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STUDY OF LIPID PEROXIDE, ANTIOXIDANTS AND TRACE ELEMENTS IN ACUTE MYOCARDIAL INFARCTION

Jagtap V.R.*

Department of Biochemistry, Government Medical College, Miraj-416410, Maharashtra, India.

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Cardiovascular Disease (CVD), Erythrocyte Catalase, Acute Myocardial Infarction (AMI), Malondialdehyde (MDA), Superoxide Dismutase (SOD)

For Correspondence:

Dr. Vanita R. Jagtap

Department of Biochemistry, Government Medical College, Miraj-416410, Maharashtra, India

E-mail:

ms.vanita_jagtap@rediffmail.com

ABSTRACT

Cardiovascular Disease, one of the chronic, non-communicable diseases, has become a major public health problem in many developing countries. Of the CVD, acute myocardial infarction is the predominant entity contributing to mortality and morbidity. Therefore, rapid diagnosis and treatment as well as assessment of the prognosis are very essential and challenging in acute myocardial infarction. Oxidative stress is implicated in the etiopathogenesis of acute myocardial infarction. Measurement of lipid peroxidation is of value in estimating oxidative stress. Therefore, the aim of this study is 1) To assess oxidative stress by determination of MDA as a lipid peroxidation marker in acute myocardial infarction and controls. 2) To measure trace elements such as iron, copper, and zinc and antioxidant enzymes i.e. erythrocyte superoxide dismutase and erythrocyte catalase levels in 30 patients with acute myocardial infarction & 30 controls. We observed that significantly increased levels of serum iron ($P < 0.001$), copper ($P < 0.001$) and lipid peroxide ($P < 0.001$) where as the levels of serum zinc and erythrocyte SOD and catalase were significantly decreased ($P < 0.001$) in acute myocardial infarction as compared to controls. Iron/zinc ratio, copper/zinc ratio were elevated in AMI patients. Significant positive correlation was observed between MDA and iron as well as MDA and copper levels. Negative correlation between MDA & zinc levels was found. This study indicated that the antioxidant status of AMI patients was low; suggesting the role of free radical mediated oxidative stress in AMI. Iron/zinc ratio, copper/zinc ratio may provide an additional index for prognosis of the AMI.

INTRODUCTION

Cardiovascular Disease (CVD) is the most frequent cause of death in adult life in developed countries, and is increasingly becoming important in developing countries like India [1]. According to World Health Report 2002, cardiovascular diseases will be the largest cause of death and disability by 2020 in India. In 2020 AD, 2.6 million Indians are predicted to die due to coronary heart disease which constitutes 54.1% of all CVD deaths. Nearly half of these deaths are likely to occur in young and middle aged individuals (30-69 years). Currently Indians experience CVD deaths at least a decade earlier than their counterparts in countries with established market economies (EME). The Global Burden of Disease (GBD) study estimates that 52% of CVD deaths occur below the age of 70 years in India as compared to 23% in EME, resulting in a profound adverse impact on its economy.

The contributing factors for the growing burden of CVDs are increasing prevalence of cardiovascular risk factors especially hypertension, dyslipidemia, diabetes, overweight or obesity, physical inactivity and smoking etc. [2, 3]. Other factors such as micronutrients may be involved in lipid peroxidation. Thus there is scope for other dependent and independent risk factors which may contribute to the onset of CVD.

In the development of AMI and evolution of atheroma (atherogenesis) emphasis is given on oxidative stress and damage caused by it. Trace elements and free radicals may play an important role in the pathogenesis of atherosclerosis and also affect the lipid profile in patients with AMI [4]. All trace elements are harmful to human body beyond a certain level. Copper and iron ions are powerful promoters of free radical damage, accelerating lipid peroxidation and causing formation of hydroxyl radical [5]. Zinc acts as a biological antioxidant by decreasing lipid peroxidation and stabilizing the membrane [6]. Thus trace elements may play a vital role resulting in either harmful or beneficial effects by damaging or protecting the vessel wall and altering the lipid profile.

"Lipid peroxidation" is the most intensively studied process for assessment of free radical mediated oxidative stress. Chemical compounds and reactions disposing of pro-oxidants scavenging them, suppressing their formation or opposing their actions are "antioxidants" [7, 8]. Hence it was thought worthwhile to study the levels of iron, copper, zinc & lipid peroxide, correlation among them, and to assess the levels of antioxidants in AMI

MATERIAL AND METHODS

The present study was carried out in the Department of Biochemistry, Govt. Medical College, Miraj. In these study 30 patients with AMI in the age group 40-70 years and 30

healthy controls, age and sex matched were studied. Cases of AMI were diagnosed by clinicians. In our study, renal diseases, liver diseases, chronic debilitating illnesses (cancer, AIDS), diabetic patients were excluded.

The Institutional Ethical Committee approved the plan of study and informed consent was obtained from each participant in the study. Blood samples were collected after an overnight fast, by taking aseptic precautions. Heparinised blood samples were centrifuged, and after separation of plasma, RBC's were washed thrice with normal saline, Hemolysate was prepared by adding 4 volumes of D/W and mixing. Haemoglobin concentration was adjusted to 10 Gm/dl. Erythrocyte SOD activity was determined by Winterbourn C.C. method [9]. Erythrocyte catalase activity in the hemolysate was determined by the spectrophotometric method of Hugo Aebi [10]. Lipid peroxide in serum was determined by estimating malondialdehyde (MDA) produced using thiobarbituric acid (Kei Satoh method) [11]. Serum iron, copper and zinc were estimated by atomic absorption spectrophotometer [12]. All data were expressed as mean $\pm$ SD. Statistical significance was analyzed by using "Z" test.

RESULTS AND DISCUSSION

Serum iron, copper and lipid peroxide levels were significantly increased ($P < 0.001$) in AMI patients as compared with control (Table no 1). Iron ions themselves free radicals, and ferrous ions can take part in electron transfer reactions with molecular oxygen, generation of superoxide and hydroxyl radicals by Fenton chemistry, can initiate lipid peroxidation and progressive damage was occur in AMI patients [13].

Rise in the iron/zinc ratio in AMI (Table no 2) is due to raised iron and lowered zinc levels. This supports the significantly positive correlation between serum iron and lipid peroxidation product observed in our study. Iron may play an important role in lipid peroxidation required for atherogenesis. The availability of free iron enhances oxidative stress and alters the antioxidant defence system rendering the myocardium more susceptible to oxidative injury. Ishwarlal Jialal et al. [14] reported that oxidation of LDL is a key step in atherogenesis. This LDL can be modified oxidatively in the presence of transition metals such as copper and iron, which can promote rapid lipid peroxidation.

Copper/zinc ratio in AMI patients were higher (Table no 2) due to elevation of serum copper and decrease in serum zinc level. The level of serum copper in AMI patient correlates significantly and positively with serum MDA. Membrane peroxidation can be progressively increased by copper. Copper ions are powerful promoters of free radical damage, accelerating lipid peroxidation and causing formation of hydroxyl radical by Fenton reaction.

Guttridge [13] and Sushamakumari S. et al. [15] showed that an alteration in the metabolism of lipid peroxides is closely and strongly associated with myocardial damage as indicated by increasing malondialdehyde in the heart tissue on induction of myocardial infarction. Reasons for this increased peroxidizability of damaged tissues, includes inactivation of some antioxidants, leakage of antioxidants from the cells and the release of metal ions (especially iron and copper) from storage sites and from metalloproteins hydrolyzed by enzymes released from damaged lysosomes. Increased lipid peroxidation leads to multiple membrane damage and disturbance in cardiac metabolism, structure and function. Hence measurement of lipid peroxidation may therefore, be excellent marker of cardiovascular diseases.

Serum zinc levels were significantly decreased (P‹ 0.001) in AMI patients as compared with controls (Table No1). Findings of Comar CL and Chvapil M [4, 16] support our result. Zinc can compete with iron, by Fenton reaction, in production of free radicals [6]. Thus zinc can "interfere with metal catalyzed lipid peroxidation". Zinc diminishes the weakening effect on the membrane caused by the peroxidative damage. Significant negative correlation between MDA & zinc were found in AMI. In our study, erythrocyte superoxide dismutase and erythrocyte catalase levels were significantly lowered (P‹ 0.001) in AMI as compared with controls (Table no 1). Rao et al. [17] and Meerson et al. [18] reported that the accumulation of lipid peroxides in myocardial tissue during ischaemia induced injury, along with simultaneous loss of myocardial SOD, catalase and glutathione peroxidase.

OBSERVATIONS

Table No. 1 Serum iron, copper, zinc, MDA, erythrocyte SOD & catalase levels in controls and acute myocardial infarction

Sr. No	Biochemical Parameters	Healthy controls Mean ± SD	AMI Mean ± SD	"P" value
1	Iron (µg/dl)	119.2 ± 37.698	204.71 ± 24.64	P<0.001
2	Copper (µg/dl)	95.40 ± 15.70	156.85 ± 22.79	P<0.001
3	Zinc (µg/dl)	91.200 ± 19.99	70.28 ± 5.472	P<0.001
4	MDA ("n" moles/ml)	3.700 ± 0.273	7.914 ± 4.069	P<0.001
5	SOD (U/G Hb)	4.08 ± 0.307	2.781 ± 0.038	P<0.001
6	Cat (U/G Hb)	497.43 ± 58.79	271.96 ± 34.59	P<0.001

Table No. 2 Iron / Zn ratios and Copper / Zn ratios in controls and acute myocardial infarction

Sr. No	Ratios	Healthy controls	AMI
1	Iron / Zn ratio	1.2	2.8
2	Copper / Zn ratio	1.0	2.2

CONCLUSION

It is concluded that nutritional disturbances of trace elements and antioxidants is to be considered as major risk factor for AMI patients. Our study supports the hypothesis that defective antioxidant status, low levels of zinc and increased levels of iron, copper which catalyze the Fenton reaction in generation of free radicals, which in turn increased free radical mediated oxidative stress. This increased oxidative stress, which is confirmed by assaying increased levels of oxidative stress marker i.e. MDA as a lipid peroxidation and decreased levels of antioxidants. Our findings will definitely help the clinicians in the determination of oxidative stress in AMI.

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