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OXIDATIVE STRESS AND SOME INFLAMMATORY BIOMARKERS IN PATIENTS WITH CORONARY HEART DISEASE

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ABSTRACT

Myeloperoxidase is a marker of oxidative stress and is released after neutrophils Energizing. It has potent pro-oxidative and proinflammatory properties. This study was objectives to investigate the impact of myeloperoxidase and some inflammatory biomarkers on the incidence of coronary heart disease. The study was done on 50 patients (30 males and 20 females), aged 55 years ±8 with acute coronary heart disease and 40 healthy subjects (22 males and 18 females), aged 45 years±5 recruited from Ibn Albitar Center for Cardiac Surgery. Lipid profile, myeloperoxidase, many inflammatory biomarkers and cardiac troponin I levels were measured and studied. The results of this study showed that the total cholesterol to HDL cholesterol ratio, inflammatory biomarkers like high sensitive C-reactive protein, interleukin -6 and myeloperoxidase were substantially higher in cases than in non-cases subjects. As well the mean level of cardiac troponin I was higher in patients with acute coronary disease than in control subjects. Conversely, the concentrations of adiponectin were insignificantly altered in cases as compared with control subjects. On conclusion, a combination of myeloperoxidase, cardiac troponin I and inflammatory markers allowed the recognitions of a greater proportion of patients at risk for coronary cardiac events than the use of cardiac troponin I alone.

KEYWORDS: Myeloperoxidase, cardiac troponin I, inflammatory markers and acute coronary disease.

INTRODUCTION

The pathogenesis of coronary artery disease (CAD) and thereafter-acute coronary syndrome (ACS) is mostly associated with inflammation and oxidative stress. Many study found that infiltrating macrophages and neutrophils causing releases of Myeloperoxidase (MPO) protein and may facilitate the conversion of long-standing coronary plaques into movable lesions.[1,2]

Myeloperoxidase seems to share in many steps of oxidation reaction that involved in the initiation, propagation and other consecutive and intricate steps of plaque formation[3] and oxidation of lipids within low density lipoprotein thereby production of atherogenic lipoprotein form.[4]

It has been shown that MPO is presented within atherosclerotic plaque and contributes to injure of the culprit and prone to rupture[2] due to the protease cascades activation which interfere with the stability and thrombogenicity of culprit.[5] As well, the utilization of endothelial-derived nitric oxide by myeloperoxidase causing impairing of endothelial functions.[6]

Interleukin -6 (IL-6) has proinflammatory and procoagulant properties. It induces C- reactive protein (CRP) and other markers of inflammation and it seems to associate with the strength of recondite culprit inflammation and its susceptibility to rupture.[7]

The goal of this case–control study was to analyze the impact of myeloperoxidase levels and other inflammatory biomarkers on the existence of acute coronary disease.

PATIENTS AND METHODS

A case–control study was directed among the participants of Ibn Albitar Center for Cardiac Surgery which involved fifty patients, (20 females,30 males), aged 55 year to 65 year with acute coronary disease and forty control healthy subjects (18 females,22 males), aged 40 year to 50 year.

Diagnoses were basing on clinical symptoms and tests like Electrocardiogram (ECG), Echocardiogram stress test and Coronary angiography. exclusion criteria were comprise all patients with liver disease, renal failure and heart failure.

Venous blood samples are aspirated after 12 hours fasting and plasma samples were stored at -20^{0}C no longer than 6 months. Patients were informing to

discontinue all drugs and caffeine-containing food or beverages for about 12 hours before blood sample aspiration.

Plasma concentrations of myeloperoxidase, adiponectin, high sensitivity C-reactive protein (hs-CRP) and interleukin-6 (IL-6) were measured on thawed frozen plasma from cases and controls by an enzyme-linked immunosorbent assay (ELISA) according to procedures recommended by manufacturer. Whereas cardiac troponin I (cTnI) was measured on entrance to the hospital and after 6 hours. The levels of total cholesterol and high-density lipoprotein cholesterol (HDL-C) were measured by spectrophotometric assay.

All eligible participants provided written informed consent to partake in this study. The study protocol accords to the ethical guidelines of the Declaration of Helsinki and approved by the college's ethics committee.

All data were analyze and express as mean ± SD with 95% confidence interval (CI) and *P* values of (0<0.05) were deemed to be statistically significant. All statistical analyses were performed using series Statistical Package for Social Sciences (SPSS) version 18.

RESULTS

Clinical data and demographic characteristics of the studied participants are stratified in Table 1.

As expected, the mean of the ratio of total cholesterol to HDL cholesterol was considerably higher in cases than in control subjects. In addition, the mean levels of necrosis biomarkers (cTnI) were considerably higher in patients with acute coronary disease on entrance to the hospital than in control subjects.

As well the mean levels of inflammatory biomarkers, high sensitive C-reactive protein, myeloperoxidase and interleukin -6 were substantially higher in cases than in non-cases subjects. Conversely, the mean levels of adiponectin were insignificantly altered in cases as compared with control subjects.

Concerning the number of folded changes as compared to control levels, the mean level of plasma myeloperoxidase in patients with acute coronary syndrome exhibited high folded increases (5.04) more than other biochemical and inflammatory parameters as stratified in Fig. 1.

The power analysis for the minimum detectable difference percentage between the mean levels of control and patients for high sensitive C-reactive protein (hs-CRP), Interleukin -6 (IL-6) and myeloperoxidase (MPO) where elucidated in Fig. 2.

Table 1: Clinical data and demographic characteristics of the studied participants.

Variables	Control	Acute coronary disease
Number(M/F)	40(22/18)	50(30/20)
Age (year)	45±5	55±8
TC/HDL-C ratio	4.54±0.05	5.62±0.21**
cTnI (ng/ml)	0.0	0.37±0.28*
hs- CRP (mg/L)	1.3±0.8	2.78±1.12**
MPO (ng/ml)	82.5± 6.5	416 ±22.3***
IL-6 (pg/ml)	2.01±1.02	3.24±1.08**
Adiponectin (µg/ml)	10.35±4.5	9.55±3.6

*Data are presented as mean ±SD (standard deviation) for continuous variables; * P<0.05 significant difference versus control,** P<0.01 high significant difference versus control, *** P<0.001 high significant difference versus control.*

Abbreviations: *mg/L, milligram per liter; ng/ml, nano gram per milliliter; pg/ml, picogram per milliliter; µg/ml, microgram per milliliter; Number, sample size of the participants; hs- CRP, high sensitive C-reactive protein; IL-6, Interleukin-six; TC/HDL-C ratio, total cholesterol to high density lipoprotein cholesterol ratio; cTnI, cardiac troponin I; MPO, myeloperoxidase.*

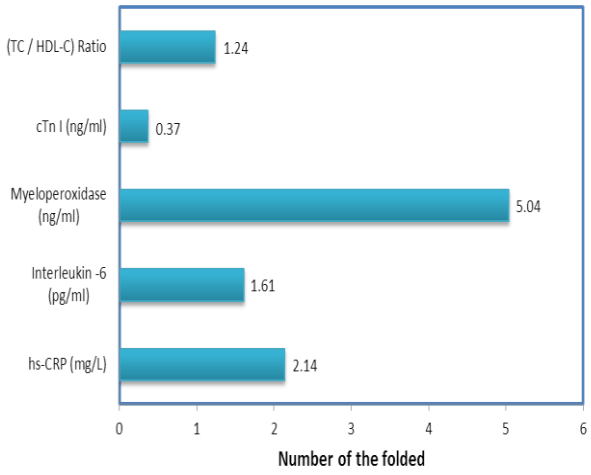

Fig. 1: Bar graph elucidated the number of the folded increases in cardiac troponin I (cTnI) and in plasma levels of high sensitive C-reactive protein (hs-CRP), Interleukin -6 (IL-6), myeloperoxidase (MPO) and total cholesterol to high density lipoprotein cholesterol ratio (TC/HDL-C ratio) for acute coronary disease patients versus control levels.

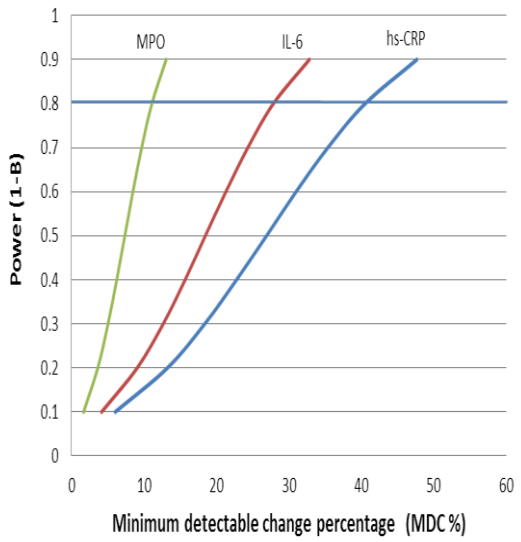

Fig. 2: Power analysis for the minimum detectable change percent (MDC %) between the mean levels of control and of acute coronary disease patients for high sensitive C-reactive protein (hs-CRP), Interleukin -6 (IL-6) and myeloperoxidase (MPO). Assuming alpha =0.05 and power = 80%.

DISCUSSION

In this study, the elevated levels of several inflammatory markers such as C-reactive protein, myeloperoxidase and IL-6 after early onset of chest pain were associated with acute coronary disease risk, whereas plasma levels of adiponectin did not appear to be associated with acute coronary disease events.

This result was conform with other studies that showed a highly elevated level of myeloperoxidase within 2 hours of symptom on set in patients with myocardial infarction[8] and in patients with acute coronary disease presenting within 3–12 hours of their last episode of chest pain.[9,10,11]

The initial measurement of myeloperoxidase in patients with chest pain and with negative- troponin test, may have a predictive value.[12]

Many studies found that increased levels of myeloperoxidase in patients with coronary disease may lead to myocardial injury as a result of movable plaque formation and coronary stenosis.[9]

Activation of neutrophils and macrophages and increase production of MPO can also occurs in any inflammatory or infiltrative diseases; therefore, high level of MPO is not necessary to be associated with cardiac diseases.

Concerning C-reactive protein which is another marker of inflammation, although many studies found a moderate correlation and a low predictive value of C-reactive protein level with cardiovascular risk specially in older patients and in patients with ischemic cardiac disease[13,14,15], other study found a potent correlation of C-reactive protein level with unstable atheroma.[16]

Additionally, IL-6 which induces the migration and differentiation of activated macrophages[17] and regulates the expression of adhesion molecules and other cytokines such as IL-1*b* and tumor necrosis factor.[18] Thereby increased levels of IL-6, may contribute to the development of an acute coronary syndrome.

CONCLUSIONS

Myeloperoxidase is a global marker of inflammation and oxidation. It is level was specifically elevated in patients with acute episode of chest pain of coronary disease therefore it can be used as a diagnostic test in acute coronary disease patients with or without negative-troponin test.

REFERENCES

1. Takahiko N., Makiko U., Kazuo H., et al. Neutrophilin filtration of culprit lesions in acute coronary syndromes. Circulation, 2002; 106(23): 2894–2900.
2. Sugiyama S, Okada Y, Sukhova GK, Virmani R, Heinecke JW, Libby P. Macrophage myeloperoxidase regulation by granulocyte macrophage colony-stimulating factor in human atherosclerosis and implications in acute coronary syndromes. AmJ Pathol, 2001; 158: 879–91.
3. Brydon L, Magid K and Steptoe A. Platelets, coronary heart disease and stress. Brain, Behavior, and Immunity, 2006; 20: 113–119.
4. Podrez EA, Schmitt D, Hoff HF, Hazen SL. Myeloperoxidase –generated reactive nitrogen species convert LDL into an atherogenic form in vitro. J Clin Invest, 1999; 103: 1547–1560.
5. Fu X, Kassim SY, Parks WC, Heinecke JW. Hypochlorous acid oxygenates the cysteine switch domain of pro-matrilysin (MMP-7). A mechanism for matrix metalloproteinase activation and atherosclerotic plaque rupture by myeloperoxidase. J Biol Chem, 2001; 276: 41279–41287.
6. Vita JA, Brennan ML, Gokce N, Mann SA, Goormastic M, Shishehbor MH, Penn MS, Keaney JFJr, Hazen SL.: Serum myeloperoxidase levels independently predict endothelial dysfunction in humans. Circulation, 2004; 110: 1134–1139.
7. Lindmark E, Diderholm E, Wallentin L, Siegbahn A. Relationship between interleukin 6 and mortality in patients with unstable coronary artery disease: effects of an early invasive or noninvasive strategy. JAMA, 2001; 286: 2107–2113.
8. Goldmann BU, Rudolph V, Rudolph TK, Holle AK, Hillebrandt M, Meinertz T, *et al.* Neutrophil activation precedes myocardial injury in patients with acute myocardial infarction. Free Radic Biol Med, 2009; 79: 47-83.
9. Baldus S, Heeschen C, Meintertz T, Zeiher A, Eiserich J, Mu ¨ nzel T, Simoons M and Hamm C.

Myeloperoxidase serum levels predict risk in patients with acute coronary syndromes. Circulation, 2003; 108: 1440–1445.
10. Eggers KM, Dellborg M, Johnston N, Oldgren J, Swahn E, Venge P, *et al.* Myeloperoxidase is not useful for the early assessment of patients with chest pain. Clin Biochem, 2010; 43: 240–5.
11. Morrow DA, Sabatine MS, Brennan ML, deLemos JA, Murphy SA, Ruff CT, et al. Concurrent evaluation of novel cardiac biomarkers in acute coronary syndrome: myeloperoxidase and soluble CD40 ligand and the risk of recurrent ischaemic events in TACTICS-TIM 18. Eur Heart J, 2008; 29: 1096–102.
12. Brennan ML, Penn MS, Van Lente F, Nambi V, Shishehbor MH, Aviles RJ, *et al.* Prognostic value of myeloperoxidase in patients with chest pain. N Eng lJ Med, 2003; 349: 1595–604.
13. Pawlus J, HOŁUB M, Kozuch M, Dabrowska M, Dobrzycki S. Serum myeloperoxidase levels and platelet activation parameters as diagnostic and prognostic markers in the course of coronary disease. Int. Jnl. Lab. Hem, 2010; 32: 320–328.
14. Wang TJ, Gona P, Larson MG, Tofler GH, Levy D, Newton-Cheh C, Jacques PF, Rifai N, Selhub J, Robins SJ, Benjamin EJ, D'Agostino RB, Vasan RS. Multiple biomarkers for the prediction of first major cardiovascular events and death. N Eng l JMed, 2006; 355: 2631–2639.
15. Kistorp C, Raymond I, Pedersen F, Gustafsson F, Faber J, Hildebrandt P. N-terminal pro-brain natriuretic peptide, C-reactive protein and urinary albumin levels as predictors of mortality and cardiovascular events in older adults. JAMA, 2005; 293: 1609–1616.
16. Ridker PM. Clinical application of C-reactive protein for cardio vascular discare detection and prevention. Circulation, 2003; 107: 363–369.
17. Galis ZS, Muszynski M, Sukhova GK, et al. Cytokine-stimulated smooth muscle cells stimulate a complement of enzymes required for extracellular matrix digestion. Circ Res, 1994; 75: 181–189.
18. Kishimoto T, Akira S, Narazaki M, Taga T. Interleukin 6 family of cytokines and gp130. Blood, 1995; 86: 1243–1254.