Research Article

Assessment of ferritin and its association with C - reactive protein and malondialdehyde in acute myocardial infarction

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ABSTRACT

Background: There is increasing evidence that moderately elevated body iron stores, below levels commonly found in genetic hemochromatosis, may be associated with adverse health outcomes. Ferritin status has been implicated in atherosclerotic cardiovascular disease and hypothesis is that high iron status is associated with increased oxidation of LDL. The main objective of study is to evaluate the ferritin status and its association with C - reactive protein, malondialdehyde and serum lipids in acute myocardial infarction patients compared with healthy volunteers.

Methods: Sixty seven acute myocardial infarction (AMI) patients in the age group of 30 to 50 years were selected for this study and 40 healthy age matched subjects were selected as control group. Diagnosis of AMI was made using guidelines of American College of Cardiology and European Society of Cardiology. The comprised group of 67 consecutive patients was divided based on the C - reactive protein (CRP) level into two groups (Group I <5 mg/L and Group II ≥5mg/L). Serum ferritin was assessed by ELISA method, C-reactive protein by turbilatex method and malondialdehyde (MDA) by Thiobarbituric Acid Reactive Substances (TBARS) method. Routine investigations were analysed by ERBA EM-360 fully automated analyzer.

Results: The mean serum ferritin level was significantly increased in AMI patient groups compared with controls. The group II patients showed significantly increased serum ferritin levels compared to group I. In both the groups ferritin levels positively correlated with CRP and malondialdehyde. In group II serum ferritin levels showed positive correlation with serum Cholesterol, TGL, LDL and negative correlation with and HDL. In group I serum ferritin levels showed positive correlation with triglycerides and LDL and there was no statistical significant correlation with HDL and total cholesterol.

Conclusions: Iron, an essential dietary constituent is now considered as a pro oxidant. Higher levels of ferritin, seems to be a strong risk factor for AMI. Regular monitoring of serum ferritin level can be useful in reducing cardiovascular morbidity and mortality.

Keywords: Acute myocardial infarction (AMI), Ferritin, Malondialdehyde (MDA)

INTRODUCTION

Acute myocardial infarction (AMI) is a potentially fatal event and one of the commonest causes of death in adults. Sudden coronary artery occlusion results in ischemic related death of cardiomyocytes and triggers regional and systemic inflammatory responses.[1] Ischemic and necrotic cardiomyocytes release a range of pro-inflammatory cytokines and chemokine's that recruit inflammatory cells to the ischemic area, facilitating the wound healing process. However, excessive regional inflammatory responses may amplify tissue damage by promoting cardiomyocytes death.[2] Mortality data from Global Burden of Diseases Studies has revealed that cardiovascular disease, especially coronary heart disease is important contributor of death. Of the 17.5 million deaths from cardiovascular diseases worldwide, 20% occurred in high income countries, 8% in upper-middle income countries, 37% in lower-middle income countries and 35% in low income countries including India.[3]

Acute phase reaction is a systemic response which usually follows a physiological condition that takes place in the beginning of an inflammatory process.[4] The most important component of this response comprises the acute phase proteins, which are a heterogeneous group of plasma proteins. Most of the components of the acute phase response reflect the defense and adaptation mechanisms, which take place before the body gives an immunological response.[5,6] Ferritin, is the major iron storage protein plays a key role in iron metabolism. Serum ferritin senses the body iron stores and serves as the early sensitive marker for iron deficiency.[7] Ferritin makes iron available for critical cellular processes while protecting lipids, DNA, and proteins from the potentially toxic effects of iron.[8] Recent epidemiologic studies have found a positive relationship between body iron stores and coronary artery disease (CAD).[9-12] Previous studies have not found association between ferritin and other cardiovascular risk factors such as C-reactive protein (CRP), malondialdehyde (MDA) and serum lipids. So the objective of the present study was to evaluate serum ferritin levels and its association with CRP, MDA and serum lipids in AMI patients.

METHODS

A total of 67 consecutive AMI patients in the age group of 30 to 50 years admitted to the Department of Emergency Medicine and Cardiology, Mamata Medical College &General Hospital, Khammam, Telangana state, India were selected for this study and 40 healthy age matched subjects were selected as control group after approval of Institutional Human ethics committee. Diagnosis of AMI was based on American College of Cardiology and European Society of Cardiology guidelines. The comprised 67 consecutive patients were

divided based on the C - reactive protein (CRP) level into two groups (Group I <5 mg/L and Group II ≥5 mg/L). We excluded the patients based on the following criteria: subjects with hemochromatosis, hypertension, diabetes mellitus, chronic inflammatory diseases, renal dysfunction and patients on medication such as iron therapy, antioxidant supplements, lipid lowering drugs and those having past history of AMI or other cardiovascular diseases.

Biochemical analysis: Blood samples were analyzed for random glucose, CK-MB, lipid profile (Total Cholesterol, HDL, LDL, triglycerides), creatinine using ERBA EM-360 fully automated analyzer. Serum ferritin was assessed by Enzyme Linked Immuno Sorbent Assay (ELISA), C-reactive protein was assessed by turbilatex method, malondialdehyde (MDA) assessed by Thiobarbituric Acid Reactive Substances (TBARS) method.[13]

Statistical analysis: Statistical analyses were carried out with SPSS 20.0. Values were expressed as mean ± standard deviation (SD) and t-test. p value <0.05 was considered statistically significant. The Pearson correlation test was used for correlation analysis.

RESULTS

Table 1 shows base line parameters in control and study subjects. CK-MB levels were significantly elevated in AMI patients when compared to healthy controls and also significantly elevated Group II AMI patients compared to Group I AMI patients.

Table 2 shows ferritin, CRP, MDA and lipid profile levels in controls and AMI patients. The measured parameters are significantly elevated in the AMI patients except HDL which was found to be decreased when compared to controls. Our study also exhibits disturbances in lipid profile as in the earlier studies. And also serum ferritin and malondialdehyde levels were significantly elevated Group II AMI patints compared to Group I AMI patients (P<0.001).

Table 3 shows correlation of serum ferritin wit parameters like CRP, MDA and lipid profile. Serum ferritin levels showed strong positive correlation with CRP and MDA in both groups of AMI patients (P<0.01). Triglycerides and LDL levels were showed strong positive correlation with serum ferritin in both the groups of AMI patients and group II AMI patients exhibited positive correlation with cholesterol and negative correlation with HDL.

Table 1: Baseline parameters in controls and AMI patients.

Parameters	Controls (n=40)	Group I AMI patients (n=32)	Group-II AMI patients (n=35)
Age	45.7±3.8	46.4±4.1	46.2±4.5
Males (%)	80	81	83
Females (%)	20	19	17
Systolic BP (mm Hg)	121±7.3	128.3±9.2	126.7±10.1
Diastolic BP (mm Hg)	80.4±6.3	82.2±9.4	83.5±9.8
Random plasma glucose RPG (mg/dl)	110.8±9.3	112.3±18.7	116.3±15.5
Serum Creatinine (mg/dl)	0.74±0.15	0.80±0.24	0.84±0.29
CK-MB (IU/L)	15.2±3.7	42.8±5.9 [a**]	47.8 ±6.4 [b**,c*]

Data are expressed as mean ±SD, **$p<0.001$,*$p<0.05$ was considered statistically significant;a= comparison between Controls and Group I AMI patient;b=comparison between Controls and Group II AMI patient ;c=comparison between Group I and Group II AMI patients.

Table 2: Ferritin, CRP, MDA and Lipid profile levels in controls and AMI patients.

Parameters	Controls (n=40)	Group I AMI patients (n=32)	Group-II AMI patients (n=35)
Serum ferritin(µg/L)	130.4±20.5	197.8±38.3 [a**]	242.3±49.5 [b**,c**]
CRP (mg/L)	1.8±0.9	3.9±1.4 [a**]	9.4±3.2 [b**,c**]
Malondialdehyde (µ mol/L)	1.42±0.67	4.94±0.34 [a**]	5.74±0.76 [b**,c**]
Serum cholesterol (mg/dl)	156.3±9.2	187.1±15.4 [a**]	210.7±18.7 [b**,c**]
Serum Triglycerides (mg/dl)	97.6±14.5	137.5±39.4 [a**]	165.9±42.8 [b**,c*]
HDL cholesterol (mg/dl)	42.4±5.4	37.5±4.1 [a**]	37.7±3.9. [b**]
LDL cholesterol (mg/dl)	113.6±10.2	134.8±14.5 [a**]	148.1±29.4 [b**,c*]

Data are expressed as mean ±SD, **$p<0.001$,*$p<0.05$ was considered statistically significant;a= comparison between Controls and Group I AMI patients;b=comparison between Controls and Group II AMI patients;c=comparison between Group I and Group II AMI patients.

Table 3: Correlation between Serum ferritin and measured parameters in AMI patients.

Parameters	Group-I AMI patients	Group II AMI patients
CRP	0.759**	0.838**
Malondialdehyde	0.498**	0.522**
Cholesterol	0.198	0.545**
TGL	0.467**	0.826**
HDL	-0.131	-0.392*
LDL	0.492**	0.782**

Data values representing Correlation Coefficient(r) ;**Correlation is significant at the 0.01 level (2-tailed);*Correlation is significant at the 0.05 level (2-tailed).

DISCUSSION

Incidence of acute myocardial infarction is increasing across the globe among all ages and both sexes with increasing morbidity and mortality. In AMI, irreversible tissue injury occurs due to sustained ischemia and recent pivotal studies have shown that the innate immune system is activated sequentially mediating both injury and repair mechanisms.[14,15] The role of ferritin in pathogenesis of coronary artery disease (CAD) has generated considerable interest in recent times.

In the present study it has been observed that mean serum ferritin and MDA levels are significantly increased in both groups of AMI patients compared to control subjects. Among the groups mean serum ferritin and MDA levels are significantly increased in group II patients compared with group I AMI and patients. Kiechl et al reported that serum ferritin was associated with cardiovascular disease and cardiovascular mortality.[16] Salonen et al,also reported that increased serum ferritin levels accelerate the oxidation of LDL-cholesterol.[17] The oxidized LDL induces inflammation in blood vessels, including the progression of atherosclerosis.[18] So it implies that serum ferritin indirectly enhances the role of LDL-cholesterol in the induction of cardiovascular diseases such as AMI.

We have observed a strong positive correlation between ferritin and CRP in both groups of AMI patients (Group I correlation coefficient (r) = 0.759, Group II correlation coefficient (r) = 0.838, p value <0.01). Sano et al,

investigated the relation between lesion morphology as seen under pre intervention intravascular ultrasound and CRP in the phase of AMI.[19] They found that elevated CRP concentrations may be related to the presence of ruptured plaque and concluded that in the setting of AMI, elevated CRP levels may reflect the inflammatory activity of a ruptured plaque. Experimental studies have shown that short periods of ischemia followed by reperfusion elicit a cascade of proinflammatory reactions that include production of oxygen-derived free radicals, activation of the complement system, adherence of neutrophils to the coronary endothelium, leukocyte-mediated injury of the myocardial cells, and production of cytokines and acute phase proteins.[20,21]

In addition we observed ferritin levels showed strong positive correlation with malondialdehyde, triglycerides and LDL cholesterol in both groups of AMI patients, and in group II, serum ferritin levels showed positive correlation with total Cholesterol and negative correlation with HDL. Free Iron, as well as other transition metals, can catalyze free radical formation. For this reason iron is tightly bound to transport and storage proteins to prevent their involvement in free radical formation. It has been hypothesized that increased iron intake or iron stores may promote atherogenesis by increasing free radical formation and oxidative stress.[23] Oxidative stress increases the peroxidation of low-density lipoprotein (LDL) thereby increasing its uptake by macrophages with increased foam cell formation and atherosclerosis.[23,24]

CONCLUSION

Iron is considered as an essential dietary constituent still now, is considered a pro oxidant. Higher levels of ferritin, seems to be a strong risk factor for AMI. Regular monitoring of serum ferritin levels may help in reduction of cardiovascular morbidity and mortality.

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