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Original Research Article

Correlation between plasma myeloperoxidase and hs-troponin I, C-reactive protein and CKMB in acute coronary syndrome

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ABSTRACT

Background: Acute coronary syndrome (ACS) is a group of clinical syndromes ranging from unstable angina pectoris to acute myocardial infarction (AMI) and death. Early prediction of ACS is frequently a challenging task. Myeloperoxidase is involved in oxidative stress and inflammation which plays an important role in the pathogenesis and course of ACS.
Methods: The study was conducted in 30 male patients in the age group 20 - 80 years who were diagnosed as ACS and admitted to CCU. Twenty age matched normal subjects were taken as controls. Plasma MPO, hsTnI, hsCRP, CKMB, lipid parameters, urea, creatinine, glucose, AST and LDH were estimated in patients and control subjects.
Results: Plasma MPO level was found to be 155.5±19.5 ng/ml and 62.4±11.8 in ACS patients and normal controls respectively and that of hsTnI was 133.3±10.1 ng/L and 20.7±1.8 ng/L, hsCRP to be 13.1±1.38 mg/L and 0.51±0.12 mg/L, CKMB to be 166.3±16.7 ng/dl and 12.8±1.51 ng/dl respectively. The values plasma of glucose, cholesterol, triglycerides, HDL-cholesterol, LDL-cholesterol, urea and creatinine were found to be slightly elevated in patients but, were not statistically significant when compared to controls. AST and LDH showed statistically significant increase in patients compared to controls. Direct linear correlation was observed between plasma MPO level and hsTnI, hsCRP and CKMB levels.
Conclusions: Plasma MPO which is a predictor of early cardiovascular events and also severity of myocardial damage linearly correlates with the values of hsTnI, hsCRP and CKMB.

Keywords: Acute coronary syndrome, High sensitivity troponin I, Myeloperoxidase

INTRODUCTION

Acute coronary syndrome (ACS) is a group of life threatening clinical syndromes ranging from unstable angina pectoris to acute myocardial infarction and death.[1] Cardiovascular disease (CVD) has an increasing role as the main cause of mortality and morbidity worldwide. The death rate due to CVD in 1990 was 28.9%, which is predicted to increase to 36.3% in 2020. Approximately 1.4 million patients with ACS without ST segment elevation are admitted to hospital annually in the US. As stated by WHO, Middle East Nations will face considerable increase in burden of CVD in the world. ACS including unstable angina and myocardial infarction are forms of CHD that constitute common cause of CVD death.

The risk factors of ACS are mainly diabetes mellitus, C-reactive protein, obesity, metabolic syndrome, dyslipidemia, depression, renal insufficiency, smoking, family history of CAD, stress and hypertension. These risk factors contribute to the damage of blood vessel

endothelium and thereby resulting in dysfunction of endothelium which in turn plays a crucial role in commencement of atherosclerotic plaque.

Atheromatous plaque is the principal cause of ACS, which is seen in more than 90% of patients. Oxidative stress and inflammation play an important role in the pathogenesis of ACS. Inflammation has been implicated in all stages in the development of atherosclerotic disease. Since ACS is a life threatening condition, early and proper diagnosis is important. Cardiac markers can evaluate heart function and are useful in early prediction and risk stratification of the disease. The main cardiac markers which have been studied are myoglobin, CKMB, cardiac troponins, B-type natriuretic peptides (BNP), glycogen phosphorylase BB isoenzyme, hsCRP and myeloperoxidase.[2]

In inflammatory processes the enzyme myeloperoxidase (MPO) is released into extracellular fluid, which is stored in azurophilic granules of polymorphonuclear neutrophils. MPO as a marker for plaque instability has been used to evaluate patients with coronary heart disease. Goldmann et al postulated that elevated MPO and rapid peak of MPO after onset of symptoms suggest neutrophil activation occurring early after ischemia onset and preceding myocardial infarction.[3] Zhang et al showed that leucocyte and blood MPO level was significantly higher in patients with CAD than controls.[4] Another case control study of 680 ACS patients and 194 controls with angiographic CAD showed that MPO level was significantly higher in cases than controls.[5] According to Duzguncinar et al, plasma MPO correlated with Gensini score (an index of atherosclerosis burden) and coronary calcium.[6] Fong et al in their study concluded that MPO levels in systemic circulation directly reflects those in coronary circulation and is a potential marker in predicting coronary artery diseases.[7] Hence, predominance of evidence supports an association between MPO level and CAD and dose-response relationship between MPO level and CAD severity.[8]

Cardiac troponin levels are very sensitive and specific for myocardial damage regardless of underlying cause.[9] During myocardial injury, depending on severity, troponins are released from the small cytosolic pool and large muscular pool and their levels in plasma can be correlated with severity of ACS.[10,11] Implementation of high sensitivity cardiac troponin I assay due to its superior analytical performance has revolutionised the diagnosis, risk stratification, triage and management of patients with suspected myocardial infarction.[12] Hence, the study was undertaken to;

- Estimate the concentrations of MPO, hsTnI, hsCRP and CKMB in ACS patients and normal controls and compare the values obtained for patients and controls.
- To find the correlation between MPO and hsTnI, hsCRP and CKMB levels in ACS patients.
- To estimate routine parameters such as plasma glucose, lipid profile, urea, creatinine, AST and LDH in ACS patients and normal controls.

METHODS

The study was conducted at the departments of Cardiology and Laboratory Medicine as a prospective analytical study. Thirty male ACS patients were selected for the study.

Inclusion criteria

- Adult male patients in the age group 20 - 80 years.
- Patients presented with typical symptoms of coronary heart disease, resting ECG findings and raised Troponin T levels.
- Diagnosed as acute coronary syndrome and admitted to CCU.

Exclusion criteria

- Female patients
- Asymptomatic patients
- Patients who had previous revascularisation
- Patients being evaluated for other cardiac diseases
- Patients having autoimmune diseases
- Patients having renal dysfunction
- Patients with diabetes
- Patients with liver diseases

Twenty age matched healthy subjects without previous history of CHD were included as controls. Ethical consent for the study was obtained from the institutional ethics committee. Written consent was obtained from the participants in English/vernacular language. A questionnaire was framed to obtain anthropometric parameters and relevant clinical data. Blood (4.0 ml) was collected in lithium heparin vacutainers. Plasma was separated by centrifugation and stored in vials at -200C. Plasma MPO was estimated by ELISA technique and hsTnI by immunoassay method. CKMB, hsCRP, lipid parameters, glucose, urea, creatinine, AST and LDH were estimated by standard methods. Data obtained was analysed by Prism 6.0 software. Independent t-test was done to compare patient and control values.

RESULTS

The values of plasma MPO, hsTnI, hsCRP and CKMB obtained for ACS patients and control subjects are presented in Table 1. The values obtained for ACS patients are compared with those obtained for control subjects and statistically significant increase was observed in the case of ACS patients.

The values of plasma glucose, lipid parameters, urea, creatinine, AST and LDH obtained for ACS patients and control subjects are presented in Table 2. The values

obtained for ACS patients are compared with those obtained for control subjects. Glucose, cholesterol, triglycerides, HDL-cholesterol, LDL-cholesterol, urea and creatinine showed no statistically significant difference between CAD patients and control subjects. AST and LDH showed statistically significant increase in ACS patients when compared to normal controls.

Table 1: Plasma myeloperoxidase (MPO), high sensitivity troponin I (hsTnI), high sensitivity C- reactive protein (hsCRP) and creatine kinase-MB (CKMB) values of patients with acute coronary syndrome (ACS) and control subjects.

Parameters	ACS patients (n=30) Mean±SD	Control subjects (n=20) Mean±SD	p value
MPO (ng/ml)	155.5±19.5	62.4±11.8	<0.001
hsTnI (ng/dl)	130.3±10.1	20.7±1.8	<0.001
hsCRP (mg/l)	13.1±1.38	0.51±0.12	<0.001
CKMB (ng/dl)	166.3±16.7	12.8±1.51	<0.001

The values obtained for patients with acute coronary syndrome are compared with those of control subjects. p<0.001 = statistically significant

Table 2: Concentration of routine parameters - plasma glucose, lipid profile, urea, creatinine, AST and LDH levels in patients with acute coronary syndrome (ACS) and normal controls.

Parameters	ACS Patients (n=30) (Mean±SD)	Control subjects (n=20) (Mean±SD)	p value
Random Glucose (mg/dl)	96.3±15.4	94.6±13.9	NS
Urea (mg/dl)	25.9±8.7	24.2±9.2	NS
Creatinine (mg/dl)	1.09±0.22	1.02±0.25	NS
Cholesterol (mg/dl)	175±29.3	171±32.1	NS
Triglycerides (mg/dl)	109±26.5	106±30.5	NS
HDL-cholesterol (mg/dl)	42.1±9.7	44.8±10.5	NS
LDL-cholesterol (mg/dl)	110±19.1	104±17.6	NS
AST (U/L)	185±38.6	32±8.5	p<0.001
LDH (U/L)	1085±218	240±50.2	p<0.001

The values obtained for patients with acute coronary syndrome are compared with those of control subjects. NS: Not statistically significant, p<0.001: Statistically significant

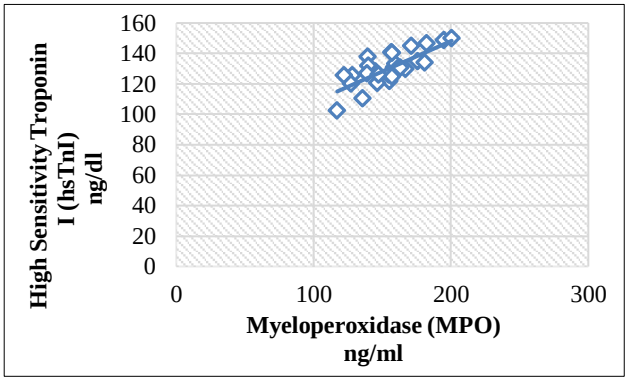

Figure 1: Correlation between plasma myeloperoxidase (MPO) and high sensitivity troponin I (hsTnI) in patients with acute coronary syndrome (ACS).

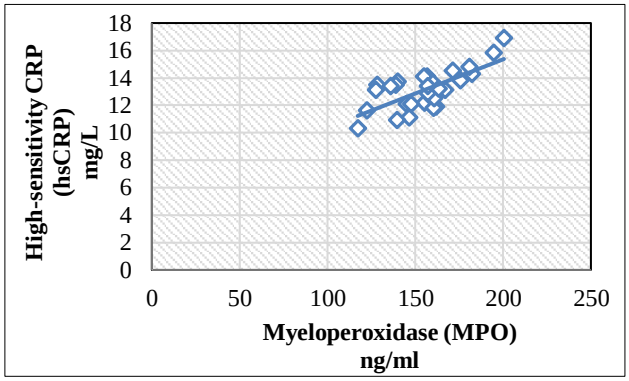

Figure 2: Correlation between plasma myeloperoxidase (MOP) and high sensitivity C-reactive protein (hsCRP) in patients with acute coronary syndrome (ACS).

Correlation between plasma MPO and hsTnI levels in ACS patients is presented in Figure 1.

Correlation between plasma MPO and hsCRP levels in ACS patients is presented in Figure 2.

Correlation between plasma MPO and CKMB levels in ACS patients is presented in Figure 3. Linear correlation was observed between plasma MPO level and hsTnI, hsCRP and CKMB levels in patients with acute coronary syndrome.

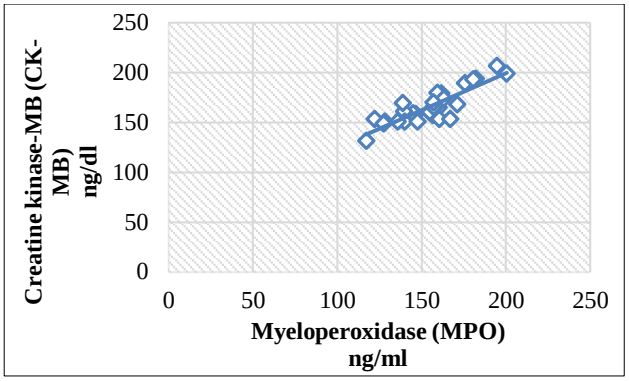

Figure 3: Correlation between plasma myeloperoxidase and creatine kinase-MB in patients with acute coronary syndrome (ACS).

DISCUSSION

Goldmann et al found that plasma MPO level remained elevated until 4 hours after the onset of symptoms, declined thereafter and increased again after 24 hrs in ACS patients.[3] MPO increases oxidative potential by the nitrogen peroxide radical generated by myeloperoxidase - hydrogen peroxide - nitrite system and promotes lipid peroxidation of low density lipoproteins.[13] Another important role of MPO in leucocytes is to activate metalloproteinases that bring about plaque rupture.[4] Leucocytes play a central role in atherosclerotic plaque rupture.[14] Sugiyama et al in their studies on atherosclerotic plaques of patients with sudden death demonstrated larger expression of MPO in rupture sites, in superficial erosions and in the lipid core while fatty streaks exhibited smaller expression.[15] Shiu et al suggested that LDL could be modified by MPO promoting the formation of foam cells and plaque formation and subsequent rupture.[16] Meuwese et al in the Epic-Norfolk Prospective population study suggested that higher MPO levels could be a risk factor for coronary artery disease even in healthy individuals.[17] Mocatta et al, Heslop et al and Tang et al predicted MPO as a marker for cardiovascular events.[18-20]

Elevated cardiac troponins in patients with acute ischemic presentations are related to more extensive coronary artery disease.[21] Joshua et al is of the opinion that the addition of hsTnI to conventional risk factors improve risk prediction.[22] Highly sensitive assays for cardiac troponins have revealed that the majority of older individuals have levels of circulating troponin T and I well below those used as the clinical threshold for the diagnosis of myocardial ischemia.[23,24] hsCRP and CKMB have already been established as cardiac markers of ischemic heart disease. Niskanen et al studied the correlation between MPO and hsCRP and suggested that elevated levels of MPO and hsCRP can be used to identify subjects who have an increased risk of developing myocardial infarction.[25]

In the present study we observed elevated plasma levels of MPO, hsTnI, hsCRP and CKMB in ACS patients which are in agreement with earlier studies. In addition, there is direct linear correlation between MPO levels and hsTnI, hsCRP and CKMB values. Hence, MPO can be included as a highly useful predictive marker in the armamentarium of cardiac markers. Serial estimations of plasma myeloperoxidase level and other cardiac markers would have helped in predicting which parameter showed the peak value early. This would have helped in early diagnosis and effective management.

CONCLUSION

Early detection of ACS is a challenging task, while immediate risk stratification remains crucial for the prompt implementation of appropriate therapy. Inflammation and oxidative stress are both linked to MPO. MPO can be proposed as a useful risk marker and diagnostic tool in ACS and in patients admitted in emergency department with chest pain. High sensitive cardiac troponin I assay due to its superior analytical performance has helped in the diagnosis, risk stratification, triage and management of patients with suspected myocardial infarction. Thus MPO and hsTnI may comprise an excellent combination in the early diagnosis of acute coronary syndrome.

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