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Low superoxide dismutase and catalase is associated malondialdehyde and ischemia modified albumin in patients with Non-ST elevated myocardial infarction (NSTEMI)

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ABSTRACT

Non-ST elevated myocardial infarction (NSTEMI) diagnosis is difficult when the electrocardiography (ECG) normal and troponin parameters are slightly higher than the normal reference range. This study aimed to assess the IMA (ischemia modified albumin), MDA (malondialdehyde), SOD (superoxide dismutase), and catalase in patients with NSTEMI.

The present study included 55 patients with NSTEMI and 55 healthy subjects prospectively. IMA, MDA, SOD, and catalase levels were measured from venous blood obtained from each patient within twelve hours after the onset of symptoms. Differences between the two groups were evaluated with Student's unpaired t-test for parameters with a normal distribution.

IMA (3.14 ± 0.06 vs. 1.49 ± 0.03) and MDA (3.14 ± 0.06 vs. 1.49 ± 0.03) were higher, and SOD (1.10 ± 0.03 vs. 2.31 ± 0.02) and catalase (0.54 ± 0.02) vs. 0.22 ± 0.02) were lower in NSTEMI patients than control subjects. There was a significant correlation among IMA, MDA, SOD and catalase.

Our data reveal that levels of MDA and IMA were increased, and SOD and catalase levels were decreased significantly in patients with NSTEMI. Blood concentrations of oxidant and antioxidant parameters could assess the oxidative state in patients with NSTEMI.

Key Words: NSTEMI, ischemia modified albumin, malondialdehyde, superoxide dismutase, catalase

Introduction

NSTEMI diagnosis is difficult when the electrocardiography (ECG) normal and troponin parameters are slightly higher than the normal reference range. Ischemia modified albumin (IMA), which is serum albumin is modified by ischemia, is a newer biomarker for the detection of myocardial ischemia. It is known that IMA increase within minutes from the onset of ischemia, stayed 6-12 hours high, and returned to normal within 24 hours (1).

Malondialdehyde (MDA), which is a marker of lipid peroxidation, is known as an oxidative stress marker. MDA level could be used as early biomarkers of ischemia and in coronary artery disease (CAD) (2). MDA is a predictor of future cardiac events in patients with angina pectoris who undergo percutaneous coronary intervention (PCI) (3). Moreover, Serum MDA level is a useful biomarker for reflecting the presence of vulnerable plaques (4).

Superoxide dismutase (SOD) removes the superoxide radicals by converting them to hydrogen peroxide (H_2O_2). Catalase catalyzes the conversion of hydrogen peroxide to water and oxygen (5). It has been reported that SOD and catalase levels were decreased in acute myocardial infarction (AMI) patients (6). This study aimed to assess the oxidative state with the IMA, MDA, SOD, and catalase in patients with NSTEMI.

Materials and Method

The study was designed as a cross-sectional and prospective observational design. The convenience sampling method was used in this study. From October 2016 to December 2018, 55

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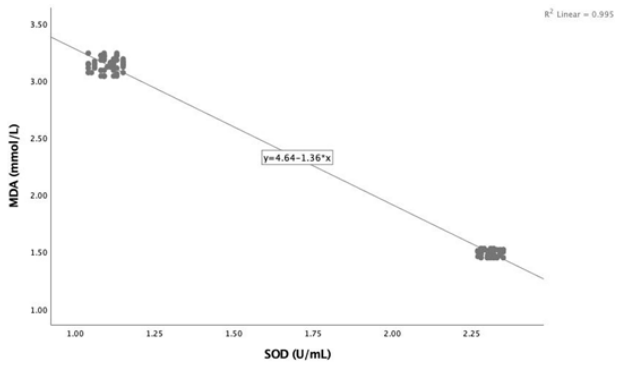

Fig. 1. The correlation analyzes between MDA and SOD levels

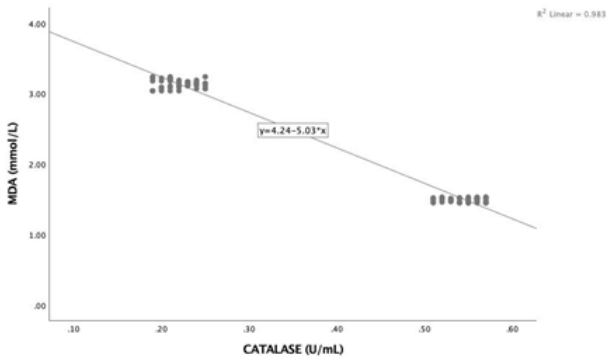

Fig. 2. The correlation analyzes between MDA and catalase levels

patients with angina pectoris who were admitted to Van training and research hospital emergency service were included. Additionally, 55 healthy subjects formed a control group. A cardiologist examined all subjects, and information on medical histories was obtained via a questionnaire. All the enrolled patients had an ECG within one h of admission. The diagnosis of NSTEMI patients included in the study was made by the height of myocardial necrosis markers (troponin I and Troponin T) and the presence of ischemic changes (ST segment depression or prominent T wave inversion) on the ECG. The exclusion criteria included patients younger than 18 years old, acute or chronic infection, myocardial infarction with ST-elevation, those with symptom onset longer than six h, stable or unstable angina pectoris, previous myocardial infarction or myocardial revascularization, systolic heart failure (ejection fraction <40%), severe valvular disease, tachyarrhythmia, patients with end-stage renal insufficiency, and inflammatory diseases.

Informed consent was obtained from all patients before the study. This study was performed by the principles stated in the Declaration of Helsinki and approved by the local Ethics Committee of the Van Training and Research Hospital, and informed consent was obtained from participants in the study.

The levels of troponin I, CKMB, creatinine, low-density lipoprotein-cholesterol (LDL), and whole blood count were measured from venous blood obtained from each patient within twelve h after the onset of symptoms. CK-MB and cardiac TnI levels were measured in serum by Simens ADVIA Centaur Cp analyzers in the emergency laboratory.

Venous blood samples obtained for the measurement of levels of IMA were centrifuged at 4,000 rpm for 10 min and stored at -80 °C until needed. For the determination of the IMA level, the albumin cobalt binding test was used. The test developed by Bar-Or et al. was based on measuring descending albumin cobalt binding capacity (7). The result of absorbance was reported as absorbance units (ABSU). Serum MDA concentrations were determined by high-performance liquid chromatography (HPLC) (Shimadzu LC-10AT), using the technique of Young and Trimble (intra-assay CV 4.2%, inter-assay CV 6.8%) (8). Superoxide dismutase (SOD; EC 1.15.1.1) was measured by the spectrophotometric method, as described by Elstner et al. (9). The serum catalase activity was determined by the method described by Goth (intra-assay CV 3.8%, inter-assay CV 4.5%) (10).

Statistical Analysis: Data were analyzed with SPSS software version 25.0 for Windows (SPSS Inc, Chicago, Illinois). The Kolmogorov-Smirnov test was used to verify that continuous variables were normally distributed. Normally distributed variables were expressed as mean ± standard deviation (SD). The categorical variables are presented as percentages. Differences between the two groups were evaluated with Student's unpaired t-test for parameters with a normal distribution. The frequencies of nominal variables were compared using Fisher's exact test or chi-square test. The Pearson and Spearman tests were used for correlation analysis. Statistical significance was defined as $p<.05$.

Results

The demographic, clinical, and angiographic data of the study participants were shown in table 1. Smoking was higher in the patient group compared to the control group ($p = 0.01$). LDL and platelet counts were significantly higher in the control group than the patient group. MDA values were significantly higher in the patient group ($p <0.001$). SOD levels were significantly lower in the patient group ($p <0.001$). Catalase levels were significantly higher in the control group compared

Table 1. The demographic and clinical data of the study population

	NSTEMI (n=55)	Control (n=55)	p
Age (years)	55.6±12.6	52.9±9.3	0.09
Body mass index (kg/m2)	25.9±3.3	25.5±2.6	0.51
Male/Female n	37/18	29/26	0.11
Smoking n(%)	20(36)	9(16)	0.01
Diabetes mellitus n(%)	23(42)	14(25)	0.06
Hypertension n(%)	24(44)	15(27)	0.07
Hyperlipidemia n(%)	9(16)	3(5)	0.06
Statin	8(15)	1(2)	0.02
Creatinine (mg/dl)	0.9±0.3	0.7±0.2	<0.001
Low density lipoprotein (mg/dl)	100.6±37.7	115.5±29.5	0.02
CKMB (ng/ml)	44(29-78)	12.9±4.8	<0.001
Troponin (ng/ml)	3.7(1.6-22.0)	0.016±0.005	<0.001
White blood cell count (103/mm3)	10.3±4.2	7.2±1.9	<0.001
Hemoglobin (g/dL)	14.3±1.7	13.2±2.0	0.002
Platelet count (103/mm3)	239.0±71.6	262.7±39.5	0.03
IMA(U/ml)	1.8±0.3	0.9±0.1	<0.001
MDA (μmol/L)	3.14±0.06	1.49±0.03	<0.001
SOD (U/ml)	1.10±0.03	2.31±0.02	<0.001
Catalase (U/ml)	0.22±0.02	0.54±0.02	<0.001

NSTEMI, non-ST elevated myocardial infarction; CKMB, creatine kinase-MB; IMA, ischemia modified albumin; MDA, malondialdehyde; SOD, superoxide dismutase

to the patient group (p <0.001). CKMB, troponin, white blood cell, hemoglobin, and IMA levels were significantly higher in the patient group than in the control group. While IMA levels were positively and significantly correlated with MDA and troponin levels, it was negatively and significantly correlated with SOD and catalase levels. MDA levels were positively correlated with troponin levels (r = 0.571 p <0.001). There was an inverse correlation between MDA and SOD levels (r = -0.997 p <0.001). The correlation analyzes between MDA and SOD was shown in Figure-1. MDA levels were inversely correlated with catalase levels (r = -0.991 p <0.001). Figure-2 shows the correlation between MDA and catalase. On the other hand, SOD levels were positively correlated with catalase, and inversely correlated with troponin levels (r = 0.992 p <0.001; r = -0.559 p <0.001; respectively). Catalase levels were significantly and inversely correlated with troponin levels (r = -0.567 p <0.001) (table 2-3).

Discussion

In this study, we found that MDA and IMA levels were higher in patients with NSTEMI compared to healthy subjects. Also, we showed that SOD and catalase levels were lower in the patient group than the control group. These findings indicate that oxidative stress is higher, and the antioxidative defense was lower in patients with NSTEMI.

Serum MDA levels were a significant prognostic factor in ACS patients undergoing PCI (11). Darbroud et al. evaluated IMA levels in 52 NSTEMI patients and 52 healthy controls. The authors showed that MDA was statistically higher in NSTEMI patients compared to the control group (12). A previous study showed that there is an inverse correlation between MDA, which is an oxidative parameter, and antioxidant enzymes (13). Moreover, Ito et al. presented that MDA levels were increased in coronary artery spasm (14). In the present study, we have shown that MDA levels were higher and significantly correlated with troponin levels in NSTEMI patients. We also presented that MDA and catalase inversely were correlated in this study, and these findings were compatible with the results of the one study, which was performed by Serdar et al. (13).

It is known that oxidative stress increases in AMI. In the present study, we reported that SOD levels were reduced in NSTEMI patients compared to healthy subjects. Similarly, Gammoudi et al. reported a decreased SOD activity associated with

Table 2. Correlation analyzes among the IMA (ischemia modified albumin), MDA (malondialdehyde), SOD (superoxide dismutase), catalase and troponin

	IMA		MDA		SOD		Catalase		Troponin	
	r	p	r	p	r	p	r	p	r	p
IMA	-	-	0.907	<0.001	-0.905	<0.001	-0.900	<0.001	0.505	<0.001
MDA	0.907	<0.001	-	-	-0.997	<0.001	-0.991	<0.001	0.571	<0.001
SOD	-0.905	<0.001	-0.997	<0.001	-	-	0.992	<0.001	-0.559	<0.001
Catalase	-0.900	<0.001	-0.991	<0.001	0.992	<0.001	-	-	-0.567	<0.001
Troponin	0.505	<0.001	0.571	<0.001	-0.559	<0.001	-0.567	<0.001	-	-

Table 3. Correlation analyzes among the affected coronary vessels, IMA (ischemia modified albumin), MDA (malondialdehyde), SOD (superoxide dismutase) and catalase

	One-vessel		Two-vessels		Three-vessels	
	r	p	r	p	r	p
IMA	-0.339	0.011	0.136	0.321	0.329	0.014
MDA	-0.170	0.216	0.243	0.073	-0.026	0.848
SOD	-0.186	0.174	0.266	0.050	0.005	0.973
Catalase	0.193	0.157	-0.118	0.390	-0.140	0.308

increased oxidative stress in coronary patients (15). In one study, Sabah et al. showed that peroxynitrite, nitric oxide, and superoxide anions are high, and SOD activity is low in ACS patients. They also showed that peroxynitrite levels, which are oxidative markers, correlate negatively with SOD activity (16). Diaz-Araya et al. have determined lower SOD activities in plasma from AMI patients as compared with controls (6). In our study, we showed that antioxidant levels were lower in NSTEMI patients than in control subjects. So, our findings suggest that the significantly reduced levels of antioxidant SOD levels represent a state of the heightened oxidative state in NSTEMI patients.

The increase in oxidative stress was probably a result of the elevation in reactive oxygen species (ROS) production due to the ischemic-reperfusion event that occurs in NSTEMI with the decrease of enzymatic antioxidant defenses. Serdar et al. presented that catalase levels were lower in patients with multivessel coronary artery disease compared to single coronary artery disease. Besides, they showed that the decreases in the activity of the catalase and SOD in serum and erythrocytes were parallel to the increase in the severity of CAD. In the same study, they also showed that there is an inverse correlation between MDA, which is an oxidative parameter, and antioxidant enzymes (13). We found that catalase levels were lower in NSTEMI patients compared to the control group. Moreover, we presented that MDA and catalase and ischemia biomarkers are inversely correlated in NSTEMI patients.

IMA is one of the biomarkers which allows physicians to diagnose ischemia before myocardial necrosis. In the case of oxidative stress, hydroxyl radicals damage the amino acids in the albumin and impair its ability to copper bind. In NSTEMI, intracoronary thrombus reduces coronary blood supply and causes IMA formation by causing a chemical change in the albumin. A previous study showed that IMA levels were increased within minutes from the onset of ischemia, remained 6-12 hours higher, and returned to normal within 24 hours (1). In this study, the oxidative stress was higher in NSTEMI patients compared to the control group, and IMA values were correlated with MDA levels. These findings support that oxidative status and impaired coronary perfusion play a role in the formation of IMA.

Limitations: One of the limitations was that the study group was confined to patients with NSTEMI. Therefore, our findings cannot be generalized to include all patients with ACS. The relatively limited number of patients could limit the strength of results and conclusions obtained from this study. The lack of high-sensitivity troponin in our institution was another limitation,

and conventional cardiac troponin I levels were measured.

In conclusion, our data reveal that levels of MDA and IMA were increased, and SOD and catalase levels were decreased significantly in patients with NSTEMI. The potential usefulness of blood concentrations of oxidant and antioxidant parameters in understanding the relationship with NSTEMI needs further studies.

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Conflict of interest: The authors declare that they have no conflict of interest.

Ethical approval: All procedures performed in this study were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent: Informed consent was obtained from all individual participants included in the study.

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