

Antioxidant Status in Blood of Patients with Elevated C - reactive protein in Acute Myocardial Infarction.

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ABSTRACT

Background: C-reactive protein (CRP) is well known as a marker of inflammation associated with cardiovascular diseases (CVD). **Methods:** The study group included was patients whose CRP level was above 7 mg/L diagnosed with acute myocardial infarction as case and normal healthy donors were taken as control. **Results:** In our study we have found that antioxidant such as glutathione (GSH) and Glutathione peroxidase (GPx) activity was decreased in blood of patients with acute Myocardial infarction (AMI) with elevated CRP compared to healthy control. We have also found that prooxidant molecule such as malondialdehyde (MDA) was increased in AMI in comparison with control. **Conclusion:** The study concluded that in acute MI associated with inflammation there is imbalance in redox balance.

Keywords: CRP, acute myocardial infarction, Glutathione.

INTRODUCTION

C – reactive protein (CRP) has been the most extensively studied biomarker associated with inflammation. CRP is produced in the liver, vascular smooth muscle cells and macrophages in response to stimulation by interleukins.^[1] However, increased CRP level in blood are not disease specific but may indicate the severity of inflammation associated with various diseases.^[2-4] The mechanisms by which free radicals and inflammation are connected are still unknown, even with the clear cut scientific evidence that both are biochemically linked.^[4] Inflammatory process induces oxidative stress with the generation of free radicals and as a result the antioxidant machinery may be severely exhausted.^[5] Various studies have shown that severity of inflammation often complicates diseases in association with higher lipid peroxidation and subsequent damage to functional proteins involved in antioxidant defence machinery.^[6,7] It is reported in a study that peroxiredoxin will be released in glutathionylated form in response to inflammation both in vivo and in vitro.^[8] The severity of lipid peroxidation in relation

to coronary heart disease which is highly connected with inflammation has been studied and established in many studies.^[9-14]

MATERIALS AND METHODS

Approximately 5 mL blood was collected in heparinised tubes and centrifuged at 3000 rpm for 7 minutes and plasma separated was used for biochemical analysis. The study group included was patients whose CRP level was above 7 mg/L diagnosed with acute myocardial infarction as case and normal healthy donors were taken as control. Estimation of glutathione in plasma was done by standard protocol by Rahman I et.al and glutathione peroxidase activity was assayed by continuous spectrophotometric method by Mohamed A et.al.^[15,16] The lipid peroxidation in blood was assayed by measuring the concentration of thiobarbituric acid substances by colorimetric method according to Kei S et.al.^[17]

Statistical Analysis

Statistical analysis was done using Microsoft excel version 2007. For comparison between groups student t-test was used and P < 0.05 was considered as significant. The sample size was n = 22 in each group.

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RESULTS

Estimation of glutathione in plasma

The result showed that there was a significant decrease ($P < 0.01$) of glutathione level in plasma of patients with elevated C-reactive protein, > 7 mg/L diagnosed with acute myocardial infarction. From the depleted state of glutathione in plasma of patients with acute myocardial infarction with elevated CRP it can be inferred that the antioxidant balance during cardiac muscle injury associated with inflammation will be disturbed. Since glutathione is the molecule which can detoxify hydrogen peroxide (H_2O_2) in tissues to non toxic water (H_2O) molecules, the depleted glutathione would cause elevated H_2O_2 subsequently leading to generation of more toxic free radicals such as superoxide anion.

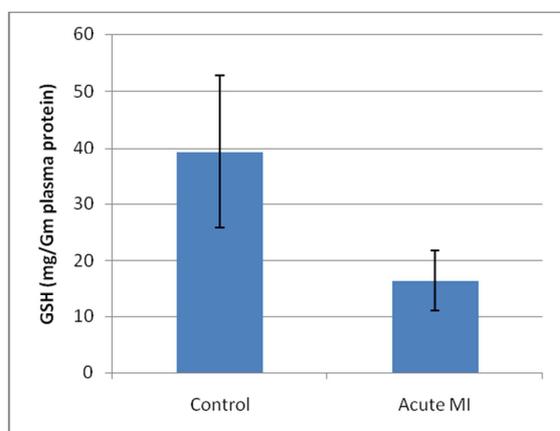


Figure 1: GSH Levels.

Glutathione peroxidase activity in plasma

The result showed that there was significant decrease ($P < 0.05$) of glutathione peroxidase activity in plasma of patients with elevated C-reactive protein, > 7 mg/L diagnosed with acute myocardial infarction. The decreased activity of glutathione peroxidase in plasma of patients with acute myocardial infarction could be attributed to the non availability or lesser availability of its substrate, glutathione in cardiomyocytes.

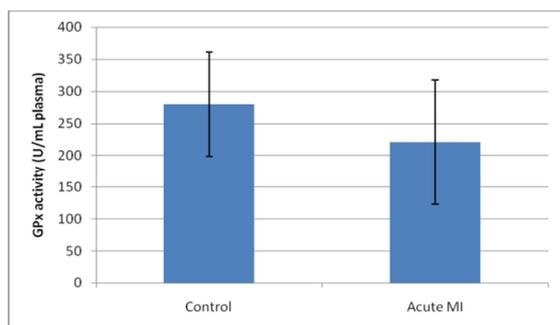


Figure 2: Glutathione peroxidase activity.

Estimation of Malondialdehyde

The result showed that there was significant increase ($P < 0.01$) of thiobarbituric acid reacting substances

such as malondialdehyde in plasma of patients with elevated C-reactive protein, > 7 mg/L diagnosed with acute myocardial infarction. The result showed that lipid peroxidation in blood was elevated in patients with acute myocardial infarction which could damage the cell membranes or cardiomyocytes.

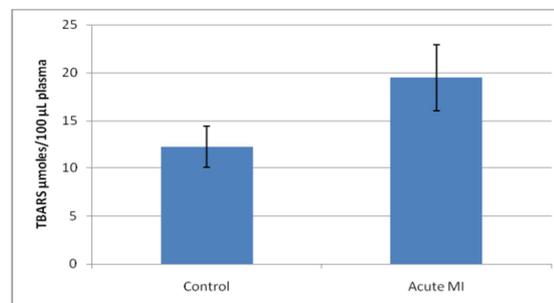


Figure 3: TBARS.

DISCUSSION

Glutathione is an important antioxidant defense molecule in our body to neutralise the free radicals such as hydrogen peroxide. Any compromise in redox balance is associated with various systemic diseases like cardiovascular diseases, lung disease, liver diseases and kidney diseases in association with activation of inflammatory molecules. It was reported in previous studies that antioxidant defense was disturbed in cardiovascular diseases and serum glutathione peroxidase activity was reduced in cardiovascular mortality cases with low HDL-cholesterol.^[18,19] During such condition there is a great possibility in imbalance of prooxidant and antioxidant molecules. In present study we found that patients diagnosed with acute myocardial infarction with elevated CRP had depleted glutathione concentration as well as reduced glutathione peroxidase activity. The decreased glutathione peroxidase activity could be attributed to depleted level of glutathione, the known substrate of glutathione peroxidase. The depleted glutathione and reduced glutathione peroxidase activity indicated that patients with acute myocardial infarction with elevated inflammation marked by enhanced by CRP level had poor compatibility to deal with free radicals generated. This was evident in our study that there was significant increase in thiobarbituric acid reactive substances such as malondialdehyde in acute myocardial infarction. The amount of thiobarbituric acid reactive substances could reflect the malondialdehyde status in blood, as MDA is well known as a stable lipid peroxidation end product. Henceforth, the study throws light on the importance of antioxidant defense mechanism in neutralising free radicals generated in inflammatory states associated with cardiovascular diseases. The generated free radicals in blood will be elevated due to the attenuated presence of antioxidant levels. This

could be deleterious to cell membrane in cardiomyocytes resulted in injury to cardiac muscles which was a classic feature of acute myocardial infarction.

CONCLUSION

The antioxidant molecules such as glutathione and glutathione peroxidase was attenuated in plasma of patients with acute myocardial infarction marked with increased CRP levels. It is also found that there is increased presence of thiobarbituric acid reacting substances in plasma which indicated the extent of lipid peroxidation in cardiac failure.

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