STUDY OF C - REACTIVE PROTEIN, MALONDIALDEHYDE AND URIC ACID LEVELS IN PREDICTING OUTCOME IN ACUTE MYOCARDIAL INFARCTION

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ABSTRACT

Acute Myocardial Infarction (AMI) is an important health problem with poor outcome despite impressive advancement in diagnosis and management. Objective: The purpose of this study is to investigate the role of C-reactive protein (CRP), Malondialdehyde (MDA) and serum Uric Acid as a predictor of outcome in Acute Myocardial Infarction (AMI). Materials & Method: A study was conducted in 72 subjects; 42 patients with AMI (35 years to 81 years), of which 6 patients expired during the study (4 Males, 2 Females) and 30 age and sex matched healthy control. These subjects are divided into among 3 groups, Group I- 6 AMI patients who expired after 7th day, Group II -36 patients with AMI; and Group III- 30 control group. Serum CRP, Uric acid & MDA readings were taken on day 1, 3 & 7 from the onset of symptoms. Result: Group I and II readings are found statistically significant (p<0.01) on all days as compared to the control (Group III). All the parameters in Group I showed an increasing trend and remained significantly elevated on day 1, 3 & 7 compared to Group II and controls. Conclusion: Our results suggest that inflammation and oxidative stress play important role in AMI and can be used in predicting outcome in AMI.

Keywords: Death, Acute Myocardial Infarction (AMI), C-reactive protein (CRP), Malondialdehyde (MDA), Uric acid, Lipid Peroxidation, Oxidative Stress.

INTRODUCTION

AMI an interruption of blood supply to a part of the heart which causes damage and potential death of heart tissue become an important health problem despite of advancement in management of this disease over the last few decades. This disease is often premature and severe, with serious complication and increase morbidity and mortality irrespective of age. CRP is labelled as a predictor of outcome in AMI and correlated with infarct size and host (immune) response factors [1,2] i.e the total circulating C-reactive protein levels in the setting of acute myocardial infarction is likely represents a marker of chronic vascular inflammation as well as the inflammatory response to acute myocardial injury. Studies have shown that uric acid is an important independent risk factor for cardiovascular mortality [3]. Under ischaemic conditions, Xanthine oxidase activity [4] and uric acid synthesis [5] are increased invivo and therefore elevated serum uric acid may act as a marker of underlying tissue ischaemia. The three carbon dialdehyde Malondialdehyde (MDA) is a highly reactive marker of lipid peroxidation due to production of free radical. Any imbalance between prooxidant and antioxidant defences in which the former dominates defined as “oxidative stress” of which lipid peroxidation is
one important manifestation [6]. Oxidative stress in relation with ROS is involved in LDL oxidation, platelet aggregation, thrombus formation and thereby atherosclerosis and AMI [7,8].

MATERIALS AND METHODS
The study is conducted in a group of 72 subjects; 42 patients with cases of Acute Myocardial Infarction (35 years to 81 years) of which 6 patients expired during the study (4 Males, 2 Females) and 30 age and sex matched healthy control, irrespective of age and sex taken randomly from the admitted patients of Cardiology department of Gauhati Medical College (GMC), Assam. All procedures for the study is followed and Informed consent was obtained from all patients and control subjects participating in this study.

Inclusion criteria- history of Squeezing or Crushing central chest pain, characteristic electrocardiogram (ECG) changes and elevated creatine kinase isoenzyme MB (CK-MB) and troponin-t within 12 hrs of onset of pain [9].

Exclusion criteria - Renal failure, Rheumatic fever, Rheumatoid Arthritis, Inflammatory Bowel disease, Gout, Neoplastic disease and Bacterial Infection. Antioxidant, vitamin supplements, probucol, quinidine, disopyramide, or other drugs were not given to the Patients or controls group which may affect the study.

Beta blockers, oral ACE inhibitors, antiplatelet therapy (aspirin or clopidogrel), unfractionated heparin, and GP (Glycoprotein) IIb/IIIa inhibitors, were used in treating the AMI Patients.

Blood samples for estimation of Serum C-Reactive Protein, Uric acid & Malondialdehyde were collected on day1 and day3 from the onset of the symptoms. 3 ml of blood is drawn from the Ante cubital vein under aseptic precautions. Biochemical estimations were done based on colorimetric principles.

- Serum C - reactive protein was estimated by using the Turbidimetric Immunoassay method [10].
- Serum Malondialdehyde (MDA) was measured as thiobarbituric acid reactive substance by colorimetric method by modified procedure of Yagi’s and Satoh’s methods [11].
- Serum uric acid is estimated by Uricase method [12] using the Crest Biosystems kits.

SPSS 16.0 statistical package were used. The results obtained were presented in Mean± SD and then compared between different groups of the study by applying students ‘t’ test, probability (p) less than 0.05 is considered significant.

OBSERVATIONS AND RESULTS
The test group comprises of 72 subjects; 42 patients with cases of Acute Myocardial Infarction (35 years to 81 years), of which 6 patients expired during the study (4 Males, 2 Females with a mean of 56.5 years) and 30 age and sex matched healthy control (25 males and 5 females, age ranging from 38 years to 77 years) with a mean of 53.4 years comprises of the control group.

Serum C-reactive protein, Malondialdehyde and Uric acid readings were taken on Day 1, 3 and 7 from the onset of symptoms. Table 1 shows statistically significant value of Serum C - reactive protein, Malondialdehyde and Uric acid on days 1, 3 and 7 in Death and AMI compared to Controls group.

Figure I show mean CRP values in Death, AMI and Control. Figure II shows a mean MDA values in Death, AMI and Control, Figure III shows a mean Uric acid levels in Death, AMI and Control on Day 1, 3 and 7. CRP, MDA and Uric acid peaks around 3rd day with subsequent decline but Group I showed an increased trend in all the parameters.

DISCUSSION
An inflammatory risk marker of acute phase protein is C-reactive protein. Studies have interpreted that an elevated levels of CRP to be a predictor of outcome in AMI [1, 13, 14]. Our
results are also comparable with them. Our results showed elevated levels of C-reactive protein in Death patients (group I) on day 1,3,7 as compared to the AMI (group II) and control group (group III).

Castelli P et al, 1995 has labelled elevated Uric acid as a marker of tissue ischemia. Studies also reveal that uric acid level as a risk factor for AMI [15] and also increases in cardiac failure [16]. In the present study, there is a statistically significant high level of serum uric acid concentration in death patients as compared to AMI and control subjects on day 1, 3 and 7.

Lipid peroxidation marker (MDA), has significantly higher values in death patients (group I) on all days compared to Group II and III. Our study showed that MDA has a definite pattern in AMI and its level continues to rise and peaks around 3rd which matches with the result obtained by Justo aznar et al 1983 [17].

CRP, MDA and Uric acid reading remain significantly elevated in Death patients (group I) with an increasing trend without subsequent decline as compared to other AMI subjects (group II) as seen in figure I,II and III respectively.

Markedly elevated levels of CRP, MDA and Uric acid in death and AMI patients should be cautiously taken and considerably important in the serial measurement of these parameters should be given to patients admitted with AMI. Thus the increasing rise of these parameters should be taken as alarming signs in management of AMI.

CONCLUSION

All the 6 patients who died had very high CRP, MDA and Uric acid at presentation and remained highly elevated during the course compared to other AMI patients who had gradual elevation of all three parameters and subsequent decline in AMI.

As a result of this we conclude that CRP, Uric acid and MDA at presentation may be considered as alarming and should be taken as a serious marker in predicting outcome including death of the patients, as the line of treatment and lab diagnosis can go hand in hand to increase the life expectancy of the individuals.

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Table 1: Clinical and biochemical indexes in the study group

<table>
<thead>
<tr>
<th>Group</th>
<th>AMI Obs (n)</th>
<th>CRP (mg/dl) DAY 1</th>
<th>MDA (nmol/ml) DAY 1</th>
<th>Uric Acid (mg/dl) DAY 1</th>
<th>CRP (mg/dl) DAY 3</th>
<th>MDA (nmol/ml) DAY 3</th>
<th>Uric Acid (mg/dl) DAY 3</th>
<th>CRP (mg/dl) DAY 7</th>
<th>MDA (nmol/ml) DAY 7</th>
<th>Uric Acid (mg/dl) DAY 7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>Death Patients (n=6)</td>
<td>8.28±1.56*#</td>
<td>3.41±0.90*#</td>
<td>8.98±1.39*#</td>
<td>9.53±0.77*#</td>
<td>3.66±0.96*#</td>
<td>9.58±0.88*#</td>
<td>10.53±0.77*#</td>
<td>3.66±0.96*#</td>
<td>9.88±0.88*#</td>
</tr>
<tr>
<td>Group II</td>
<td>AMI Patients(n=36)</td>
<td>3.94±2.77*</td>
<td>2.58±0.83*</td>
<td>5.56±1.56*</td>
<td>5.53±3.24*</td>
<td>3.01±0.90*</td>
<td>6.23±1.70*</td>
<td>4.03±3.01*</td>
<td>2.97±0.82*</td>
<td>5.69±1.54*</td>
</tr>
<tr>
<td>Group III</td>
<td>Control Subjects(n=30)</td>
<td>0.43±0.19</td>
<td>1.85±0.22</td>
<td>3.94±1.10</td>
<td>0.43±0.19</td>
<td>1.85±0.22</td>
<td>3.94±1.10</td>
<td>0.43±0.19</td>
<td>1.85±0.22</td>
<td>3.94±1.10</td>
</tr>
</tbody>
</table>

Legend—Values are given as mean ± S.D. (*p<0.01—Highly Significant when compared to Control Subjects; *# death Group is highly significant when compared to AMI & Control group; NS—Not significant)
Figure: 1- Comparison of Mean CRP in Death, AMI and Control subjects in Day 1, 3& 7

Figure: 2- Comparison of Mean MDA in Death, AMI & Control subjects in Day 1, 3& 7

Figure: 3- Comparison of Mean Uric acid in Death, AMI & Control subjects in Day 1, 3& 7

Legend: From the above graph it can be seen that all the three parameters (MDA, CRP, Uric acid) are significantly elevated in Death patients.