the interval of 0–6 hours after symptom onset, the other cardiac markers such as creatine kinase, CK-MB mass or activity, cardiac cTnI and cTnT will only be starting to accumulate in the plasma and their sensitivity has been reported to be around 64%.[96]

Urinary H-FABP and acute myocardial infarction

H-FABP is eliminated from the circulation by the kidney, but the precise mode of renal handling of H-FABP is unknown. A rise in serum and urine H-FABP concentration above normal values is seen in patients who present with AMI as early as 1.5 hours after the symptom onset. [10]Assays that measure H-FABP in urine samples were able to accurately diagnose

patients with AMI and provide reliable estimation of infarct size[9]. However, the measurement of infarct size based upon urinary H-FABP may be influenced by several factors, such as renal blood flow, perfusion pressure, glomerular filtration rate, tubular absorption and diseases of the kidney. Measurement of urinary and plasma H-FABP in the presence of kidney diseases may lead to underestimation and overestimation, respectively, of the size of infarct due to impairment of excretion of H-FABP [97]. H-FABP circulates for longer (>25 hours) after AMI in the presence of renal failure[11]. Several sensitive assays that can measure H-FABP in urine samples are available.[10,12]

Limitations of H-FABP assays

H-FABP is excreted by the kidney and renal insufficiency results in decreased clearance of H-FABP, thereby elevating the concentration and prolonging the circulation time. In situations of AMI and renal failure, measurement of plasma H-FABP could lead to overestimation of myocardial infarct size and could interfere with its use for the detection of re-infarction [97]. However, renal failure is readily detectable in standard biochemical analysis and should not confound the diagnostic specificity of H-FABP, for the vast majority of patients. The main disadvantage of myoglobin or H-FABP as early markers of myocardial injury is lack of complete specificity, due to the presence of both in skeletal muscles. Severe skeletal muscle injury may result in the release of both proteins in sufficient

quantity to interfere with the specificity of the assay. Both proteins are released into the plasma after injury at about the same time and in a ratio similar to the concentration of the proteins in the tissue of origin, therefore the measurement of the myoglobin: H-FABP ratio could be useful for discriminating between cardiac and skeletal muscle damage. A myoglobin:H-FABP ratio ~5 is considered to be specific for the heart; a ratio ~21–70 is more indicative of skeletal muscle damage[6]. The combination of the two markers in a ratio has been reported by some investigators to increase the diagnostic specificity for the diagnosis of AMI more than relying on either marker alone. However, the use of this ratio should not be a rigid criterion, as overlaps do occur. Some investigators did not find any additional value in myoglobin:H-FABP ratio over the measurement of H-FABP alone [6,92].

H-FABP and acute myocardial infarction after surgery

H-FABP peaks early and may be useful for the early detection of myocardial injury after surgery. The plasma concentration of H-FABP is increased relatively early, compared to CK-MB and cTnT, after aortic declamping in CABG surgery. The time to peak concentration was significantly shorter for plasma H-FABP (1.4 ± 0.5hours) than for

CK-MB (2.5±0.5hours) or cTnT (6.6±1.3hours). Similar findings were reported in other studies.[98] H-FABP was not increased in low-risk patients after CABG surgery without cardiopulmonary bypass.[99]

H-FABP and detection of reperfusion

H-FABP has been reported to be a sensitive marker for the detection of reperfusion after thrombolytic treatment. Abe et al. (1996) demonstrated that a rise of H-FABP ratio of ≥1.5 (compared to pre-treatment concentration), 30minutes after thrombolytic treatment, was associated with 100% accuracy for the detection of reperfusion. This accuracy dropped to 94% at 60 minutes after thrombolytic treatment.[95] The advantage of using H-FABP is that reperfusion is ascertained very quickly, in some studies as early as 15 minutes. In a study by Ishii et al (1995), the predictive accuracy of H-FABP ratio > 1.8 for the detection of reperfusion within 60 minutes of initiation of treatment was 93% at 15 minutes, 98% at 30 minutes and 100% at 60 minutes after reperfusion.[100]

H-FABP and detection of re-infarction

The features of an ideal marker for early re-infarction are early release and clearance from the circulation, thus permitting a prompt return to pre-infarction concentrations. H-FABP fulfills these features, appearing within 3 hours after infarction, peaking early at about 5 hours and returning to baseline concentrations about 20 hours after symptom onset.[11] Re-infarction is shown by a rapid rise in H-FABP concentration in serum

compared to the previous value. H-FABP can detect re-infarction when it occurs 10 h after symptom onset.[6] Other cardiac biomarkers such as cTnI, cTnT and LDH take several days to return to the pre-infarction levels and thus are not sufficiently sensitive for the detection of re-infarction.

H-FABP and estimation of infarct size

Accurate measurement of infarct size is possible using nuclear studies, but is not practical for routine use because it is expensive, requires high technology and exposes patients to additional radiation. Cardiac markers offer an alternative for the estimation of infarct size. The rapid and quantitatively robust release of H-FABP into plasma after symptom onset and its rapid clearance from the circulation within 24 hours, makes it potentially suitable for the early estimation of infarct size, provided that blood is sampled sufficiently frequently.[97] Sohmiya et al. (1993) showed good correlation between myocardial infarct size measured from plasma H-FABP and infarcted myocardium estimated from triphenyl tetrazolium chloride (TTC) staining.[9] A study by Glatz et al. (1994) using H-FABP for the early estimation of infarct size, showed a good correlation between H-FABP, CK-MB and α-hydroxybutyrate dehydrogenase (α-HBDH) for the estimation of infarct size. The advantage of H-FABP is that this measurement is completed much earlier than with the other two markers: 24

hours, 48 hours and 72 hours for H-FABP, CK-MB, and α-HBDH, respectively.[101]

Excretion of heart type fatty acid binding protein

It is not clear at present whether H-FABP reaches the circulation trans-endothelially or via the lymphatic system or both, after its release from the cell into the intercellular space. The rapid appearance in the blood may suggest the first route. The route of elimination from the circulation is assumed to be the kidney, based on direct and indirect evidences.

Supporting literatures :

Some studies are discussed here to enlighten the present study:

In a study by Okamoto et al[3] to compare the role of H-FABP in AMI with that of Myoglobin and CK-MB, the overall sensitivity within 12 hours of symptom onset was 92.9% for H-FABP,88.6% for myoglobin and 18.6% for CK-MB. The overall specificity was 67.3% for H-FABP, 57.1% for myoglobin and 98.0% for CK-MB. The diagnostic efficacy with these markers were 86.2%(H-FABP),80.4%(myoglobin) and 39.2%(CK-MB) respectively.

A study by Priya Gururajan et al[102] at Chennai showed H-FABP to be a good discriminator between patients with and without IHD. It also showed that whereas troponin levels rise more than 6 hours after symptom onset, H-FABP is usually positive within the first 4 hours.

A study by Ruzgar et al[103] showed sensitivity of 38% with troponin, 76% with CK-MB and 95% with H-FABP in patients admitted within 6 hours of symptom onset.

A study by Seino Y et al [104] showed 89% sensitivity of H-FABP within 2 hours of symptom onset compared to 22% with troponin and 38% with myoglobin.

In a study by Mad P et al [105] , in 280 patients presenting to the hospital with a median time of 3 hours after symptom onset, H-FABP had a sensitivity of 69% and specificity of 74% and AMI was diagnosed significantly earlier than by troponin.

A study by Karthik Viswanathan et al[106]showed that elevated H-FABP is an independent prognostic marker in patients with suspected acute coronary syndrome and that it identifies high risk troponin negative chest pain patients reliably.

But a study by Jonathan Rosman et al [107]failed to show any advantage of H-FABP over troponin.

MATERIALS AND METHODS

This study was carried out in the Department of General Medicine and Cardiology at Government Kilpauk Medical College & Hospital, Chennai –10 during the period between November 2009 and October 2010.This study was ethically approved by the Ethical committee of Government Kilpauk Medical College and Hospital, Chennai – 10.

This is a cross sectional study. 50 patients admitted to the Intensive Cardiac Care Unit (ICCU) with ischaemic symptoms were enrolled. They were categorised in to those coming to the hospital within 4 hours of symptom onset and those coming in between 4 to 12 hours.

INCLUSION CRITERIA:

1. All the patients with ischaemic symptoms admitted to the ICCU.

EXCLUSION CRITERIA:

1. Patients with Cerebrovascular accident.
2. Patients with Renal diseases.
3. Patients coming after 12 hours of symptom onset .

Applying these criteria, 50 eligible patients were selected and included in the study after informed consent.

METHODOLOGY

A detailed history was taken and clinical examination was done in all the patients with particular reference to the cardiovascular system. Relevant urinary and blood investigations were done.ECG was taken in all the patients.CK-MB was measured. Qualitative estimation of Cardiac troponin I (cTnI) and Heart type fatty acid binding protein (H-FABP) was done using Cardiodetect qualitative immunological rapid test combi kit. Echocardiography was done. Treatment given, complications and course in the hospital were recorded. Data collected was analysed statistically.

1. Socio-demographic data:

Age Sex Occupation

Family H/O hypertension, diabetes, IHD (Father/Mother/Siblings)

H/O Alcohol, Smoking, Tobacco use, Diet history.

2. Clinical data:

A detailed clinical examination was done. Pulse, BP,JVP, respiratory rate, temperature recorded. Pallor, icterus, cyanosis, clubbing, pedal oedema, lymphadenopathy were looked for.BMI was calculated.

BMI:[108]Body Mass Index(BMI) = Weight (kg) /(Height in metre) ^{2}.

Values 18.5 - 22.9 kg / m^2 was taken as normal weight.

23- 24.9 kg / m^2 was taken as overweight.

$\geq$ 25 kg / m^2 was taken as obesity.

General & Systemic examination done.

3. Laboratory data:

Urine analysis: Urine sample was collected for urine routine analysis which included sugar, protein, cytology and urinary sediments.

Blood sugar: Blood sugar was estimated by Trinder's (Glucose oxidase) method and read at 505/670 nm.

Renal function test: The blood urea was estimated using DAM method (Diacetyl Monoxime). Serum creatinine was estimated using Modified Jaffe's method. Electrolytes were measured by absorption spectrophotometry.

Lipid Profile: Total cholesterol and triglycerides measured using Trinder's method. Total cholesterol <200mg/dl taken as normal and triglycerides <150mg/dl taken as normal.

ECG: Standard 12 lead ECG taken for all the patients.

Echocardiography: Two dimensional Echocardiography was done for all the patients included in this study.

CK-MB: Estimated using Immunoinhibition method. Values <25 IU/L considered as normal.

ESTIMATION OF TROPONIN I AND H-FABP :

Estimation was done using Cardiodetect qualitative immunological rapid test combi kit. The test may be performed with capillary or venous whole blood, serum or plasma.The test field for both troponin I and H-FABP is filled with 3 to 4 drops of whole blood, serum or

plasma. The result is read after 15 minutes. If both the test (T) and control (C) lines are seen then it is taken as positive result. If only control (C) is seen then it is taken as negative result. If no line is seen then it is taken as invalid result.

The test principle:

H-FABP: The test contains two different monoclonal antibodies specific for H-FABP, of which one is gold-labelled. The sample liquid releases the gold-labelled anti-FABP antibody from its matrix. This antibody forms an intermediary complex with the FABP present in the sample. This complex spreads across the test strip up to the position marked by 'T' where a second antibody is located. The intermediary complex and the second antibody form a sandwich complex showing up as a red line. A sample without H-FABP does not form a sandwich complex and therefore, forms no red line.

cTnI: If the sample contains cTnI , it interacts with anti cTnI antibodies and particles coated with the biotynilised anti cTnI antibodies. This complex passes over the test strip up to the position marked with 'T' where a line is coated with Streptavidin. The complex reacts with the Streptavidin showing up as a red line. A sample without cTnI forms no red line.

Integrated Function Control: The functioning of the test is indicated by the red control line at the position of the 'C' mark, because the excessive

gold-labelled antibodies gather here. The control line is formed if the sample has properly passed across the test field.This occurs irrespective of the concentration of the analyte in the sample. The test result is only valid if this line appears.

Evaluation of the test:

For H-FABP:

If 2 lines seen (at 'C' and 'T') - Positive (HFABP>7ng/ml).

If only one line at 'C' - Negative (H-FABP<7ng/ml).

No line or one line at 'T' only- Invalid test.

For cTnI: :

If 2 lines seen (at 'C' and 'T') - Positive (cTnI>1ng/ml).

If only one line at 'C' - Negative (cTnI<1ng/ml).

No line or one line at 'T' only- Invalid test.

4. Statistical analysis:

Data was entered in Microsoft excel spread sheet and analysed statistically using SPSS software version 17.

Results were considered significant if the 'p' value was below 0.05.

The following tests were used for statistical analysis:

1. Chi – square test.
2. Diagnostic Accuracy test
3. Pearson's correlation.

RESULTS

- A total of 50 patients were selected. They were divided into two groups those presenting within 4 hours after the symptom onset and those presenting during 4-12 hours.
- Out of 50 patients 22 presented within 4 hours (44%) and 28 patients presented during 4-12 hours (56%).There was no statistical difference between males and females with regard to time window of presentation to hospital after symptom onset.
- 39 patients were males (78%) and 11 were females (22%).
- 6 patients were aged <40 years (12%), 15 were in 40-50 years age group (30%), 17 in 50-60 years age group (34%) and 12 were aged >60 years (12%).
- Totally 22 patients (44%) had hypertension. Prevalence of hypertension was more among females (8 out of 11 i.e.72.7%) compared to males (14 out of 39 i.e. 35.9%).But there was no statistically significant difference between males and females with regard to diabetes mellitus. (10 among males and 5 among females).
- Smoking and alcohol consumption were more common among the males. 34 males were smokers (87.2%), while only 2 females were smokers (18.2%).22 males used to consume alcohol (56.4%), while no females reported consuming alcohol.

- 32 males and 6 females were positive for H-FABP (82.05% v/s 54.55%).23 males and 5 females were positive for cTnI (59% v/s 45.5%) while 16 males and 6 females had elevated CK-MB (41% v/s 54.5%). This was statistically not significant.
- Out of 22 patients presenting within 4 hours H-FABP was positive in 16 patients (72.73%), cTnI was positive in 5 patients (22.73%) and CK-MB was positive in 2 patients (9.1%).The sensitivity was 60% for H-FABP, 18.8% for cTnI and 12.5% for CK-MB. The specificity was 23.53% for H-FABP, 66.67% for cTnI and 100% for CK-MB.
- Out of 28 patients presenting during 4-12 hours, H-FABP was positive in 22 patients (78.57%), cTnI was positive in 23 patients (82.1%) and CK-MB was positive in 20 patients (71.43%).The sensitivity was 86.96% for H-FABP, 90.9% for cTnI and 77.3% for CK-MB. The specificity was 60% for H-FABP, 50% for cTnI and 50% for CK-MB.
- Diagnostic accuracy of H-FABP was 31.82% within 4 hours and 82.14% during 4-12 hours. Overall diagnostic accuracy compared to troponin was 60% and compared to CK-MB was 56%.
- There was statistically significant correlation between ECG changes and Echocardiographic findings with H-FABP positivity (P value 0.000).

- Number of death was 3 out of 38 patients who were positive for H-FABP (7.9%) and nil among 12 patients who were negative for H-FABP. All the 3 deaths were in females (3 out of 11= 27.27%)
- The mean age group among H-FABP positive patients was 51.92 ± 9.437 years and 55.92 ± 9.931 among H-FABP negative patients.
- H-FABP was positive among 20 alcoholics (90.9%) and 18 nonalcoholics (64.3%). This was statistically significant. But H-FABP positivity did not show any statistically significant difference between smokers and non-smokers, hypertensives and normotensives, diabetics and normoglycaemics or those with elevated or normal BMI, triglycerides and cholesterol.

TABLE- 1

COMPARISON OF H-FABP WITH TROPONIN (0-4 HOURS)

H-FABP	TROPONIN		TOTAL
	POSITIVE	NEGATIVE	
POSITIVE	3(60%)	13(76.47%)	16(72.73%)
NEGATIVE	2(40%)	4(23.53%)	6(27.27%)
TOTAL	5(100%)	17(100%)	22(100%)

Sensitivity = 60% Positive Predictive Value=18.75%

Specificity= 23.53% Negative Predictive Value=66.67%

Diagnostic Accuracy= 31.82%

TABLE-2

COMPARISON OF H-FABP WITH CK-MB DURING 0-4 HOURS

H-FABP	CK-MB		TOTAL
	POSITIVE	NEGATIVE	
POSITIVE	2(100%)	14(70%)	16(72.73%)
NEGATIVE	0	6(30%)	6(27.27%)
TOTAL	2(100%)	20(100%)	22(100%)

Sensitivity = 100% Specificity= 30%

Positive Predictive Value=12.5% Negative Predictive Value=100%

Diagnostic Accuracy= 36.36%

TABLE-3

COMPARISON OF H-FABP WITH TROPONIN (4-12 HOURS)

H-FABP	TROPONIN		TOTAL
	POSITIVE	NEGATIVE	
POSITIVE	20(86.96%)	2(40%)	22(78.57%)
NEGATIVE	3(13.04%)	3(60%)	6(21.43%)
TOTAL	23(100%)	5(100%)	28(100%)

Sensitivity = 86.96% Positive Predictive Value=90.91%

Specificity= 60% Negative Predictive Value=50%

Diagnostic Accuracy= 82.14%

TABLE-4

COMPARISON OF H-FABP WITH CK-MB DURING 4-12 HOURS

H-FABP	CK-MB		TOTAL
	POSITIVE	NEGATIVE	
POSITIVE	17(85%)	5(62.5%)	22(78.57%)
NEGATIVE	3(15%)	3(37.5%)	6(21.43%)
TOTAL	20(100%)	8(100%)	28(100%)

Sensitivity = 85 Specificity= 37.5%

Diagnostic Accuracy= 71.43% Negative Predictive Value=50%

Positive Predictive Value=77.27%

TABLE-5

OVERALL COMPARISON OF H-FABP WITH TROPONIN

H-FABP	TROPONIN		TOTAL
	POSITIVE	NEGATIVE	
POSITIVE	23(82.14%)	15(68.18%)	38(76%)
NEGATIVE	5(17.86%)	7(31.82%)	12(24%)
TOTAL	28(100%)	22(100%)	50(100%)

Sensitivity = 82.14% Positive Predictive Value=60.53%

Specificity= 31.82% Negative Predictive Value=58.33%

Diagnostic Accuracy= 60%

TABLE-6

OVERALL COMPARISON OF H-FABP WITH CK-MB

H-FABP	CK-MB		TOTAL
	POSITIVE	NEGATIVE	
POSITIVE	19(86.36%)	19(67.86%)	38(76%)
NEGATIVE	3(13.64%)	9(32.14%)	12(24%)
TOTAL	22(100%)	28(100%)	28(100%)

Sensitivity = 86.36% Specificity= 32.14%

Diagnostic Accuracy= 56% Negative Predictive Value=75%

Positive Predictive Value=50%

TABLE-7

DISTRIBUTION OF H-FABP AMONG AGE GROUPS

AGE GROUP(YEARS)	H-FABP		TOTAL
	POSITIVE	NEGATIVE	
<40	5(83.33%)	1(16.67%)	6(100%)
40-50	11(73.33%)	4(26.67%)	15(100%)
50-60	15(88.24%)	2(11.76%)	17(100%)
>60	7(58.33%)	5(41.67%)	12(100%)
TOTAL	38(76%)	12(24%)	50(100%)

P Value is 0.298. statistically not significant.

There was no statistically significant difference in H-FABP positivity in various age groups. (P>0.05).

TABLE-8

DISTRIBUTION OF H-FABP AMONG MALES AND FEMALES

SEX	H-FABP		TOTAL
	POSITIVE	NEGATIVE	
MALE	32(82.05%)	7(17.95%)	39(100%)
FEMALE	6(54.55%)	5(45.45%)	11(100%)
TOTAL	38(76%)	12(24%)	50(100%)

P value is 0.06. Statistically not significant.

No statistically significant difference was noted between males and females with regard to H-FABP positivity. (P>0.05).

TABLE-9

DISTRIBUTION OF H-FABP AMONG HYPERTENSIVES

HYPERTENSION	H-FABP		TOTAL
	POSITIVE	NEGATIVE	
YES	17(77.27%)	5(22.73%)	22(100%)
NO	21(75%)	7(25%)	28(100%)
TOTAL	38(76%)	12(24%)	50(100%)

P value is 0.852. Statistically not significant.

No statistically significant difference was noted between hypertensives And normotensives with regard to H-FABP positivity. (P>0.05).

TABLE-10

DISTRIBUTION OF H-FABP AMONG DIABETICS

DIABETES MELLITUS	H-FABP		TOTAL
	POSITIVE	NEGATIVE	
YES	9(60%)	6(40%)	15(100%)
NO	29(82.86%)	6(17.14%)	35(100%)
TOTAL	38(76%)	12(24%)	50(100%)

P value is 0.083. Statistically not significant.

No statistically significant difference was noted between diabetics and normoglycaemic patients with regard to H-FABP positivity. (P>0.05).

TABLE-11

DISTRIBUTION OF H-FABP AMONG SMOKERS

SMOKING	H-FABP		TOTAL
	POSITIVE	NEGATIVE	
YES	30(83.33%)	6(16.67%)	36(100%)
NO	8(57.14%)	6(42.86%)	14(100%)
TOTAL	38(76%)	12(24%)	50(100%)

P value is 0.052. Statistically not significant.

No statistically significant difference was noted between smokers and Non-smokers with regard to H-FABP positivity. (P>0.05).

TABLE-12

DISTRIBUTION OF H-FABP AMONG ALCOHOLICS

ALCOHOL CONSUMPTION	H-FABP		TOTAL
	POSITIVE	NEGATIVE	
YES	20(90.90%)	2(9.10%)	22(100%)
NO	18(64.30%)	10(35.71%)	28(100%)
TOTAL	38(76%)	12(24%)	50(100%)

P value is 0.029. Statistically significant.

There was statistically significant difference in H-FABP positivity between alcoholics and non alcoholics. (P<0.05).

TABLE-13

DISTRIBUTION OF H-FABP AMONG KILLIP CLASSES

KILLIP CLASS	H-FABP		TOTAL
	POSITIVE	NEGATIVE	
I	23(79.31%)	6(20.69%)	29(100%)
II	12(66.67%)	6(33.33%)	18(100%)
III	2(100%)	0	2(100%)
IV	19(100%)	0	1(100%)
TOTAL	38(76%)	12(24%)	50(100%)

P value is 0.576. Statistically not significant.

There was no statistically significant difference in H-FABP positivity in patients of various Killip classes . (P>0.05).

TABLE-14

DISTRIBUTION OF H-FABP WITH REGARD TO BMI

BMI	H-FABP		TOTAL
	POSITIVE	NEGATIVE	
NORMAL	23(69.70%)	10(30.30)	33(100%)
INCREASED	15(88.24%)	2(11.76%)	17(100%)
TOTAL	38(76%)	12(24%)	50(100%)

P value is 0.146. Statistically not significant.

No statistically significant difference was noted between patients with normal BMI and elevated BMI with regard to H-FABP positivity. (P>0.05).

TABLE-15

DISTRIBUTION OF H-FABP IN RELATION TO TRIGLYCERIDES

TRIGLYCERIDES	H-FABP		TOTAL
	POSITIVE	NEGATIVE	
NORMAL	7(64.64%)	4(36.36%)	11(100%)
INCREASED	31(79.49%)	8(20.51%)	39(100%)
TOTAL	38(76%)	12(24%)	50(100%)

P value is 0.277. Statistically not significant.

No statistically significant difference was noted between patients with normal triglycerides and elevated triglycerides with regard to H-FABP positivity. (P>0.05).

TABLE-16

DISTRIBUTION OF H-FABP IN RELATION TO CHOLESTEROL

CHOLESTEROL	H-FABP		TOTAL
	POSITIVE	NEGATIVE	
NORMAL	3(60%)	2(40%)	5(100%)
INCREASED	35(77.78%)	10(22.22%)	45(100%)
TOTAL	38(76%)	12(24%)	50(100%)

P value is 0.377. Statistically not significant.

No statistically significant difference was noted between patients with normal cholesterol and elevated cholesterol with regard to H-FABP positivity. (P>0.05).

TABLE-17

DISTRIBUTION OF H-FABP IN RELATION TO ELECTROCARDIOGRAPH

ECG	H-FABP		TOTAL
	POSITIVE	NEGATIVE	
ST ELEVATION	26(89.66%)	3(10.34%)	29(100%)
OTHER CHANGES	12(85.71%)	2(14.29%)	14(100%)
NO CHANGES	0	7(100%)	7(100%)
TOTAL	38(76%)	12(24%)	50(100%)

P value is 0.000. Statistically significant.

Statistically significant difference was noted between those patients with and without ECG changes with regard to H-FABP positivity. ($P<0.05$).

TABLE-18

DISTRIBUTION OF H-FABP IN RELATION TO ECHOCARDIOGRAPH

ECHO	H-FABP		TOTAL
	POSITIVE	NEGATIVE	
RWMA	32(91.43%)	3(8.57%)	35(100%)
NO RWMA	6(40%)	9(60%)	15(100%)
TOTAL	38(76%)	12(24%)	50(100%)

P value is 0.000. Statistically significant.

Statistically significant difference was noted between those patients with and without regional wall motion abnormality in echocardiograph with regard to H-FABP positivity. ($P<0.05$).

TABLE-19

DISTRIBUTION OF H-FABP IN RELATION TO THROMBOLYSIS

THROMBOLYSIS	H-FABP		TOTAL
	POSITIVE	NEGATIVE	
YES	25(89.29%)	3(10.71%)	28(100%)
NO	13(59.09%)	9(40.91%)	22(100%)
TOTAL	38(76%)	12(24%)	50(100%

P value is 0.013. Statistically significant.

Statistically significant difference was noted between those patients who were thrombolysed and who were not thrombolysed, with regard to H-FABP positivity. ($P<0.05$).

TABLE-20

DISTRIBUTION OF H-FABP IN RELATION TO DEATH

DEATH	H-FABP		TOTAL
	POSITIVE	NEGATIVE	
YES	3(100%)	0	3(100%)
NO	35(74.47%)	12(25.53%)	47(100%)
TOTAL	38(76%)	12(24%)	50(100%)

P value is 0.315. Statistically not significant.

There was no statistically significant difference in H-FABP positivity between those patients who died of MI and those who improved. ($P> 0.05$).

DISCUSSION

Acute myocardial infarction remains one of the most common causes of morbidity and mortality throughout the world and its incidence is increasing in developing countries including India [1].

Early diagnosis and treatment is very important in preserving the myocardium and in limiting the ischaemic damage. Studies have shown that the serum levels of Gold standard cardiac biomarkers start to rise relatively late (3-4 hours in case of cardiac troponins and 4-6 hours in case of CK-MB) and myoglobin which can be detected early is nonspecific to myocardium. Studies also have shown that nondiagnostic ECGs are recorded in approximately half of the patients presenting to emergency department with chest pain who ultimately are shown to have AMI. Hence an early biomarker is essential for the accurate diagnosis of AMI. Heart type fatty acid binding protein (H-FABP) has shown promise in this regard in various studies.

This study compared the role of H-FABP in diagnosing AMI with that of cardiac troponin I and CK-MB.

In this study, in patients presenting within 4 hours of symptom onset, the sensitivity of H-FABP was 60% which was significantly higher than that of cTnI (18.8%) and CK-MB (12.5%).But specificity was only 23.53% in the initial 4 hours which was less than that of cTnI (66.67%) and CK-MB (100%). In patients presenting during 4 to 12 hours of symptom onset, the

sensitivity of H-FABP was 86.96% which was comparable to that of cTnI (90.9%) and CK-MB (77.3%).The specificity was 60% in the 4-12 hours group which was comparable to that of cTnI (50%) and CK-MB (50%). Diagnostic accuracy of H-FABP was 31.82% within 4 hours and 82.14% during 4-12 hours. Overall diagnostic accuracy compared to troponin was 60% and compared to CK-MB was 56%.

This observation is supported by some of the following studies.

According to a study by Okamoto et al[3] the overall sensitivity within 12 hours of symptom onset was 92.9% for H-FABP,88.6% for myoglobin and 18.6% for CK-MB. The overall specificity was 67.3% for H-FABP, 57.1% for myoglobin and 98.0% for CK-MB.

A study by Priya Gururajan et al[102] at Chennai showed H-FABP to be a good discriminator between patients with and without IHD. It also showed that whereas troponin levels rise more than 6 hours after symptom onset, H-FABP is usually positive within first 4 hours. At the optimum cut-off value(17.7 ng/ml) , the sensitivity and specificity were found to be 87% and 93% respectively.

A study by McCann CJ et al [109] showed, in patients presenting within 4 hours of symptom onset, sensitivity of H-FABP higher than cTnT (73% v/s 53%). Specificity of H-FABP was 71%.Combined use of H-FABP and cTnT significantly improved the sensitivities of both to 85%.

In a study by Umut Cavus et al [110],H-FABP had a sensitivity equal to that of CK-MB and superior to that of myoglobin (97.6% v/s 96.7% v/s 85.4%) in initial 4 hours.H-FABP was more specific than CK-MB, myoglobin and Troponin T at the first hour (38.5%,34.6%,34.6%,23.1% respectively).

In a study by Ecollan P et al [111], a positive H-FABP using cardiodetect assay had a significantly better sensitivity than cTnI, myoglobin and CK-MB (87.3% v/s 21.8%, 64.2% and 41.5% respectively).

A study by Ruzgar et al[103] showed sensitivity of 38% with troponin, 76% with CK-MB and 95% with H-FABP in patients admitted within 6 hours of chest pain onset.

A study by Seino Y et al [104] showed 89% sensitivity of H-FABP within 2 hours of symptom onset compared to 22% with troponin and 38% with myoglobin.

In a study by Mad P et al [105] , in 280 patients presenting to the hospital with a median time of 3 hours of symptom onset, H-FABP had a sensitivity of 69% and specificity of 74% and AMI was diagnosed significantly earlier than by troponin.

LIMITATIONS OF THE STUDY:

1. The sample size was small.
2. Each patient was tested only once. Serial evaluation of the biomarkers was not done.
3. Quantitative assay for troponin and H-FABP was not performed.
4. Cardiac Troponin T and myoglobin not measured.
5. This being a cross sectional study follow up was not done.

SUMMARY

The present study aimed at evaluating the role of heart type fatty acid binding protein in the diagnosis of acute myocardial infarction and also to compare it with the standard biomarkers troponin and CK-MB. It also aimed at finding out the distribution of H-FABP with regard to variables like age and sex of the patient, BMI, lipid levels, smoking, alcoholism and in those with systemic hypertension and diabetes mellitus. It also aimed at correlating the H-FABP positivity with ECG and echocardiographic findings. With rigid criteria 50 patients were selected and enrolled in the study.

The H-FABP was found to be more sensitive but less specific compared to cardiac troponin I and CK-MB during the initial 4 hours of symptom onset. During the 4-12 hours of symptom onset the H-FABP showed similar sensitivity and specificity compared to cardiac troponin I and CK-MB. It did not show any significant difference between males and females, between different age groups, between diabetics and non-diabetics, between hypertensives and normotensives, between smokers and non-smokers, between those having hyperlipidaemia and those having normolipidaemia.It showed significant difference between alcoholics and non-alcoholics but most probably it is an error due to small sample size.

This study recommends the selective and judicious use of heart type fatty acid binding protein along with the established biomarkers for the better diagnosis of Acute Myocardial Infarction. Further larger scale and follow up studies and further improvement in assay technique are required before it can be recommended as a single test.

CONCLUSION

1. The heart type fatty acid binding protein is a sensitive biomarker for the diagnosis of acute myocardial infarction in the initial hours after symptom onset when the standard biomarkers may not be elevated. But it is less specific.

2. During 4-12 hours of symptom onset it is as sensitive and specific as standard cardiac biomarkers troponin and CK-MB.

3. The H-FABP assay is not influenced by the age, sex, BP, glycaemic status, BMI and lipid levels of the patient.

4. Due to these factors H-FABP can be considered as a promising cardiac biomarker which can be used along with troponins and CK-MB at present. With further larger scale studies and further improvement in the assay technique it can emerge as a cardiac biomarker which can be used alone, particularly in the early hours after symptom onset.

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