Correlating Serum Ceruloplasmin and Troponin I levels in patients diagnosed with acute myocardial infarction

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Abstract
The current study was undertaken to assess the levels of serum ceruloplasmin (CP) in patients diagnosed with acute myocardial infarction (AMI) and to see if a correlation exists between serum CP which is an indicator of production of free radicals in the body and troponin I (Tn I) which is an indicator of the severity of AMI. Serum CP, was estimated by manual method of Ravin (Copper Oxidase - enzymatic method). Serum CP levels in patients with AMI was raised. Serum Tn I levels were increased in patients with AMI. The levels of serum CP had a positive correlation with serum Tn I levels.

Keywords: Ceruloplasmin, Troponin I, Acute Myocardial Infarction.

Introduction
Serum Troponin I (Tn I) concentration provide valid diagnostic information in patients with suspected myocardial infarction.¹ There are a good number of studies which have shown increased levels of serum ceruloplasmin (CP) in patients with acute myocardial infarction (AMI).² There is a growing body of evidence for the role of free radicals in mediating myocardial tissue injury during myocardial ischemia and reoxygenation. Oxidant and oxygen radical formation is greatly increased in the post-ischemic heart and serves as a critical central mechanism of post-ischemic injury. Studies have shown that free radical scavengers and enzymes like superoxide dismutase, catalase can reduce myocardial tissue that undergoes irreversible injury. Additionally, inhibitors of the enzyme xanthine oxidase, have been shown to reduce the ultimate infarct size, by reducing the xanthine oxidase generation of superoxide anion.³ CP is an acute phase protein, and is an important intravascular, extracellular antioxidant and free radical scavenger. It protects tunica intima against free radical injury.⁴ Many studies show a strong relationship of circulating CP levels and myocardial damage in patients with AMI. The levels of CP in AMI patients were significantly high as compared with controls. It is known that increased oxidative stress plays a role in the pathogenesis of AMI. Antioxidants reduce free radical damage caused by oxidative stress, which is seen in tissue inflammation and damage.⁵ Electrocardiogram (ECG) and/or cardiac TnI / creatine kinase(CK) levels are not indicative of
the load or the production of free radicals in the body. Thus, this study was undertaken to assess the levels of CP in patients diagnosed with AMI and to see if a correlation exists between serum CP which is an indicator of production of free radicals in the body and Tn I which is an indicator of the severity of AMI.

The objective of this study was to estimate serum ceruloplasmin levels and serum troponin I in patients diagnosed with acute myocardial infarction (AMI) and correlate these results.

**Materials and methods**

The study was a cross sectional study. The sources of data were cases diagnosed with acute myocardial infarction based on clinical/ electrocardiogram/ echocardiography/ laboratory findings by cardiologist, in a tertiary care hospital. The study was conducted after getting clearance from the institutional ethics committee. A total of thirty (30) cases were selected for the study. Venous blood sample of patients who met the inclusion criteria were collected within 24hours of admission in the coronary care unit under aseptic condition. Written informed consent was obtained from them for analysis of Ceruloplasmin. The serum was separated and assayed\(^6\) for serum CP, which was done by the method of Ravin (Copper Oxidase - enzymatic method). Tn I data was collected from the patient records.

“R software” was used for descriptive statistical analysis of the data. Microsoft word and Excel have been used to generate graphs, tables etc. Significance is assessed at 5 % level of significance. Test for Pearson’s correlation (\(\rho\)) has been used to find the significance between the serum CP levels and Tn I levels in patients.

**Inclusion criteria**

- Male and female patients aged between 35-80yrs diagnosed to have acute MI based on Electrocardiogram (ECG)/ echocardiography findings.

**Exclusion criteria**

- Patients with any known inflammatory or infectious disease.
- Patients on drugs like anticonvulsant (carbamazepine, phenobarbital, phenytoin, valproic acid), steroids, estrogens, methadone, oral contraceptive pills, tamoxifen.
- Patients on antioxidant vitamin supplementation.
- Patients with Wilson’s disease.
- Patients with congenital disorders of CP deficiency.

**Results**

The mean value of serum CP in AMI patients is 45.08 ± 7.83 mg/dl. Serum CP levels in cases ranged from 26.02 to 60.50 mg/dl (Table 1). The level of serum Tn I in cases ranged from 0.011 to 7.1 ng/mL. The mean value of serum Tn I is 1.14 ng/mL .The pearson’s correlation (\(\rho\)) between serum Tn I and serum CP obtained was 0.62 which is shown using a scatter plot in figure 1. The p value for comparison of the variables serum Tn I and serum CP in AMI patients was 0.0004 , which being lesser than 0.05 is statistically significant.

| Parameter | CP | Tn I |
|-----------|----|------|
| Mean value | 45.08 mg/dl | 1.14 ng/mL |
| Range | 26.02 to 60.50 mg/dl | 0.011 to 7.1 ng/mL |

**Table 1**: Serum CP and Tn I levels in AMI cases

**Figure 1**: Scatter plot depicting the serum CP and serum Tn I levels in AMI patients.
Discussion

CP is an acute phase protein, has ferroxidase activity and also plays a role in scavenging of oxygen derived free radicals. Our study demonstrated, CP levels was higher than the biological reference interval in AMI cases. The mean value of serum CP in AMI patients is 45.08 mg/dl. The serum CP levels showed a positive correlation with serum Tn I levels in AMI patients, which could indicate increase in antioxidant activity in response to oxidative stress in AMI.

HB Sirajwala et al also observed that Serum CP level in all patients of AMI was abnormally high. Their study proposed that rise in ceruloplasmin could be due to its property of an APP; hence, after necrosis or inflammation of the tissue, the level rises immediately. W.H. Wilson Tang et al noted that patients with elevated CP were more likely to be older, female gender, with more cardiovascular risk factors including dyslipidemia, history of diabetes mellitus, and poorer renal function at baseline. There was no gender-specific difference in prognostic value despite higher serum levels of CP observed in women versus in men. G.Venkataramana et al. concluded that serum CP levels were statistically significantly elevated in patients with AMI as compared to controls. Patients with symptoms and signs suggestive of AMI supported by ECG and cardiac markers (increased CK, CK-MB and Tn I) were included in the study.

In a study done by Abdullah Kh. Ibrahim et al, serum CP were significantly higher in patients with AMI than those of control group. They concluded that serum bilirubin and serum CP may be considered biochemical risk factors for AMI. Fox et al suggested that CP could be an independent risk factor for cardio-vascular disease. It is an abundant protein that participates in the acute phase reaction to stress, but its physiological function(s) is unknown. An antioxidant activity of CP has been described, but recent evidence suggests that the protein may also exhibit potent prooxidant activity and cause oxidative modification of low density lipoprotein (LDL). The pro-oxidant activity is highly dependent on the structure of the protein; removal of a single one of the seven integral copper atoms, or a specific proteolytic cleavage event, completely suppresses LDL oxidation. This newly described pro-oxidant activity may help to explain epidemiological studies indicating that ceruloplasmin is an independent risk factor for cardiovascular disease. An increased level of serum CP in AMI patients (p<0.001) suggests that this molecule may act as an oxidative stress indicator. It was also seen that AMI patients had significantly lower levels of vitamins E and C. Imbalance between oxidant and antioxidant molecules is observed in AMI patients, and magnitude of imbalance is greater in diabetic AMI patients, possibly because of greater inflammation in diabetic patients.

In a study done by P.T Komala, there was a significant increase in serum malonaldehyde, uric acid, CP levels in MI cases compared to controls which showed a significant decrease after thrombolysis. Oxidative stress is present in patients with MI. Serum malonaldehyde is one of the significant marker to indicate the oxidative stress associated with myocardial infarction. There is adaptive increase in stress is decreased due to reperfusion by the thrombolytic therapy. A similar study, demonstrated an increase in substances reactive to thiobarbituric acid (TBARS) and carbonyl protein levels in the AMI and risk groups. In addition, a positive correlation was found between TBARS, carbonyl protein levels, and Tn I in AMI patients.

Recently, diagnostic strategies using a combination of biomarkers have been evaluated in hope of identifying high risk patients with chest pain. The combination of troponin and a biomarker that does not arise from myocardial necrosis but by a different mechanism such as myocardial stretch, inflammation, or stress is appealing. In our study we have seen that serum CP levels in patients with AMI and correlated with serum Tn I levels (ρ = 0.6).

Limitations: As the sample size was small, more studies with a larger sample size would give more information. Also, this study involved a onetime testing. Serial estimation of CP and Tn I during the reperfusion phase would enable us to know the peak
and trend of this analytes, in the clinical course of AMI.

Conclusion
The level of CP was found to rise in AMI patients. This rise may be in response to the free radical damage and oxidative stress seen in AMI. There is a positive correlation between serum CP levels and serum Tn I levels in AMI patients in this study. As increased level of CP could indicate severity of atherogenicity, early detection of high levels of CP can moot in an early intervention, thereby, reducing the mortality and morbidity from AMI cases. Moreover, discerning the anti oxidant property of ceruloplasmin, the study could be extended to find out the need for initiation of supplementation of antioxidant therapy at the earliest.

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