Evaluation of Body Iron and Oxidative Stress Status in Smoker/Hypertensive/ Diabetic Patients Suffering Acute Myocardial Infarction Episode

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Abstract

The relationship between serum ferritin, body iron indices, and the coronary heart disease (CHD) or stroke remains controversial. The role of diabetes mellitus, smoking, and hypertension on serum ferritin and other iron monitoring molecules in acute myocardial infarction (AMI) has been under active consideration. The present study addresses the alterations in the body iron status and the lipid peroxidation (LPO) activity in AMI, particularly in the diabetics, hypertensives, and smokers. The study also evaluates the correlation between them. This study is comprised of AMI patients with or without diabetes/hypertension/smoking and healthy controls of ages 29 to 79. Blood hemoglobin, hematocrit (HCT) values, serum iron, total iron binding capacity (TIBC), ferritin and erythrocytes LPO were analyzed. An elevation in total iron, ferritin and erythrocyte LPO, and a decline in TIBC were observed in AMI patients irrespective of whether they are with or without diabetes, hypertension, or smoking while Haemoglobin (Hb) decreased in AMI non-smokers, and HCT remained unchanged when compared to controls. A positive correlation existed between total iron, ferritin and erythrocyte LPO, between hemoglobin and hematocrit, but a negative correlation of TIBC with ferritin and LPO in the AMI experimental groups is observed. A statistical significant increase in Hb and HCT values were noted in AMI smokers in comparison to AMI non-smokers, while other parameters remained unchanged between the complimentary AMI groups. AMI females had lower levels of Hb and HCT than AMI males. Diabetes, hypertension, smoking, and AMI are inflammatory processes. Elevated Ferritin, an acute phase reaction protein and associated LPO activity might be attributed to AMI progression.

1. Introduction

High blood pressure is no less than an epidemic and it remains a major cause of cardiovascular morbidity and mortality worldwide (Wang and Wang,2004; Lawes *et al.*, 2006). It is still unknown whether iron itself has a role in the development of hypertension or not. Recently, non-haem iron has been reported to have an inverse relation with blood pressure while heme iron intake, on the other hand, elevates blood pressure (Tzoulaki, *et al.,* 2008). Serum ferritin and dietary iron are reported to be associated with the increased incidence of myocardial infarction (Klipstein-Grobusch, *et al.,* 1999a). Recently, a link has been established between increased dietary iron intake, particularly eating red meat as well as increased body iron stores, and the development of diabetes. A causative link with iron overload is suggested to improve insulin sensitivity and insulin secretion with frequent blood donation and decreased iron stores (Jiang, *et al.*, 2004; Fernandez-Real, *et al.,* 2005). The role of tissue iron and elevated body iron stores in causing type 2 diabetes and or the pathogenesis of its important complications, particularly diabetic nephropathy and cardiovascular disease is now being investigated elaborately. Several epidemiological studies have analyzed the involvement of iron in coronary heart disease but with inconclusive results (Vander, *et al.,* 2005; Tavani *et al.,* 2006; Qi, *et al.*, 2007). Smoking, current or past, has been associated with higher plasma/serum ferritin concentrations among various populations (Rodger, *et al.,* 1985; Touitou, *et al,* 1985). The mechanism of increased plasma ferritin concentrations among current smokers remains to be investigated. Considering the inconclusive literature reports on the role of ferritin, indices of body iron stores, in relevance to the development of acute myocardial infarction, the present study aims at investigating and evaluating the total iron, ferritin, total iron binding capacity (TIBC), hematocrit (HCT), hemoglobin (Hb) and lipid peroxidationin activity (LPO), and their correlations, if any, in acute myocardial

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infarction (AMI) group of patients with or without hypertension/ smoking/ diabetes.

Despite of the traditional use of *Aloysia triphylla* as an analgesic, no systemic studies concerning the antinociceptive effects are available. In the present study, we are reporting the antinociceptive effects of two flavonoids (artemitin and hesperidin) which were isolated from the *Aloysia triphylla*.

2. Materials and Methods

2.1. Subjects

This study includes patients who were admitted in the Jamahyria hospital, Benghazi, during the period from June, 2007 to December, 2007 with acute myocardial infarction (AMI) and were between 29–59 years old with a mean value ± S.D., 55±13. The patients were subjected to clinical examination. The detailed medical history, blood pressure and ECG tracing were recorded. These patients (AMI patients) were divided into the following subgroups: AMI Smokers (10), AMI hypertensive (10), AMI diabetics (10), AMI non-smokers (20); AMI normotensives (20), and AMI non-diabetics (20); with AMI only males (21) and with AMI only females (9). The control group included 30 (15 males and 15 females), healthy subjects with a mean age 50±10 for males, 48.5±10.5 for females. They were normotensive nonsmoking and non-diabetics with normal ECG tracing and were devoid of heart, liver, kidney and any other endocrine related diseases.

2.2. Criteria for smoking patients

The selection criteria for the smoking group with AMI included those who had a history of smoking of ten or more cigarettes per day during the last ten years or more.

2.3. Criteria for Hypertension and anemia

Hypertension was defined as a resting systolic blood pressure >140 mm Hg and diastolic blood pressure >90 mm Hg, and anaemia was defined, using World Health Organization (WHO) criteria, as a hematocrit value at initial presentation < 39 % for men and < 36 % for women.

2.4. Criteria for diabetes mellitus

The AMI patients having fasting blood glucose level more than 126mg/dl and post absortive blood glucose levels above 200mg/dl were included.

2.5. Exclusion criteria

None of the subjects in the study groups and the control group had a previous history of myocardial infarction, angina, coronary artery surgery, transient ischemic attack and peripheral arterial diseases, liver, kidney and thyroid related diseases. None of the study subjects had undergone blood transfusions/ donations throughout their life time.

The present study was conducted after obtaining the written informed consent of the participating subjects. The study was approved by the ethical committee of the hospital, and procedures were followed in accordance with the ethical standards laid down on human experimentation (institutional and national) and with the Helsinki Declaration of 1975.

2.6. Blood specimen collection

Blood samples were collected from the study subjects and the controls after overnight fasting. One part of the blood was placed into plain tube for the serum separation by centrifugation at 3500 rpm for 10 minutes and stored at -30 C till the analysis was conducted. Another blood aliquot was collected in EDTA containing tubes for the plasma separation by centrifugation. The packed cells were washed with an equal volume of the physiological saline and centrifuged again. The supernatant was removed and the cells were analyzed for the lipid peroxidation.

2.7. Analytical methods

The complete blood count, hemoglobin (Hb), serum iron (Makino, 1988), (TIBC) total iron binding capacity (Ramsey, 1958), ferritin (Zuyderhoudt and Linthorst, 1984) and the (LPO) lipid peroxidation in erythrocytes (Quinlan *et al.*, 1988) were analyzed by employing the authentic methods. The hemoglobin (Hb) and the hematocrit values (HCT) were estimated by the established hematological methods (Dacie and Lewis, 1986).

2.8. Statistical analysis

All the biochemical parameters were statistically analyzed using software SPSS version 11 (statistical package for social sciences) for calculation of student's 't' test for obtaining the p values and pearson's correlation coefficient 'r'.

3. Results

The data on serum iron, total iron binding capacity (TIBC), ferritin, blood hemoglobin, hematocrit and erythrocyte lipid peroxidation in the AMI patients, AMI males and females, AMI smokers/hypertensives/diabetics patients, AMI non-smokers/ normotensive/non-diabetics patients and the healthy controls, Correlation coefficient between these experimental groups are presented in table-1-4.

3.1. Body iron status and LPO activity in AMI patients

The AMI patients showed a significant increase in serum iron, ferritin and erythrocyte LPO activity along with a significant decline in serum TIBC when compared to healthy controls. The hemoglobin and hematocrit values remained unaltered in AMI patients as shown in table I.

3.2. Body iron status and LPO activity in AMI males and females patients

No significant difference was noticed in serum iron, TIBC, ferritin and erythrocyte LPO activity in AMI males and females while a significant decrease in hemoglobin and hematocrit values was observed in female AMI patients when compared to male AMI patients as shown in table 2.

3.3. Body iron status and LPO activity in AMI non-smokers, AMI normotensive and AMI non-diabetic patients

The AMI non-smokers, AMI normotensive and AMI non-diabetic patients groups when compared with corresponding healthy nonsmoking, normotensive and non-diabetic controls, there was a significant increase in

Table 1: Iron status, hematocrit and erythrocyte lipid peroxidation activity (Mean values±SD) in AMI patients

Parameters	Controls N=30	AMI Patients N=30
Serum Iron (mg/dL)	62.07±18.05	79.50±22.34 $p< 0.002$
Serum TIBC (mg/dL)	341.43±47.36	313.60±49.41 $p< 0.03$
Serum Ferritin (ng/dL)	71.60±33.23	185.50±57.92 $p <0.001$
Hemoglobin (g/dL)	13.07±1.67	12.73±1.57
Hematocrit (%)	38.26±5.33	37.57±4.77
Erythrocyte LPO (Absorptive value)	0.36±0.14	0.50±0.32 $p<0,03$

AMI: Acute myocardial infarction

TIBC:Total iron binding capacity ; LPO: erythrocyte lipid peroxidation

$P<0.05$, significant when compared to control group; N, the number of subjects

the level of the serum iron and serum ferritin while the TIBC decreased significantly with the exception of AMI normotensiove patients where the decline was statistically nonsignificant. The erythrocytes lipid peroxidation activity was raised in these groups but it was observed to be significant only in AMI smoker group. There was a significant decrease in serum hemoglobin in AMI nonsmoker group while it remained unchanged in AMI normotensive and AMI nondiabetic groups. Hematocrit levels of AMI nonsmokers, AMI normotensive and AMI nondiabetic patients groups did not differ significantly from that of healthy controls. The data are presented in table3.

3.4. Body iron status and LPO activity in AMI smoking patients

The AMI smoker patients group showed a significant increase in the level of serum ferritin and non-significant changes in the levels of serum iron, serum TIBC, hemoglobin, hematocrit and erythrocyte lipid per-oxidation when compared to nonsmoking healthy controls. AMI smokers group showed a significant increase in hemoglobin and hematocrit values than the AMI nonsmoking group, while iron, TIBC and ferritin and lipid per-oxidation (LPO) activity remained unchanged when compared to AMI nonsmoker group of patients. The data are given in table 3.

3.5. Body iron status and LPO activity in AMI hypertensive group of patients

There was a significant increase in total serum iron, ferritin levels, and LPO activity in AMI hypertensive patients while TIBC though declined, yet remained statistically unchanged when compared to healthy controls. Hemoglobin and hematocrit levels did not alter when compared to healthy controls. None of the parameters altered in AMI hypertensive patients when compared to AMI normotensive patients. The data are shown in table 3.

3.6. Body iron status and LPO activity in AMI diabetic group of patients

AMI diabetic group of patients observed a significant increase in iron, ferritin, and LPO activity while the decline in TBIC was not statistically significant when compared to healthy controls. Hemoglobin and hematocrit values remained unaltered as compared to healthy controls. None of the parameters studied differed in their values in AMI diabetics when compared to AMI nondiabetics. The data are exhibited in table 3.

3.7. Coefficient correlations between parameters within different groups

The data on correlation coefficient and p values in various parameters in AMI smokers, AMI hypertensives, AMI diabetics and AMI non-smokers, AMI normotensives, AMI non-diabetics patient groups are presented in table 4.

There were positive correlations of iron with serum ferritin, LPO activity and a negative correlation between serum TIBC and ferritin in AMI smokers, AMI hypertensives, AMI diabetics patients and in AMI non-smokers, AMI normotensives, AMI nondiabetics patients groups. Hemoglobin showed a positive correlation with hematocrit in all these experimental groups.

Table 2: Iron status, hematocrit and erythrocyte lipid peroxidation activity (Mean values±SD) in AMI patients, both males and females

Parameters	AMI Patients Males (N=21)	AMI Patients Females (N=(9)
Serum Iron (ug/dL)	80.19±23.55	77.89±20.46
Serum TIBC (mg/dL)	315.00±52.51	310.33±44.05
Serum Ferritin (ng/dL)	187.52±61.98	180.78±50.20
Hemoglobin (g/dL)	13.26±1.54	11.5±0.73 *p* <0.003
Hematocrit (%)	39.04±4.75	34.12±0.31 *p* <0.05
Erythrocyte LPO (Absorptive value)	0.52±0.33	0.45±0.31

AMI: Acute myocardial infarction; TIBC: Total iron binding capacity

LPO: erythrocyte lipid peroxidation; N: Number of subjects

p<0.05 denotes significant on comparison with AMI males

p>0.05 denotes non-significant on comparison with AMI males

Table 3: Iron status, hematocrit and erythrocyte lipid peroxidation activity (Mean values±SD) in AMI patients and controls.

Parameters	Control N=30	AMI Non Diabetics N=20	AMI Diabetics N=10	AMI Non Smokers N=20	AMI Smokers N=10	AMI Normo-tensive N=20	AMI Hyper-tensive N=10
Serum Iron (µg/dL)	62±18	81±23 *p*<0.003	77±22 *p*<0.02	81.20±21.68 *p*<0.001	76.10±24.42	77±24 *P*<0.02	85±17 *P*<0.001
Serum TIBC (mg/dL)	341±47	308±46 *p*<0.03	320±54	310.50±47.20 *p*<0.03	319.80±55.68	316±51	309±47 *P*<0.05
S. Ferritin (ng/dL)	72±33	190±58 *p*<0.001	180±59 *p*<0.001	189.45±59.87 *p*<0.001	177.60±56.03 *p*<0.001;	188±64 *p*<0.01	181±46 *p*<0.001
LPO (absorptive value)	0.36±0.14	0.49±0.03	0.52±0.32 *p*<0.03	0.54±0.32 *p*<0.001	0.43±0.33	0.47±0.34	0.56±0.29 *p*<0.01;
Hemoglobin (g/dL)	13±1.6	13±1.8	12±0.99	12.00±0.91 *p*<0.001	14.19±1.6 3 *p*2<0.001	12.7±1.5	13±1.8
Hemato- crit(%)	38±5.3	37.8±2.5	36±3.40	35.60±3.54	41.51±4.57 *p*2<0.001	37.4±4.5	37.7±5.5

AMI: Acute myocardial infarction; TIBC: Total iron binding capacity;

LPO: erythrocyte lipid peroxidation; N: Number of subjects;

Non significant at p>0. 05

p<0.05, significant when compared with controls

p_1<0.05, significant when compared with AMI non-diabetic patients

p2<0.05, significant when compared with AMI non-smoker patients

p3<0.05, significant when compared with AMI normotensive patients

Table.4. Correlation coefficient (r) between the Analytes in AMI patients

Coefficient Correlation	AMI Groups					
	Diabetics	NonDiabetics	Smokers	Nonsmokers	Hypertensive	Normotensive
Iron Vs TIBC	r, -0.75 $p<003$	r,-0.54 $p<0.03$	r,-0.51 $p<0.13$	r,-0.71 $p<0.001$	r,-0.71 $p<0.02$	r,-0.62 $p<0.04$
Iron Vs Ferritin	r, 0.70 $p<0.01$	r, 0.80 $p<0.001$	r,0.81 $p0.01$	r,0.74 $p<0.001$	r,0.67 $p<0.03$	r,0.81 $p<0.001$
Iron Vs Hb	r,0.39 $p<0.18$	r,-0.14 $p<0.59$	r,-0.04 $p<0.92$	r,-0.22 $p<0.35$	r,0.05 $p<0.89$	r,-0.27 $p<0.26$
Iron Vs HCT	r,0.29 $p<0.33$	r,-0.07 $p<0.80$	r,0.01 $p<0.99$	r,-0.09 $p<0.72$	r,0.09 $p<0.81$	r,-0.20 $p<0.41$
Iron Vs LPO	r,0.62 $p<0.02$	r,0.78 $p<0.001$	r,0.79 $p<0.01$	r,0.65 $p<0.002$	r,0.40 $p<0.25$	r,0.78 $p<0.01$
TIBC Vs Ferritin	r,-0.71 $p<0.01$	r,-0.72 $p<0.001$	r.0.70 $p<0.03$	r,-0.73 $p<0.001$	r,-0.60 $p<0.07$	r,-0.77 $p<0.001$
TBIC Vs Hb	r,0.29 $p<0.36$	r,0.15 $p<0.56$	r,0.02 $p<0.97$	r,0.19 $p<0.41$	r,0.14 $p<0.71$	r,0.14 $p<0.56$
TBIC Vs HCT	r,0.11 $p<0.72$	r,0.06 $p<0.82$	r,0.07 $p<0.85$	r,0.02 $p<0.94$	r,0.08 $p<0.85$	r,0.03 $p<0.91$
TBIC Vs LPO	r,-0.73 $p<0.01$	r,-0.56 $p<0.02$	r,-0.54 $p<0.11$	r,-0.68 $p<0.001$	r,-0.56 $p<0.09$	r,-0.65 $p<0.002$
Ferritin Vs Hb	r,-0.30 $p<0.32$	r,-0.19 $p<0.46$	r,-0.28 $p<0.43$	r,-0.06 $p<0.80$	r,-0.22 $p<0.55$	r,-0.17 $p<0.48$
Ferritin Vs HCT	r,-0.21 $p<0.50$	r,-0.09 $p<0.74$	r,-0.24 $p<0.50$	r,0.07 $p<0.78$	r,-0.17 $p<0.64$	r,-0.06 $p<0.79$
Ferritin Vs LPO	r,0.59 $p<0.04$	r,0.85 $p<0.001$	r,0.91 $p<0.001$	r,0.64 $p<0.003$	r,0.46 $p<0.19$	r,0.83 $p<0.001$
Hb Vs HCT	r,0.93 $p<0.001$	r,0.95 $p<0.001$	r,0.97 $p<0.001$	r,0.89 $p<0.001$	r,0.98 $p<0.001$	r,0.92 $p<0.001$
Hb Vs LPO	r,-0.21 $p<0.49$	r,-0.23 $p<0.38$	r,-0.31 $p<0.38$	r,-0.01 $p<0.95$	r,-0.05 $p<0.89$	r,-0.31 $p<0.19$
HCT Vs LPO	r,-0.06 $p<0.86$	r,0.18 $p<0.49$	r,-0.24 $p<0.50$	r,0.06 $p<0.80$	r,0.03 $p<0.93$	r,-0.24 $p<0.31$

Non significant at $p>0.05$

$p<0.05$, significant when compared with controls

4. Discussion

Epidemiological studies have established risk factors for coronary heart disease which include cigarette smoking, hypertension, diabetes and elevated serum cholesterol levels. Hypertension was strongly associated with both ischemic heart disease and stroke mortality not just in middle age but also among people in their seventies and eighties (Lewington, *et al.,* 2002). The present study observed a significant elevation in the levels of ferritin and total serum iron and a decline in iron binding capacity in AMI patients irrespective of whether the patients were smokers or nonsmokers; hypertensives or normotensive and diabetics or non-diabetics when compared to healthy controls (table 1-3). Excessive iron has been proposed to be a potent risk factor for CHD, especially for acute myocardial infarction in several earlier investigations (Salonen, *et al*., 1992; Salonen, *et al*., 1994) which provide support to the present findings. A couple of reports showed a marked increase in ferritin levels in smoker population (Touitou, *et al*., 1985; Rodger *et al.,*1985). Serum ferritin may additively affect ischemic

heart disease risk in the elderly. The risk of acute myocardial infarction was associated with the highest tertile of ferritin which was most evident in current or former smokers along with other risk factors (Klipstein-Grobusch *et al.,* 1999). In diabetics, serum ferritin levels are elevated, which may increase the risk of coronary heart disease (Mert *et al*., 2005)

An analysis of NHANES III data showed elevated serum ferritin in persons with newly diagnosed or previously diagnosed diabetes and in all ethnic groups and age groups combined (Ford and Cogswell,1999). The serum ferritin level has been found to be associated with decreased insulin sensitivity and increased fasting serum insulin and blood glucose (Fernandez-Real *et al.*, 1998; Ford and Cogswell,1999). Iron depletion improves vascular dysfunction in type 2 diabetic patients with high ferritin concentrations (Fernandez *et al.*, 2002.). Raised ferritin levels among patients of myocardial infarction suggest a role of increased iron stores in myocardial infarction but iron overload was not an independent risk factor for coronary heart disease patients (Clys *et al*, 2002). In myocardial infarction, a gradual increase in

serum ferritin levels can be detected. Furthermore, a significant increase in ferritin content can be found in peripheral blood monocytes. Peripheral blood monocytes activated by steroids during stress could be the cause of increased serum ferritin levels following AMI (Moroz *et al.*, 1997). Body iron storage in males increases progressively with a proportional rise in serum ferritin, whereas serum ferritin levels are lower and more stable in females during reproductive period. Ferritin levels only increase after the menopause. In the present study, ferritin levels were not statistically different in AMI females compared to males AMI patients group. It might be due to the inclusion of post-menopausal age group subjects in the present study. However, the levels of Hb and HCT were significantly higher in males AMI patients (table II). The difference in hemorheological properties in female blood is caused by the increased concentration of younger red blood cells (RBCs) and the reduced population of older RBCs. Higher viscosity, increased RBC aggregation and decreased RBC deformability are observed in male compared with female blood (Mert *et al.*, 2005).

Iron induced oxidative stress in the form of increased generation of reactive oxygen species, in a series of fenton like reactions, does not make the pancreatic islets only but it also makes the vascular endothelium vulnerable to dysfunctional injury, leading to the development of diabetes and increased susceptibility to AMI. Moreover, total serum iron in acute myocardial infarction with or without hypertension, with or without diabetes, with or without smoking correlated positively with the elevation observed in ferritin concentration and negatively with a decline in total iron binding capacity in the present study (table 4). It suggests that due to an acute reaction response to inflammation and with the more availability of free iron on account of declined total iron binding capacity, the formation of ferritin gets markedly induced in a protective, body defense measure to sequester the free iron along with its known anti-oxidative properties (Crichton *et al.*, 2002). It is the free ionic form of iron that is harmful due to its pro-oxidative properties, which generates reactive free radicals. Superoxide produced during oxidative stress can mobilize free catalytic iron from ferritin (Halliwell, 1994) and facilitate the formation of Hydroxyl ion ($OH^.$). Reactive oxygen species, superoxide cause lipid peroxidation and endothelial dysfunction in vessels (Salonen *et al.*, 1994).

In addition, hypertension, which is considered to be a risk factor, may exacerbate the inflammatory response on the arterial wall by increasing oxidative stress, production of oxygen-free radicals and recruitment of mononuclear cells (Chobanian and Alexander, 1996). Endothelial alterations occur early in hypertension with enhanced adherence of leukocytes to the endothelial surface and increased endothelial permeability. The risk of coronary heart disease, doubles with each increment of blood pressure by 20/10 mm Hg, beginning beyond 115/75 mm Hg. Elevated blood pressure is associated with macrophage accumulation, stimulation of smooth muscle cell proliferation and enhanced expression of cytokines and growth factors in the intima (Lewington *et al.*, 2002). Inflammatory processes play a role in the initiation of unstable coronary artery disease because they destabilize

the atherosclerotic plaque and enhance the formation of thrombus (Ross,1999).

Increased LPO activity in AMI patients of experimental groups when compared to healthy controls, in the present study, supports the generation of reactive free radicals. The erythrocyte value of LPO in the smoker group significantly increased when compared to normal healthy non-smokers individuals. In smokers, a series of free radical chain reactions were aggravated, the dynamic balance between oxidation and antioxidation was seriously disrupted, and oxidative stress was clearly exacerbated (Zhou *et al.*, 2000). The lipid peroxidation activity correlated positively with elevated total iron and ferritin levels in the present study. It was further observed that the iron homeostasis was mainly affected by altering hemoglobin concentrations, which were increased on smoking (Northrop-Clewes and Thurnham, 2007). Similar elevation in the hemoglobin level was obtained in the AMI smoking patients group when compared to the AMI nonsmoking patients group in the present study. Further hemoglobin and hematocrit values significantly correlated positively in both AMI groups with or without smoking in the present study. The increased hemoglobin could be attributed to the effect of smoking which increases carboxyhemoglobin, thereby decreasing the oxygen carrying capacity of red blood cells thus leading to tissue hypoxia. Hypoxia stimulates erythropoietin production, which induces hyperplasia of the bone marrow and to the development of secondary polycythemia (El-Zyadi, 2006). There is also a higher risk of cardiovascular disease due to decreased oxygen delivery (Kameneva, 2007). Fe^{3+} is released from ferritin and other scavengers in rough proportion to the amounts of iron stores by leukocyte-derived oxygen radicals or by oxygen-free redox systems such as hydroquinones in cigarette smoke (Northrop-Clewes CA, Thurnham *et al.*, 1995; Reif, 1992; Thomas *et al.*, 1985; Abdalla *et al.*, 1992; Biemond *et al.*, 1986). This process is stimulated by disturbances of oxygen supply in atherosclerotic lesions (Crawford and Blankenhorn, 1991). Susceptibility of LDL to oxidative modification increases as a function of serum ferritin and dietary iron supplementation and decreases in response to experimental iron depletion (Craig *et al.*,1995; Vander *et al.*, 2005)). The capacity of prominent iron stores to amplify lipid-induced atherogenesis has been verified in a hypercholesterolemic animal model (Araujo *et al.*, 1995).

Several studies have demonstrated a direct association between increased iron intake, body iron stores, and cardiovascular risk in the general population. Increased intake of heme iron is associated with increased cardiovascular events (Vander *et al.*, 2005; Ascherio *et al.*, 1994; Lee *et al.*, 2005; Ramakrishnan *et al.*, 2002). Increased body iron stores are associated with myocardial infarction in a prospective epidemiological study (Tuomainen *et al.*, 1998). However, no significant difference was observed in these parameters between AMI patients with or without smoking; AMI with or without diabetes; AMI with or without hypertension when compared in the present study. It indicated that the diabetes and AMI, hypertension and AMI, smoking and AMI did not show synergic effect in the alterations of the iron status and LPO activity in the all AMI experimental groups. The present study concludes that the significant

alterations in the iron and lipid peroxidation activity in AMI shown in the subgroups of AMI patients may contribute along with other risk factors to the development and precipitation of AMI.

Acknowledgement

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