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Study Of Antioxidant Status In Myocardial Infarction Cases Before And After Thrombolytic Therapy

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Abstract: *Free radical oxidative injury has been linked to myocardial infarction. This study has been taken to analyse the extent of oxidative injury and the antioxidant defensive mechanism by estimating Malonaldehyde and defensive markers such as serum Ceruloplasmin,serum Catalase antioxidant defence by S. Uric Acid and S. Ceruloplasmin. On 5th day of MI, oxidative and serum Uric acid at 6-12 hrs of onset of myocardial infarction and 5 days after thrombolytic therapy.Out of total 100 cases,50 age matched Control cases and 50 cases of known Myocardial infarction(with ECG report) are taken.Serum Malonaldehyde is estimated by thiobarbituric acid method.Serum Ceruloplasmin by O-diansidine method,serum Uric acid by uricase kit method.Serum Catalase activity by Spectrophotometric assay of complex of Molybdate and Hydrogen peroxide. Routine Blood sugar,blood urea,Serum creatinine,Haemoglobin %,HIV,HBs Ag also done .The data is statistically analysed and the mean,SD values are calculated. Student 't' test and 'p' values are also calculated.Statistically significant increase in Malonaldehyde, Uric acid,Ceruloplasmin in MI cases compared to controls with 'p' values <0.000 is seen.Significant decrease in serum Catalase in cases compared to patients with 'p' value <0.000 is seen.There is a significant decrease in serum Uric acid,Malonaldehyde,Ceruloplasmin and increase in serum Catalase after 5 days of Thrombolytic therapy.The area under table of the ROC curves of different parameter is compared.In present study there is significant increase in serum Malonaldehyde, Uric acid,Ceruloplasmin levels in MI cases compared to controls. Malonaldehyde is the best markers to indicate Oxidative Stress In MI.*

Key Words*: Ceruloplasmin , Malonaldehyde , MI-Myocardial infarction, Reactive oxygen species and Uric acid*

I. Introduction

Myocardial infarction (MI) is still one of the major causes of morbidity and mortality in India[1]. There are about 2.5million deaths/year in the world and 1 million deaths /year in India[2]). The incidence was 10% in 1995 and is slowly rising. MI can be defined as a disorder in which damage to an area of the heart muscle occurs because of inadequate supply of oxygen to that area. Permanant loss of blood supply always lead to cell injury and ultimately necrosis, which results in myocardial infarction[3]. Thus, MI can be defined as the necrosis of cardiac muscle as a sequalae to ischemia. Oxidative stress has defined as a loss of counter balance between free radical or reactive oxygen species production and the antioxidant systems, with negative effects on carbohydrates, lipids and proteins. It is also involved in the progression of different chronic diseases and apoptosis[4,5]. Oxidative stress has been proposed to play a role in many disease states, including cardiovascular and infectious diseases, cancer, diabetes and neurodegenerative pathologies. Early reperfusion brought about by thrombolytic agents reduces myocardial necrosis, improves ventricular function and reduces mortality in acute myocardial infarction. Paradoxically, thrombolytic therapy can in turn cause deleterious effects, termed as reperfusion injury[6]. There is now increasing evidence to suggest that free radicals play a key role in its pathogenesis [7]. It is not surprising that in recent times, attention has been given to the concept of reducing myocardial injury at the time of reperfusion by treatment with free radical scavengers[8].

Direct detection of oxygen free radicals is complicated by their highly reactive and transient nature. Indirect evidence for the presence of free radicals has been demonstrated by the estimation of markers of oxidative stress like malonaldehyde[9] and by the estimation of certain antioxidant levels during ischemia and repefusion. Eg.Catalase, Ceruloplasmin

II. Materials And Methods:

1.1 Selection of subjects

The study was conducted in three groups of subjects selected from the Department of Cardiology, Male and female wards of cardiology, acute medical Care Unit, Department of biochemistry at a Tertiary care hospital . Meenakshi Medical College,Kanchipuram,T.N.

1.2 Experimental Design

The patients were divided into three groups of 50 Patients each, R. Controls or Group-I Comprised of normal 40males and 10females. They did not have any family history of diabetes, hypertension, and did not suffer from any cardiac or renal disorder.

Group-II Comprised of subjects, 41males and 9 females diagnosed as myocardial infarction cases within 12-24hrs of onset of chest pain. Diagnosis was confirmed with an ECG

Group-III comprised of subjects, 41 males and 9 females diagnosed as myocardial infarction cases, whose blood samples were taken on 5^{th} day of group II cases of follow up.

1.3 Biochemical Analysis

The blood samples were collected in fasting state and venous blood was used throughout the study. Specimens were withdrawn with minimum of occlusion. 1 ml of blood with EDTA dipotassium salt as anticoagulant, for glycosylated hemoglobin; 1 ml blood with potassium oxalate and sodium fluoride as anticoagulant for blood glucose estimation and 10ml blood in dry bottles without any anticoagulant for all other investigations were collected. Serum was separated by centrifugation. Blood and serum samples were stored at 4`C.

Blood sugar was estimated by Asatoor and King method [14], Malonaldehyde by Thiobarbituric acid method [15], ceruloplasmine by O-diansidine method [16], Uric acid by the method of Henry, Sobel and kim, 1957).

III. Statistical Analysis

The mean values and standard deviations for each parameter group wise were calculated and provided in the tables and graphs. Analysis of variance using SPSS for multiple comparison procedures for significance of differences between the groups were used.

IV. Results and Discussion

The mean ± Standard deviation of controls and cases

Parameter	Controls	Group I	Group II
UA	3.188 ± 0.353	4.224 ± 0.94	4.882 ± 0.969
MDA	315.5 ± 26.896	699.78 ± 36.232	646.64 ± 38.466
Cer	104.8 ± 6.45	123.72 ± 10.707	102.38 ± 9.16
CAT	43.46 ± 6.876	24.62 ± 8.448	34.98 ± 7.455

Best cut off value, sensitivity, specificity of the analytes

The best cut off values were established by selecting points of best values that provided the greatest sum of sensitivity, specificity and diagnostic efficacy

Parameter	Best Cut off Value	Sensitivity	Specificity	Diagnostic Efficacy
UA	3.350 (mg/dl)	86%	80%	86%
MDA	495.00 (nmol/dl)	100%	100%	100%
Cer	112.50 (U/L)	82%	94%	56%
CAT	34.50 (KU/L)	52%	48%	42%

Reactive oxygen species have been increasingly implicated in the ageing process and in different diseases such as cancer, coronary heart diseases, Alzeimer`s Disease, Parkinson`s diseases, reperfusion injury, etc. pathogenesis is mediated by medicated by oxidative damage of bio molecules, namely DNA, lipid, protein and carbohydrate.

The present study is undertaken to estimate the oxidative stress associated with myocardial infarction.. Before treatment, the levels of MDA,Uric acid, ceruloplasmin were found to be significantly high, while levels of catalase significantly low in 12-24hrs of MI patients compared to controls. After treatment, on 5th day,the levels of MDA and ceruloplasmin decreased. Uric Acid and catalase levels increased significantly. Dousset etal., (1983),Ohlin H.M.(1995) showed increased MDA levels particularly during initial 48hrs post MI. Bickel C(2002), Culleton BF (1999), Johnson RJ (1999) showed significant increase in levels of uric acid at the onset of MI. Lazzarino-G (1992), Singh T.K. (1992) showed increase ain ceruloplasmin levels in MI cases. Looper etal (1991) reported a fall in Serum catalase during first 2 days after MI. in the present study, catalase , an antioxidant enzyme, shows a decrease in its level in cases when compared to controls. Catalase becomes very important when concentration of H2O2 is raised. It reacts rapidly with H2O2 to form water and oxygen. H2O2 although itself not an O2 free radical, it is a member of the so called ROS extremely harmful when produced in exert. Catalase plays an important role as their eliminator.

V. Conclusion

Oxidative stress is present in patients with MI. Serum MDA is one of the significant marker to indicate the oxidative stress associated with MI. There is adaptive increase in stress is decreased due to reperfusion by the thrombolytic therapy. The usefulness of antioxidant therapy as adjuvant in Myocardial Infarction for future study.

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