



Evaluation of oxidative stress factors and lipid profile in patients suffered from stroke heart disease with coronary artery obstruction

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Abstract

Introduction: Cardiovascular disease accounts for the highest number of deaths in most industrialized countries and it is increasing in developing countries. Among cardiovascular diseases, coronary heart disease (CHD) is the deadliest cardiovascular disease. High concentrations of reactive oxygen species can cause membrane lipid peroxidation, and impaired regulation of vascular and cardiac cells.

Objectives: The present study is an analytical case-control study that tried to estimate the activity of antioxidant enzymes (superoxide dismutase [SOD], catalase), malondialdehyde (MDA) content, total antioxidant capacity (TAC), triglyceride (TG), LDL-c, in CHD patients.

Patients and Methods: Seventy-four subjects (male) older than 30 years old who referred to the hospital for angiography after coronary angiography were divided into case and control groups. Subsequently, 10 cc of blood was taken from the subjects. Catalase and SOD activities in erythrocytes were measured by calorimetry and enzymatic inhibition, respectively. Total HDL-c, LDL-c, TG and total cholesterol levels were measured by Pars Azmoon kit.

Results: Regarding the *P* values, the variables of TG, HDL cholesterol, SOD, MDA, TG/HDL-c and TC/HDL-c are effective. Comparison the mean of MDA in two groups of treatment and control showed a significant difference between mean of MDA between two groups. Significant differences were also observed for TG values for the two groups of control (94.03 ± 31.06 mg/dL) and treatment (80.78 ± 160.01 mg/dL).

Conclusion: Antioxidant status of patients with CAD was lower than normal subjects. In addition, disturbance in lipid profile parameters confirmed in CAD patients; while TG increased in those patients.

Introduction

Cardiovascular disease accounts for the highest number of deaths in most industrialized countries and it is increasing in developing countries (1). In Iran, about 38% of the causes of death are related to cardiovascular disease.

Various risk factors, including blood lipid, diabetes, hypertension, smoking, and obesity, play important roles in the development of cardiovascular disease. Among cardiovascular diseases, coronary heart disease (CHD) is the deadliest cardiovascular disease (2). fatty acids are the major constituents of the membrane and the peroxidation of the membrane fat could seriously disrupts the function of the membrane. Membrane peroxidation products are a criterion of oxidative stress as the most common product is malondialdehyde (MDA) (3).

It was concluded that the capacity of the antioxidant system in patients with cardiac ischemia was lower than the control group,

Key point

Antioxidant status of patients with CAD was lower than normal subjects. In addition, subjects with CAD had lower HDL levels and higher TG levels while triglyceride increased in those patients.

which this fact could justify the increase in lipid peroxidation in patients. Additionally, the amount of lipid peroxidation could not be predicted by the amount of ceruloplasmin because there was no relationship between them (6). Considering the significant relationship between serum levels of MDA, cholesterol, triglyceride (TG), LDL-c, HDL-c and LDL-c to HDL-c ratio in coronary artery disease (CAD) patients compared to control group, it can be concluded that monitoring and controlling these factors in the above-mentioned individuals can be useful in preventing the development and progression of atherosclerotic lesions (7). In 1993, Wen et al determined serum lipids, lipoproteins, and

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MDA in 86 angiographically confirmed cardiovascular (CAD) patients and 33 controls. Correlation analysis showed that the severity of angiogenic lesions was positively correlated with serum total cholesterol, LDL-c, MDA and negatively with HDL-c (8).

Objectives

The aim of the present study was to compare the antioxidant enzymes and lipid profile in patients with coronary artery obstruction and without obstruction referring to Imam Khomeini Hospital in Tehran from 2009 to 2010.

Patients and Methods

Study design

The present study is an analytical case-control study to estimate the activity of antioxidant enzymes (superoxide dismutase [SOD], catalase), MDA rate, total antioxidant capacity (TAC), TG, total cholesterol; LDL-c and HDL-c in the blood of samples were collected from men with CAD who referred to Imam Khomeini hospital in Tehran in comparison with healthy men.

Population of the study

Control group; people who referred to the center and were matched in age with treatment or case group. The age range of the subjects was 33-65 years and the mean age was 55 years.

Case group; men who had been admitted to the center with a heart attack or with a previous diagnosis of coronary artery obstruction for angiography diagnosis had been admitted to angiography section. Their age range was 30-62 and mean age was 59.

Excluded group (outliers); men with one of the livers, diabetes, inflammatory, infectious, autoimmune, kidney, cancer and anemia diseases were excluded.

Procedure

Seventy-four subjects (male) more than 30 years old who referred to the hospital for angiography after coronary angiography were divided into case and control groups.

Subsequently, 10 cc of blood was taken from the subjects, 5 cc of which was poured into an anticoagulant tube and after centrifugation at 1500 rpm and supernatant separation, erythrocyte sediment was washed 3 to 4 times with saline and washed until the test time was maintained at -80°C . Catalase and SOD activities in erythrocytes were measured by calorimetry and enzymatic inhibition, respectively. Total HDL-C, LDL-C, TG and total cholesterol levels were measured by Pars test kit

Statistical analysis

The statistical software of Windows/Statistical Package for Social Science (SPSS) version 9 was used. Paired *t* test was used to compare the mean of quantitative variables in the two groups of controls. Independent *t* tests were used to gather the quantitative variables and compare them with

the dependent variable.

Pearson's correlation was used to correlate the variables in each control and patient group. Regression analysis was used to test the linearity of the correlations and backward regression was used to determine the most important variables affecting the dependent variable. Excel and SPSS software were used for drawing curves and graphs.

Results

Statistical analysis of Q-Q Plot for the distribution of the evaluated variables showed that the distribution of SOD and TG did not follow the normal distribution. Table 1 presents the results for variables such as age, body mass index (BMI), duration of smoking, number of cigarettes, number of exercise hours per week, history of hypertension and history of heart disease. According to *P* values reported based on the statistical analysis in the table, with 95% confidence interval, duration of smoking, number of cigarettes and history of heart disease are the most important parameters that influence the results. In fact, changing any of these parameters will result in a noticeable change in the results.

As reported in Table 2, based on *P* value values, the TG, HDL-c, SOD, MDA, TG/HDL-c, and TC/HDL-c are influential.

Comparison of mean MDA in case and control groups showed significant difference between mean of MDA between two groups. The mean MDA in the case group ($2.097 \pm 0.818 \mu\text{mol/L}$) was lower than in healthy subjects ($2.774 \pm 0.724 \mu\text{mol/L}$; $P < 0.001$). The results of correlation test showed that there is a significant correlation between MDA with cholesterol and LDL-c.

According to Table 1, significant differences were found for TG values for the two control ($94.03 \pm 31.06 \text{ mg/dL}$) and case ($80.78 \pm 160.01 \text{ mg/dL}$).

According to Table 3, the relationship between HDL cholesterol activity with LDL-c factor, cholesterol acyltransferase (CAT) with LDL-c factor and total plasma (TAC) with BMI factor in case group as well as TG activity with TC factor were significant in the control group, since in other cases, the relationship is not significant.

Table 1. Results for variables such as age, BMI, duration of smoking, number of cigarettes, number of exercise hours per week, history of hypertension and history of heart disease

Variable	Control	Case	<i>P</i> value
Age (years)	55	59	0.223
Body mass index (BMI)	25	24	0.053
Duration of smoking (y)	25	36	0.008
Number of cigarettes consumed (year per day)	26	35	0.028
Exercise hours (hours per week)	39	31	0.073
Blood pressure history (years)	35	39	0.344
History of heart disease (years)	22	52	<0.001

Table 2. Results of the evaluation of the tested variables

Variable	Control	Case	P value
Triglycerides (mg/dL)	94.03±31.06	160.01±70.87	<0.001
Total cholesterol (mg/dL)	177.14±33.57	165.03±38.24	0.153
HDL Cholesterol (mg/dL)	44.25±7.84	35.97±9.79	<0.001
LDL Cholesterol (mg/dL)	90.72±24.01	83.32±25.029	0.201
Catalase	194.78±64.99	191.71±55.81	0.829
Superoxide dismutase	942.51±349.19	1165.11±419.74	0.018
Malondialdehyde (µmol/L)	2.8±0.73	2.10±0.83	<0.001
TAS	3.94±0.94	3.83±0.74	0.346
LDL/HDL	2.09±0.58	2.40±0.73	0.470
TG/HDL	2.18±0.80	4.99±3.59	<0.001
TC/HDL	4.07±0.6	4.82±1.55	0.033

Discussion

Free radical scavenging may increase MDA, which may play an important role in exacerbating atherosclerosis and thrombosis. Increased MDA in patients may be due to increased lipid peroxidation that consequently the increase in lipid peroxidation is due to increased levels of oxidative stress. The studies showed that MDA has been shown to be a good indicator for assessing fatty acid peroxidation and it is now used as a screening parameter (13).

Numerous studies have investigated MDA levels in patients with AMI after thrombolytic therapy (14). In all cases, there was an increase in MDA after thrombolysis, although in some studies the increase was not statistically significant. There were also differences in the timing of changes in MDA levels. Beard et al (15) and Young et al (16) reported that there was a decrease in MDA level, 2–6 hours after thrombolysis after the initial increase.

Regarding the catalase enzymes, although there have been no reports of altered erythrocyte catalase activity in cardiac patients; the decrease in the activity of the enzyme in the studied patients suggests that catalase enzymes in cardiac patients may be impaired. In particular, the greater the severity of coronary artery involvement, the greater the decrease in enzyme activity.

The results of this study showed that there is a significant relationship between HDL-c and BMI. A decrease in HDL-c levels has been shown with increased BMI in men and women (17). Another study (18) investigated the decrease in HDL-c with increasing BMI in relation to HDL-c-related factors such as lipoprotein AI and membrane-bound IIpA, lipoprotein and concluded that BMI was strongly correlated with both factors, which play a role in BMI. The effect on HDL-c particles is confirmed.

Following are some studies in Iran and outside Iran. In 1989, in Tabriz, differential sequestration by dextran sulfate, HDL-c and its fractions (HDL-c, II-C and HDL-c) were studied in the plasma of 340 healthy individuals and 60 hospitalized patients with myocardial infarction. The results indicated that HDL-c measurement due to its

Table 3. Results for case and control variables

Variable	LDL	T.C	BMI	AGE
Case				
TG	-	-	-	-0.384*
HDL	0.427**	0.343*	0.355*	-
MDA				
CAT	0.431**	0.362*	-	-
SOD	-	-	-	-
TAC	-	-	0.432**	-
Control				
TG	0.363*	0.435**	-	-
HDL	-	0.337*	-	-
MDA	-	-	-	-
CAT	-	-	-	-
SOD	-	-	-	-
TAC	-	-	0.393*	-

Values are shown as correlation coefficient *r*.

* $P < 0.05$, ** $P < 0.001$.

protective role and the ratio of total cholesterol to HDL-c could be more valuable criterion than other lipoproteins and lipid fractions in predicting the risk of heart disease. There is also a strong negative association between HDL-c and TG concentrations compared to HDL-c (4).

In another study in 2005, (52 males and 36 females) with angiography for CAD were selected. The severity of the lesions was less than 50%, 50-71%, 71-90% and 91-100% by angiography, as well as the extent of lesions with angiographic results in terms of number of affected veins, one vessel, two vessels, and three vessels were classified. Statistical analyzes showed no association between the extent of atherosclerotic lesions and low total antioxidant levels and high levels of total homocysteine (5).

In 2005, a descriptive study was performed on 99 men aged 35-55 in Iran. The case group included 29 patients with cardiac ischemia and coronary artery stenosis above 70% confirmed by exercise test and angiography while the control group included 70 healthy individuals with no history of heart disease, diabetes and hypertension.

In 2006, 51 males under the age of 55 years who were confirmed by angiography were in Tabriz and 60 apparently healthy men who were at the same age and gender with 51 patients were selected as control group. Results showed a significant increase in MDA serum levels in patients compared to the control group ($P=0.03$). Additionally, evaluation of serum cholesterol concentration, TG and LDL-c and the ratio of LDL-c to HDL-c showed an increase in these factors in the patients group compared to the control group.

In 1994, Sharrett et al, conducted a study from the population of 7261 men and women without clinical signs of cardiovascular disease to evaluate the association between carotid artery aneurysm stenosis measured by ultrasound imaging and fasting level of HDL-c, LDL-c, TG and HDL-c fractions. Lipid factors showed a linear relationship with carotid stenosis (positive association

with LDL-c and negative association with HDL-c) (9).

In 2001, Takao et al conducted a pilot study to determine the association between atherosclerosis of the thoracic artery, coronary artery, and HDL-c in both age- and sex-matched healthy and patient groups. The results showed that patients showed low HDL-c and apo A-1 levels compared to healthy individuals (10).

In 2007, Kotur et al, by examining the relationship between MDA, SOD, with C-reactive protein (CRP) protein and fibrinogen in 385 CAD patients and 197 controls, showed a significant increase in plasma MDA along with a significant decrease in SOD in CAD patients compared to controls (11).

In 2008, Vishnu-Priya and Surapaneni, compared the levels of MDA, SOD, and CAT in 65 CAD patients with the control group. Finally, there was a significant increase in MDA, SOD and a significant decrease in CAT of the patients compared to the control group (12).

Conclusion

In the current study, a total of 74 men were studied, including 39 patients with coronary artery obstruction angiography, and 35 clinically healthy men who had been clinically confirmed as having no obstruction. The age range was 30-70 years. Patients with renal, thyroid, liver, infectious, inflammatory disease were excluded. Regarding the P-values, TG, HDL-c, SOD, MDA, TG/HDL-c and TC/HDL-c variables are affected.

Comparison of MDA mean in case and control groups showed significant difference between mean of MDA between two groups. Significant differences were observed for TG values for the two control (94.03 ± 31.06 mg/dL) and case (160.01 ± 80.78 mg/dL). Regarding the association of TG with cigarettes, it can be said that the serum TG level in the case group is increased compared to the control group. In some studies, serum TG levels were increased in cardiovascular patients.

The results showed a positive correlation between smoking dose and total cholesterol, TG and negative correlation with HDL-c. In this study, the level of erythrocyte SOD activity was significantly higher in patients with coronary artery occlusion compared to healthy controls (942.5 ± 352.19 and 1165.360 ± 419.74). Mean serum HDL-c was significantly different in subjects with coronary artery obstruction (44.2 ± 7.8 and 35.9 ± 9.7 mg/dL, $P < 0.001$).

There was also a significant relationship between HDL-c and BMI. A decrease in HDL-c levels with increasing BMI has been reported in both men and women.

Antioxidant status of patients with CAD was lower than normal subjects. In addition, subjects with CAD had lower HDL levels and higher TG levels while TG increased in those patients.

Limitations of the study

There is some limitation in our study that must be

acknowledged. First, heterogeneity in the severity of disease might have influenced results direct measurement of molecular intermediates facilitates evaluating changes in measured parameters more precisely. Also, small sample size is another limitation. Therefore, our findings require confirm in a study involving a larger cohort of patients.

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Authors' contribution

KN, MDJ and MJM performed the research and contributions to design of the study. KN prepared the primary draft. MDJ contributed to data analysis. MDJ and MJM edited the final draft and final approval of the manuscript. All authors participated in preparing the final draft of the manuscript, revised the manuscript and critically evaluated the intellectual contents.

Conflicts of interest

All the authors declared that they have no conflicts of interest.

Ethical issues

The research followed the tenets of the Declaration of Helsinki. The Ethics Committee of Tehran University of Medical Sciences approved this study. The institutional ethical committee at Tehran University of Medical Sciences approved all study protocols. Accordingly, written informed consent was taken from all participants before the study. This study was extracted from M.Sc. thesis at this university (Thesis #240/5333). Moreover, ethical issues (including plagiarism, misconduct, data fabrication, falsification, double publication or submission, redundancy) have been completely observed by the authors.

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