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Correlation of Serum Magnesium and Malondialdehyde Levels in Patients with Myocardial Infarction

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ABSTRACT

Serum Magnesium (Mg) plays a significant role in cardiac homeostasis, and its deficiency is capable of producing myocardial injuries. Studies have suggested that magnesium deficient myocardial tissues were rendered susceptible to oxidative stress and also caused a significant increase in lipid peroxidation products the following ischemia. The present study aimed to find the association between hypomagnesemia and serum Malondialdehyde (MDA) levels and to assess the oxidative stress due to Myocardial infarction (MI). The present study was conducted on 112 subjects, which included 61 patients who had episodes of MI and 51 controls. The blood samples were collected within 12 hours after the onset of chest pain. The samples collected were used for the estimation of magnesium using Calmagite method and cardiac markers were analyzed in Cobas 6000.MDA was measured as thiobarbituric acid reactive substance. The patients with MI were found to have low levels of serum magnesium and high levels of serum MDA. A significant correlation was found between the serum levels of magnesium and MDA. The present study showed a high significant correlation between hypomagnesemia occurring in MI with MDA levels in serum, suggesting the evaluation of serum magnesium to be considered in strategies aimed at preventing and controlling the increase in oxidative stress in these patients.

Keywords: Myocardial infarction, Malondialdehyde, Hypomagnesaemia, Oxidative stress

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INTRODUCTION

Myocardial infarction (MI) is the most common cause of morbidity and mortality worldwide. In India, 31.7% of deaths occur due to MI and smoking, alcohol, low physical activity, high blood pressure and abnormal lipids are the known cardiovascular risk factors [1]. The most common cause of MI is atherosclerotic coronary artery disease (CAD) with the erosion or rupture of a plaque, thus causing transient, partial or complete arterial occlusion [2].

Magnesium (Mg) is the second most abundant intracellular cation and is an essential cofactor in many biologically important enzymatic reactions. Serum Magnesium plays a significant role in cardiac homeostasis**,** and its deficiency is capable of producing myocardial injuries and post-MI arrhythmias. Magnesium depletion has been related to the pathogenesis of hypertension, atherosclerosis, and cardiac arrhythmias. [3]

Studies have suggested that Mg- deficient tissues were rendered susceptible to oxidative stress and also caused a significant increase in lipid peroxidation products in the myocardial tissue following ischemia or reperfusion [4].

Malondialdehyde(MDA), being the end product of lipid peroxidation, can be considered as one of the biomarkers of cell membrane damage occurring in Myocardial infarction [5].

In the current work, we have measured Mg and MDA, along with cardiac enzyme-total CK-MB in AMI patients at 12 hours after the onset of chest pain, to compare their levels with those of age-matched healthy controls. In order to explore the possibility of oxidative stress due to Mg deficiency in Myocardial infarction, this study was designed to find the correlation between serum Mg and MDA levels.

MATERIALS AND METHODS

This study was carried out in the Department of Biochemistry, Kasturba Medical College, Manipal after the approval of Institutional Ethical Committee, Manipal University. The study was conducted on 61 patients, admitted to the ICU under the Department of Cardiology, Kasturba Hospital, Manipal, had episodes of MI and 51 healthy controls. The patients having diabetes, chronic alcoholics, smokers and long-term drug therapy are excluded from the study. The age of the study group was 40-70 years. The blood sample was collected within 12 hours after the onset of chest pain. The samples collected were separated at 3000 rpm by REMI-clinical centrifuge and were used for the estimation of magnesium using Calmagite method and cardiac markers were analyzed in Cobas 6000. Reagent Kits were supplied by Roche Diagnostics, USA. MDA was measured as thiobarbituric acid reactive substance, and the absorbance was read at 535nm [11].

The reference range for magnesium was 1.5 -2.5 mg/dl, CKMB was 0.6 – 6.3 ng/ml and for MDA was 4.99 -1.39 nmol/ml[23].

Statistical Analysis

The data was analyzed statistically using SPSS software, version 16. The values were expressed as a mean and standard deviation; the independent t-test was performed to compare the mean values between test and control. Pearson's correlation was done to assess the association between various test parameters. A p-value <0.05 was considered significant.

RESULTS

As compared to control groups, the patients with AMI were found to have low levels of serum magnesium (Table I). MDA levels estimated in MI patients and controls are presented in Table I. The mean (± SD) of MDA levels (nmoles/ml) in the plasma were found to be 9.81 (± 2.75) in MI patients and 4.21 (± 1.05) in controls. The MDA levels in patients were significantly higher at $p<0.01$, compared to controls. A significant correlation was found between the serum levels of magnesium and MDA (Table 2,Fig1).

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Table 1: Mean values of different parameters in controls and AMI patients

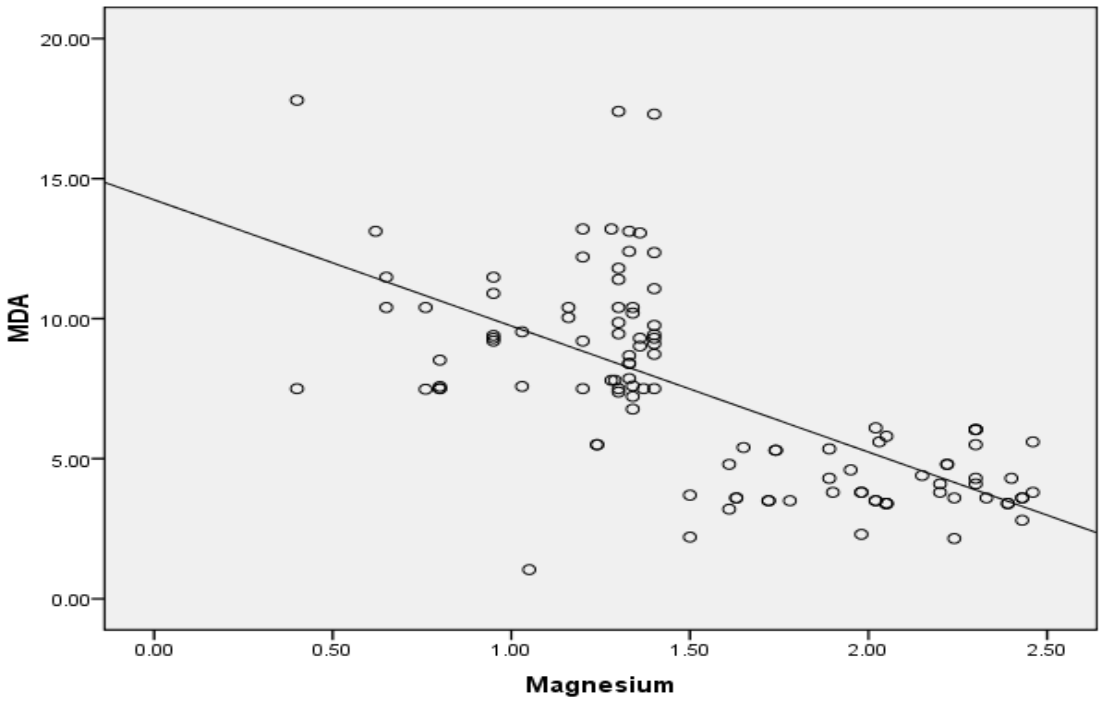
Parameters	Controls (n=51)	Tests (n=61)	P value
CK-MB (ng/ml)	3.05±1.71*	44.09±17.09*	**<0.05**
Magnesium (mg/dl)	2.02±0.32	1.15±0.26	**0.08**
MDA (nmol/ml)	4.21±1.05*	9.81±2.75*	**<0.05**

*p value <0.05 is significant

Table 2: Correlation analyses of serum Mg with cardiac markers and MDA

Parameters	r value	P value
Mg vs MDA	- 0.66	<0.001

Figure 1- Graph showing correlation between serum Mg and MDA



DISCUSSION

Previous studies have shown Reactive Oxygen Species (ROS) to be a primary cause for initiation and progression of atherosclerosis. Increased generation of ROS may, to an extent, be responsible for the irreversible peroxidative damage to the myocardial tissue [6]. During ischemia, occurring in MI, ROS produced by endothelial cells and the circulating phagocytes may initiate a self-perpetuating chain reaction of lipid peroxidation, damaging the membrane. Hence MDA, the end product of lipid peroxidation, can be considered as one of the biomarkers of cell membrane damage [10]. Mary F. Walter *et al.*,'s [24] study concludes, the serum levels of TBARS /MDA were strongly predictive of cardiovascular events in patients with stable CAD, independently of traditional risk factors and inflammatory markers. The results of this study also showed a significant increase in the MDA in the MI patients [9.81 ± 2.75nmol/ml] as compared to the controls (4.21±1.05 nmol/ml) supporting the above hypothesis.

Magnesium is a cardioprotective element because of its β-adrenoreceptor blocking action, antiplatelet action and inhibitory effect on the cardiac conducting system [8]. Magnesium also regulates LDL-cholesterol uptake and oxidation. Reduced magnesium levels in blood alter the activity of LCAT and HMG-CoA reductase, promotes increased inflammation and oxidative stress. Hypomagnesaemia alters the vascular wall biology that in turn promotes coronary artery disease and dyslipidemia [8,15].

In animal models of magnesium depletion, LDL-cholesterol particles were more susceptible to oxidative damage. [9]. At the cellular level, exposure of endothelial and smooth muscle cells to low magnesium results in increased LDL transport and uptake, increased, along with smooth muscle cell proliferation and intimal invasion; all of which are essential features of the atherogenic process. [9-14]

Magnesium has been postulated to possess antioxidant properties, and its deficiency may lead to a state of increased oxidative stress [16]. Different mechanism, including systemic reactions (inflammation and endothelial dysfunction) and cellular changes (mitochondrial dysfunction and excessive production of fatty acids), have been postulated to be involved in the development and progression of oxidative stress due to Mg deficiency.

Previous studies have shown convincingly that Mg deficiency in vitro or in vivo results in increased production of oxygen-derived free radicals in various tissues, increased free radical elicited oxidative tissue damage. Moreover, Calviello *et al.,* found that Mg deficiency in rats causes a decrease in hepatic glutathione, superoxide dismutase along with an increase in lipid peroxidation and MDA levels secondary to up-regulated NADPH oxidase activity. In the present study, a correlation ($r=-0.66$, $p<0.001$) was observed between the serum Mg and MDA levels, proving Mg deficiency as one of the several factors leading to oxidative stress seen in MI.

There is data to support the above results suggesting that Mg when present in sufficient prevents oxidative damage by scavenging free radicals and inhibiting xanthine oxidase and NADPH oxidase [17].Oral Mg supplementation has been shown to reduce serum triglycerides, apolipoprotein B, LDL-cholesterol, total cholesterol, and increase HDL-cholesterol in high-risk patients with ischemic heart disease [18].

CONCLUSION

In conclusion, the present study showed a highly significant correlation between hypomagnesemia occurring in MI with MDA levels in serum, suggesting the evaluation of serum Mg to be considered in strategies aimed at preventing and controlling the increase in oxidative stress in these patients. The results of these investigations may also enable formulation of specific antioxidant therapies as the most effective remedy against atherogenesis for an early intervention and better management of the disease.

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