ORIGINAL ARTICLE

Role of IMA in Acute Chest pain in Relation with Troponin-I and Total lipids for early diagnosis of MI in Acute Coronary Syndrome (ACS)

JAI PARKASH PANJWANI, DIAL DAS, JAGDESH, *MUHAMMED ILTAF, MUKESH KUMAR ADVANI, MUHAMMAD YOUSIF MEMON*

ABSTRACT

Aim: To evaluate the role of ischemia modified albumin (IMA) in serum in relation with cardiac troponin-I and total lipid profile in patients with chest pain for early diagnosis of myocardial ischemia prone to myocardial infarction in acute coronary artery syndrome subjects.

Methods: Present study was carried out in the Department of Biochemistry, BMSI, JPMC, in collaboration with National Institute of Cardiovascular Diseases (NICVD) Karachi. 228 patients out of 1050 were randomly selected who have continuously chest pain for three hours and were divided in three groups. In Group-A patients having chest pain continuously for three hours with normal ECG and Troponin-I, Group-B patients with chest pain have developed ECG changes within three hours, Group-C patients with chest pain followed by MI with increased Troponin-I.

Results: Positive significant good correlation ($p< 0.01$) among IMA and cTn-I in patients admitting in emergency ward with chest pain within three hours (Group-A) favour in differentiation of angina from muscular pain. While patients with chest pain & developed ECG changes (Group-B) showed that cTn-I, cholesterol, triglyceride, HDL-c and LDL-c when correlated with IMA showed some what significant positive correlation ($p< 0.01$) versus IMA while IMA, cholesterol, triglyceride, HDL-c and LDL-c when correlated with cTn-I, showed statically significant positive correlation ($p< 0.01$) versus cTn-I .

Conclusion: Serum IMA level should be routinely performed at the time when patient attending the emergency department in combination with measurement of cardiac troponin-I and ECG, to confirm or exclude a final diagnosis of ischemic heart disease and to exclude myocardial infarction.

Keywords: IMA, cTn1, ECG, CHD, IHD.

INTRODUCTION

The evaluation of acute chest pain remains challenging, despite many insights and innovations over the past two decades. The percentage of patients who attend at emergency department with acute chest pain may actually be increasing[1]. It is estimated that 30% of patients presenting with chest pain will be diagnosed with an acute coronary syndrome[2].

Ischemic heart disease (IHD) is the number one cause of mortality and morbidity in the Western world, and this unfortunate reality is unlikely to change in the future. In fact, it is believed that in 2020 acute coronary syndromes (ACS) will over-run infectious disease and cancer to become the leading cause of death and disability, not only in industrialized countries, but also in the developing world[3]. Despite these facts, the diagnostic approach to ACS remains one of the most difficult and controversial medical challenges[4].

In a clinical setting, myocardial ischemia results due to inadequate blood perfusion to the myocytes, leading to a deficiency of oxygen and nutrients[5] and is assessed by an individual's symptoms and electrocardiographic (ECG) studies. The ECG changes may include ST-T segment wave alterations[6]. There is a need for early and sensitive markers of cardiac ischemia as current diagnostic tests fail to identify many chest pain patients presenting with ACS and who are at high risk for adverse cardiac events[7]. The detection of ischemia prior to infarction is a challenging concept. It would be very helpful to be able to identify quickly and accurately which patients really have myocardial ischemia and may be in need of either treatment or intervention to prevent subsequent events[8].

Recently, a novel biochemical evaluation has been developed based on Human Serum Albumin (HSA) binding to a transitional metal, cobalt. This evaluation is called Albumin Cobalt Binding (ACB) test. This test is used to detect the presence of Ischemia Modified Albumin (IMA), an extremely early indicator of myocardial ischemia before necrosis occurred[9].

Unlike injury markers such as CK-MB, myoglobin, and troponin, IMA is believed to be a marker of cardiac ischemia. The IMA level rises within minutes after the onset of ischemia and remains elevated for several hours after the

Department of Biochemistry, BMSI, JPMC, Karachi, National Institute of Cardiovascular Diseases, Karachi
Correspondence to Dr. Jai Parkash

cessation of the ischemic event. IMA rises in the presence of ischemia and not as a result of necrosis[10]. IMA is produced when ischemia stresses released from hypoxic heart tissue induce modification of circulating albumin[8]. IMA is defined as albumin modified by the free radicals produced in ischemic tissues[11].

Cardiac Troponin T and I are cardiac regulatory proteins that control the calcium-mediated interaction of actin and myosin. An important advantage of the troponins is that their isoforms are unique to cardiac myocytes, with most of the early troponin release during an AMI coming from the cytosolic pool. Subsequent release is prolonged, with degradation of the actin and myosin filaments in the area of damage[3]. Although cardiac troponins are extremely specific for myocardial necrosis, they do not discriminate between ischemic and non-ischemic etiologies of myocardial injury[12].

Dyslipidaemia is the most important predictive factor for coronary artery disease. It is well known that increased levels of low density lipoproteins (LDL), Triacylglycerides (TG) and total cholesterol (TC) and decreased levels of high density lipoproteins (HDL) are also indicative of increased incidence of cardiac events and are considered as risk factors. The strong, independent, continuous and graded positive association between total cholesterol level or LDL cholesterol level and risk of coronary artery disease events has been clearly demonstrated both in men and women in all age groups. In general, a 1% increase in the LDL cholesterol level may lead to a 2-3% increase in coronary artery disease risk[13]

SUBJECTS AND METHODS

Present study was carried out in the Department of Biochemistry, BMSI, JPMC; in collaboration of National Institute of Cardiovascular Disease (NICVD) Karachi. 228 patients out of 1050 were randomly selected and included who have continuously chest pain for three hours and classified in three groups. In Group-A patients having chest pain continuously for three hours with normal ECG and Troponin-I (n = 66), Group-B patients with chest pain have developed ECG changes within three hours (n=72), Group-C patients with chest pain followed by myocardial infarction with increased Troponin-I (n=90), in addition 54 normal healthy controls subjects were taken from general population for comparison. After all aseptic measures, about 8 milliliters of blood was taken from the antecubital vein and was centrifuged for 5–10 minutes at a speed of 2500–3000rpm. The serum obtained was stored at -70°C till analyzed. Before analyzing serum was thawed and allowed to attain room temperature. Ischemia Modified Albumin (IMA) assayed by addition of a known amount of Co-II to a serum specimen and measurement of the unbound Co-II by colorimetric assay using dithiothreitol (DTT). Troponin-I was determined by using kit mouse monoclonal anti-TnI ELISA Kit, Product Code No. 1105Z.

RESULTS

Table 1 shows the comparison of lipid and lipoprotein profile of control and A, B & C groups. The mean values of cholesterol were 166.31±2.68, 173.62±2.19, 170.69±2.14 & 180.05±2.70 respectively. Mean value of cholesterol when compared among each other, only group-C showed statistically significant difference ($p<0.01$) with control and group-B subjects. The mean triglyceride values of control and A, B & C groups were 136.57±2.16, 135.54± 3.40, 135.80±2.98 and 138.91±3.51 respectively. When these values were compared with each other showed statistically non significant difference ($p<0.01$). The mean HDL-c in control and Group-A, Group-B & Group-C were 45.29±0.66, 46.21±0.77, 41.69±0.64 & 40.17±0.59 respectively, when these values were compared to each other group-B and C showed decreased significant difference ($p<0.01$) when compared with control and group-A. The mean LDL-c in control and Group-A, Group-B & Group-C were 93.42±2.31, 100.01±1.34, 101.94±1.42 & 111.85±2.32 respectively, when these values were compared to each other group-B showed statistically significant difference ($p<0.01$) with normal control where as group-C showed increased significant difference ($p<0.01$) when compared with control and group-A and B. As a whole table 1 shows significant changes of cholesterol, HDL-c and LDL-c in group-C patients except TG among groups, indicates that as the duration of chest pain advances biochemical disturbances occurs due to changes in ECG followed by M.I.

Table 1: Comparison of Serum Lipid and Lipoproteins profile among normal subjects and study groups

Biochemical parameters	**Normal Control** (n =54)	**Group-A** (n =66)	**Group-B** (n =72)	**Group-C** (n =90)
Cholesterol (mg/dl)	166.31±2.68	173.62 ± 2.19	170.69 ± 2.14	180.05 ± 2.70 $^{\circ\square}$
TAG (mg/dl)	136.57±2.16	135.54 ± 3.40	135.80 ± 2.98	138.91 ± 3.51
HDL-c (mg/dl)	45.29 ± 0.66	46.21 ± 0.77	41.69 ± 0.64$^{\bullet\circ}$	40.17 ± 0.59$^{\bullet\circ}$
LDL-c (mg/dl)	93.42 ± 2.31	100.01 ± 1.34	101.94 ± 1.42°	111.85 ± 2.32$^{\circ\Delta}$

$^{\circ}$Significant as compared to Controls $p<0.01$
$^{\bullet}$Significant as compared to Group A $p<0.01$
$^{\Delta}$Significant as compared to Group A and B $p<0.01$
$^{\square}$Significant as compared to Group B $p<0.01$

Table 2 shows the correlation coefficient of ischemia modified albumin (IMA) and troponin-I (cTn-I) in group-A subjects versus parameters. BMI, cholesterol, triglyceride and LDL-c showed some what weak negative correlation versus IMA, whereas Age and HDL-c showed weak positive correlation. When BMI, cholesterol, triglyceride, HDL-c and LDL-c were correlated with cTn-I, they showed somewhat weak positive correlation versus cTn-I. When Age, was correlated with cTn-I, it showed some what weak negative correlation versus cTn-I, while IMA was correlated with cTn-I, it showed statically significant positive correlation versus cTn-I. In whole positive significant good correlation among IMA and cTn-I was observed in patients admitting in emergency ward with chest pain within there hours favour in differentiation of angina from muscular pain.

Table 2: Correlation Co-efficient (r) of IMA and Troponin-I vs. Biochemical Parameters within group-A

Parameter	IMA (r– value)	cTn-I(r–value)
Age (years)	0.17	-0.03
BMI (Kg/m^2)	-0.22	0.01
IMA (u/ml)	-	0.31*
Cholesterol (mg/dl)	-0.02	0.12
TAG (mg/dl)	-0.03	0.13
HDL-c (mg/dl)	0.10	0.13
LDL-c (mg/dl)	-0.14	0.06

*Correlation is significant at p< 0.01
Group-A = Subjects having chest pain continuously three hours with normal ECG and Troponin-I.

Table 3: Correlation Co-efficient (r) of IMA and Troponin-I vs. Biochemical Parameters within group-B

Parameter	IMA(r – value)	cTn-I(r–value)
Age (years)	-0.07	-0.05
BMI (Kg/m^2)	-0.11	-0.16
IMA (u/ml)	-	0.76*
Cholesterol (mg/dl)	0.64*	0.62*
TAG (mg/dl)	0.44*	0.46*
HDL-c (mg/dl)	0.44*	0.41*
LDL-c (mg/dl)	0.61*	0.59*

*Correlation is significant at p < 0.01
Group-B = Subjects with chest pain and developed ECG changes within three hours.

Table 3 shows the correlation coefficient of ischemia modified albumin (IMA) and troponin-I (cTn-I) in group-B subjects versus parameters. Age and BMI showed weak negative correlation versus IMA, whereas cTn-I, cholesterol, triglyceride, HDL-c and LDL-c when correlated with IMA showed somewhat significant positive correlation versus IMA. When Age, and BMI were correlated with cTn-I, they showed weak negative correlation versus cTn-I. Comparatively IMA, cholesterol, triglyceride, HDL-c and LDL-c when correlated with cTn-I, they showed statically significant positive correlation versus cTn-I.

This table indicates that patients with chest pain developed ECG changes showing strongly significant (r=0.76, p<0.01) increased level of IMA early warns that such chest pain patients are prone to myocardial infarction and aware to doctor for early treatment and preventive measures.

Table 4 shows the correlation coefficient of ischemia modified albumin (IMA) and troponin-I (cTn-I) in group-C subjects versus parameters. Age and HDL-c when correlated with IMA, showed some what weak negative correlation versus IMA and BMI when correlated with IMA, showed somewhat weak positive correlation versus IMA, whereas cTn-I, cholesterol, triglyceride and LDL-c when correlated with IMA showed somewhat significant positive correlation versus IMA. When Age was correlated with cTn-I, it showed somewhat weak negative correlation versus cTn-I, while BMI and HDL-c when correlated with cTn-I, they showed weak positive correlation versus cTn-I. When IMA, cholesterol, triglyceride nd LDL-c when correlated with cTn-I, they showed statically significant positive correlation versus cTn-I. In, a whole IMA versus cTn-I, lipid and lipoprotein except HDL showed significant correlation with cTn-I.

Table 4: Correlation Co-efficient (r) of IMA and Troponin-I vs. Biochemical Parameters within group-C

Parameter	IMA(r – value)	cTn-I(r–value)
Age (years)	-0.13	-0.10
BMI (Kg/m^2)	0.04	0.14
IMA (u/ml)	-	0.31*
Cholesterol (mg/dl)	0.34*	0.44*
TAG (mg/dl)	0.30*	0.42*
HDL-c (mg/dl)	-0.17	0.01
LDL-c (mg/dl)	0.35*	0.39*

*Correlation is significant at p < 0.01
Group-C = Subjects with chest pain followed by myocardial infarction with increased Troponin-I within three hours.

DISCUSSION

Myocardial ischemia results from the lack of adequate blood perfusion of the myocytes, leading to a deficiency of oxygen and nutrients, thus compromising their vital functions. The manifestations of the myocardial ischemia are varied and multiple like chest pain, epigastric or arm discomfort, breathlessness, nausea and vomiting. However, these symptoms may be subtle and are not easily recognized. Prolonged ischemia can lead to myocardial cell death known as acute myocardial infarction[14]. Cardiac markers of cell necrosis such as myoglobin, CK-MB and troponins are highly sensitive and exhibit good specificity. They do not, however, detect myocardial ischemia in the absence of necrosis and provide no reliable information when

measured in the first 2-6 hours following an ischemic event[15].

In present study we observed increased IMA as a diagnostic factor for early diagnosis of myocardial ischemia and observed significant elevated levels of IMA in most of the chest pain patients. These findings are in agreement with the study of Sameer *et al*[16] who found high level of IMA in chest pain subjects.

On the other side we also evaluated cardiac troponin-I level and found non significant difference in chest pain with normal ECG group when compared to normal control and significant difference in chest pain with ECG changes group when compared to normal control. Age and Body Mass Index (BMI) used as a one of the biophysical parameters which was found significantly high in subjects with chest pain and diagnosed myocardial infarction (group-C) subjects.

In our study IMA and cTn-I was correlated positively with age in chest pain with ECG changes (Group-B) and chest pain and diagnosed MI subjects (Group-C), in agreement with Sameer *et al*[16] and Kim *et al*[17]. Although the underlying mechanism remains unknown, it has been suggested that the association between age and IMA could be related to age-induced changes and life style.

The symptoms of patients with myocardial ischemia and/or infarction can be diverse. Although not specific for myocardial ischemia / infarction, chest pain is one of the earliest and most common symptoms in patients presenting to the emergency department[15].

The results of our study showed that IMA is a useful marker for the diagnosis of ACS. There is a significant relationship between the results of cTn-I, a measure of myocardial necrosis and IMA a measure of ischemia, in evaluating patients with ACS.

CONCLUSION

The sensitivity of IMA for the diagnosis of acute ischemic chest pain is greater valuable than with ECG and cTn-I. Our hypothesis may propose that measurement of IMA can be used at admission, in combination with measurement of cardiac troponin-I and ECG, to confirm or exclude a final diagnosis of ischemic heart disease and to exclude myocardial infarction.

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