Comparison of Selenium, Zinc, Copper, TNF-a and IL-6 Serum Levels and Erythrocyte GSH-PX Activity in Patients with Acute and Chronic Coronary Artery Disease

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Abstract

Background- Selenium (Se) is part of the enzyme glutathione peroxidase (GSH – Px) that plays an important role in the antioxidant defense of the body. Evidence has demonstrated that populations with low intake of selenium in the diet have a 2-3 fold risk of ischemic heart disease. Positive statistically significant correlations have been found between trace element concentrations (Cu, Zn, Se) of heart tissue with physiological parameters (CO: cardiac output, EF: ejection fraction) of the heart. Increased plasma concentration of TNF-α has been found in patients with coronary artery disease. Stressed myocardium activates pro-inflammatory cytokines, such as TNF-α, which produce abnormalities in myocyte contractile function. This study was done to determine the circulating levels of Cu, Zn, Se, IL- 6, TNF - α, and erythrocyte GSH - PX activity in two groups of patients with chronic coronary artery disease (CCAD), acute myocardial infarction (AMI) and normal individuals (IHD-free).

Methods- Patients were divided into two groups: 25 with chronic CAD (CCAD) and 25 with acute myocardial infarction (AMI). The control group was 50 normal individuals that did not have any symptoms for IHD, and was gender and age-matched with the patients. Blood samples were collected during the first hours after the onset of chest pain in the acute MI group. Serum levels of Se, Cu, and Zn were determined by atomic absorption spectrometry, TNF-α and IL-6 were measured with ELISA and erythrocyte GSH-PX activity with Paglia and Valentine methods.

Results- In both groups of patients, there was a significant reduction of Se in the serum (82.36±11.31 micg/l in CCAD, 74.08±11.31 in AMI vs. 105±32.52 in control group, P-value=0.03). No statistically significant difference was found in Zn and Cu serum levels (0.98±0.22 and 112±18 in CCAD and 0.98±0.4 and 115±20 in AMI vs. 0.96±0.24 and 114±17 in control group). TNF-α titers showed a significant difference in AMI patients compared to CCAD and control groups (mean TNF-α level 37.44 pg/ml in CCAD, 914.32 pg/ml in AMI and 4.80 pg/ml in control group, P value 0.01). Serum levels of IL-6 in the two groups of CCAD and AMI patients were 3.28±15.55 and 472±207.88 pg/ml, respectively, compared to 1.28 pg/ml in the control group, P= 0.001).

Conclusion- These findings confirm the previous studies and demonstrate that patients suffering from AMI exhibit a lower plasma concentration of selenium and TNF-α and IL - 6 significantly increase during the first hours of AMI. Selenium concentration of whole blood was lower in the two patient groups (CCAD, AMI) compared to the control group. GSH - PX activity has a strong inverse association with CAD ***(Iranian Heart Journal 2007; 8 (2): 26-29).***

Key words: AMI ■ CAD ■ selenium ■ zinc ■ copper ■ TNF- α ■ IL- 6■ GSH- PX

The evidence has demonstrated that populations with low intake of dietary selenium have a 2-3 fold increased risk of Selenium is incorporated into molecules of glutathione peroxidase (GSH-PX), a vital enzyme that protects red blood cells cell

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against undesirable reactions with soluble peroxidase and has an important role against the deleterious actions of free radicals and lipid peroxidase. Selenium acts as a protective factor against atherosclerosis by changing the blood - lipid profile. Selenium therapy in the active phase of MI (first to third day) decreases left heart failure and ventricular extrasystole.[2] The relationship between whole blood selenium levels and risk of myocardial infarction was investigated in a community – based study in Auckland, New Zealand and showed that decreased selenium in the presence of cigarette smoking is a risk factor for heart disease.[3]

Statistically significant positive correlations have been found between trace element concentrations (Cu, Zn, Se) of heart tissue with physiological parameters (CO: cardiac output, EF: ejection fraction) of the heart. It is probable that free oxygen radicals and oxidatively modified particles of LDL participate in the development of atherosclerotic lesions and the potential role of natural antioxidants (vit. C - ascorbic acid; vit. E - tocopherol) is inhibition of this process.[5] TNF - α has a dose - dependent effect on ischemic myocardium. The lower dose may induce angiogenesis and higher dose may induce development of connective tissue leading to scar formation. Increased plasma concentration of TNF- α has been found in patients with coronary artery disease. Stressed myocardium activates pro-inflammatory cytokines, such as TNF-α, which produce abnormalities in myocyte contractile function and soluble TNF receptors that bind to TNF-α may be able to prevent and even reverse TNF-α damage. Patients with significantly elevated serum levels of cytokines and corresponding soluble receptor/receptor antagonist would have the best NYHA (New York Heart Association) class.[4] Pretreatment with tumor necrosis factor – alpha antibodies reduces myocardial infarct size (ischemic preconditioning).[5] This study sought to determine the circulating levels of minerals (Cu, Zn, Se), endogenous modulators (IL- 6, TNF - α), and erythrocyte GSH - PX activity in two groups of patients with chronic coronary artery disease (CCAD), acute myocardial infarction (AMI) and a control group.

Methods

This prospective, single-blind controlled study was done with cooperation of the Departments of Cardiology and Biochemistry of Ghaem Educational Hospital, Mashhad University of Medical Sciences, and Pediatric Immunology Institute of Koln. Fifty (50) patients with coronary syndromes and fifty (50) normal individuals were enrolled in this study.

Twenty five (25) patients with chronic coronary artery disease (proved with ECG, exercise tolerance test and angiography) and (25) patients with acute myocardial infarction (considering symptoms, ECG and documented with enzyme tests) and fifty (50) normal individuals without any symptoms of IHD, gender, age-adjusted were included. Blood samples were collected during the first hours after the onset of chest pain in the AMI group. Samples were centrifuged and sera were frozen at -25° C separately and were sent to Koln.

Serum concentration levels of Se, Cu, and Zn were determined by atomic absorption spectrometry. TNF – α and IL-6 were measured with ELISA and erythrocyte GSH-PX activity with Paglia and Valentine method.

Results

In both groups of patients, there was a significant reduction of Se in the serum (82.36±11.31micg/l in CCAD, 74.08±11.31 in AMI, and 105±32.52 in control group, P=0.03). No significant statistical difference was found between Zn and Cu serum levels (0.98±0.22, 112±18 in CCAD, 0.98±0.4,

115±20 in AMI and 0.96±0.24, 114±17 in control group). A significant difference of TNF-α titer was found especially in AMI patients. Mean TNF-α level was 37.44pg/ml in CCAD and 914.32pg/ml in AMI, compared to the control group (4.80pg/ml, p=0.01). TNF-α was not detectable in 46% (n=47) of cases; 24% (n= 6) in CCAD and 82% (n=41) in the control group. IL-6 was not detected in 70% (n=70) of cases; 84% (n=21) in CCAD patients, 8% (n=2) in AMI and 94% (n= 47) in the control group. Serum levels of IL-6 showed a significant difference between patients groups and control group (3.28±15.55 in CCAD, 472±207.88 in AMI and 1.28 pg/ml in control group, P=0.001).
There is considerably different erythrocyte GSH- PX activity in AMI patients (45u/g) in comparison to CCAD (25.40u/g) and control groups (24u/g, p value 0.00).

Conclusion

These findings confirm the previous studies and demonstrate that patients suffering from AMI exhibit lower plasma concentration of selenium. This level will be lower in males than females and decreases in old age. This data showed that selenium deficiency not only increases the risk of coronary artery diseases, but also increases the risk of acute events.
Laboratory examination also has established that TNF – α and IL - 6 significantly increase during the first hours of AMI.
This reveals that AMI provokes the immune system and releases pro-inflammatory modulators that result in myocardial necrosis. Selenium concentration of whole blood was lower in the two groups of patients (CCAD, AMI) compared to the control group. Erythrocyte selenium level represents a measure of the selenium status over a period of several weeks due to its long biological half – life. The GSH-PX activity has a strong inverse association with CCAD. The presence of increased erythrocyte GSH-PX activity in patients with AMI may be interpreted as an antioxidant defense against the chronic oxidant stress present before AMI.

Table I. Mean concentration of TNF-α, IL-6, erythrocyte GSH-PX, and trace element s in serum

Mean conc. in serum	CCAD	AMI	Control	P value
Se pg/l	82.36±11.31	74.08±11.31	105.36 ± 32.52	0.03
Zn pg/l	0.98 ± 0.22	0.98 ± 0.21	0.96 ± 0.24	
Cu pg/l	112 ± 18	115 ± 20	114 ± 17	
TNF- α pg/ml	37.44	614.32	4.8	0.01
IL-6 ph/ml	3.28	472	1.28	0.001
RBC Gsh-Px u/g	25.4	45	24	0.00

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