Cortisol: Testosterone ratio and homocysteine levels in patients with acute myocardial infarction.

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Abstract

Stressful experiences include major life events, trauma, and abuse and are sometimes related to the environment in the home, workplace, or neighborhood. Acute stress and chronic can both have long-term consequences. Therefore, this study was carried out to investigate cortisol, total testosterone and total homocysteine (tHcy) status in acute myocardial infarction (AMI). Thirty AMI patients were included and diagnosed based on clinical examination, laboratory investigations, electrocardiogram, angiography and other tests. The blood samples were analyzed for cortisol, total testosterone and tHcy. Significantly increased levels of serum cortisol and tHcy, and decreased level of total testosterone were noticed in the patients group as compared to control subjects. Whereas, we found positive and significant correlation between cortisol : testosterone (C/T) ratio and tHcy, and mean blood pressure in AMI patients. This study suggests that, some methods require which reduces the C/T ratio and homocysteine levels may reduce the risk of AMI.

Key Words: Acute myocardial infarction, cortisol : testosterone ratio, homocysteine
All participants completed a medical history form and provided informed consent. The presence of coronary heart disease at baseline was determined by the Rose questionnaire for myocardial infarction, the electrocardiogram results, and a self-reported confirmation of heart disease diagnosed by a physician [10]. Thirty (30) AMI patients were included in the present study. All the AMI patients were diagnosed based on clinical examination, laboratory investigations, electrocardiogram, angiography and other tests. The control group consist of 30 normal healthy subjects, having age ranging 20 to 65 years matched with the patients. All the controls were symptom less on clinical examination.

Inclusion criteria were normal renal and liver function. Exclusion criteria were use of medications (therapy involving Prednisolone, Corticosteroid, S-adenosylmethionine, carbamazepine, phenytoin, 6-azauridine, antithoerin, antifolates, anticonvulsant agents, tamoxifen, and theophylline), diabetes mellitus, cancer, anemia, and systemic illness. The Institutional Ethical Committee at the Grant Medical College and Sir J.J. Group of Government Hospitals, Mumbai, India, approved the study.

**Blood sample collection**

Venous blood samples were collected in test tube with aseptic precautions. After 2 hours of collections sample was centrifuged at 3000 rpm for 5 minutes. Serum was separated and collected in polythene tube with cork. The sera with no sign of hemolysis used for the analysis of cortisol, total testosterone and total circulating homocysteine (tHcy).

**Biochemical Analysis**

Serum cortisol estimated by the method of solid-phase, competitive chemiluminescent enzyme immunoassay. [11]. Serum total testosterone concentration was evaluated by solid-phase, competitive chemiluminescent enzyme immunoassay method [12]. Serum tHcy concentration was measured by competitive chemiluminescent enzyme immunoassay method [13]. We used fully automated enzyme amplified chemiluminescent immunoassay based Immulite 1000 analyzer. Measurement of these blood parameters by using commercial kits from Siemens Medical Solutions Diagnostics, Los Angeles, CA, USA.

**Statistical Analysis**

Numerical variables were reported in terms of mean and standard deviation. Statistical analysis of results was done by normal ‘z’ test. In this analysis, variables showing p value less than 0.05 and 0.001 were considered to be statistically significant and highly significant respectively. Pearson correlation test was used to test.

**Results**

Demographic data of AMI patients such as age, weight, body mass index (BMI), systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean blood pressure (MBP) are significantly change (p< 0.05) as compared with normal control group (Table 1).

Table 2 shows levels of serum cortisol, testosterone, homocysteine, and C/T ratio in healthy subjects and AMI patients. Study group showed a significant (p<0.001) increase in serum cortisol, homocysteine, and C/T ratio whereas, significant (p<0.001) decrease in serum testosterone (p<0.001 as compared to control subjects. Positive and significant (p < 0.001) correlations were observed between levels of cortisol : testosterone ratio and homocysteine, and MBP. (Table 3).

**Table 1. Demographic data in controls and AMI patients.**

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Biochemical Parameters</th>
<th>Control group (n=30)</th>
<th>AMI group (n=16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Age (years)</td>
<td>54.3 ± 3.32</td>
<td>56.7 ± 2.27*</td>
</tr>
<tr>
<td>2.</td>
<td>Weight (Kg)</td>
<td>65.8 ± 6.15</td>
<td>72.1 ± 12.6*</td>
</tr>
<tr>
<td>3.</td>
<td>BMI (Kg/m2)</td>
<td>23.7 ± 2.24</td>
<td>29.6 ± 4.45*</td>
</tr>
<tr>
<td>4.</td>
<td>SBP (mm of Hg)</td>
<td>122 ± 4.22</td>
<td>168 ± 6.35*</td>
</tr>
<tr>
<td>5.</td>
<td>DBP (mm of Hg)</td>
<td>80.7 ± 2.51</td>
<td>99.3 ± 5.54*</td>
</tr>
<tr>
<td>6.</td>
<td>MBP (mm of Hg)</td>
<td>101 ± 2.49</td>
<td>134 ± 4.76*</td>
</tr>
</tbody>
</table>

The results were compared between control group and study group of AMI patients. The values are presented in mean ± S.D. *P < 0.05.
Cortisol: Testosterone ratio and homocysteine levels in acute myocardial infarction.

**Table 2. Serum cortisol, testosterone and C/T ratio in controls and AMI patients.**

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Biochemical Parameters</th>
<th>Control group (n=30)</th>
<th>AMI group (n=16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Cortisol (nmol/L)</td>
<td>253±81.6</td>
<td>1237±293**</td>
</tr>
<tr>
<td>2</td>
<td>Testosterone (nmol/L)</td>
<td>11.0±2.32</td>
<td>9.49±1.68**</td>
</tr>
<tr>
<td>3</td>
<td>Homocysteine (µmol/L)</td>
<td>7.81±1.75</td>
<td>39.5±5.51**</td>
</tr>
<tr>
<td>4</td>
<td>C/T ratio</td>
<td>432±119</td>
<td>306±52.3**</td>
</tr>
</tbody>
</table>

The results were compared between control group and study group of AMI patients. The values are presented in mean ± S.D. **P < 0.001.

**Table 3. Correlation of C/T ratio and Homocysteine, and mean blood pressure in patients with AMI.**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>r</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>tHcy</td>
<td>0.899</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>MBP</td>
<td>0.457</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

**Fig 1: Correlation between cortisol : testosterone ratio and homocysteine in AMI patients**

**Fig 2: Correlation between cortisol : testosterone ratio and mean blood pressure in AMI patients.**

r = 0.457
Discussion

Excessive cardiovascular reactivity to stress may have a pathophysiological role in neurogenic hypertension [14]. In study group, age, weight, body mass index (BMI), systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean blood pressure (MBP) were showed significant (p < 0.05) increase. The present study shows that there was significant change in adrenal and cardiac functions in patients with AMI. Serum cortisol level was significantly increased (p<0.001) in cases of AMI. Kumari et al [8] studied animal model of stress-induced acceleration of atherosclerosis that provides scope for future studies into its etiology/pathogenesis, the mechanisms through which stress can increase disease risk are currently poorly understood.

Cortisol is the potential mediator between stress and cardiovascular disease that has been mostly discussed in the literature. Four small cross sectional studies suggested that early-morning plasma cortisol levels correlate with the degree of coronary artery disease detected on angiograms [15-17], but studies failed to find this association [18]. There is limited additional evidence from studies comparing poorly characterized groups of patients with various diseases (including cardiovascular disease) with subjects without these diseases, which suggests that blood cortisol levels may be related to cardiovascular disease [19]. Endogenous corticosteroid treatment has also been associated with elevated cardiovascular disease risk [20], and evidence from animal studies suggests detrimental effects on cardiovascular health of elevated cortisol [21].

Serum testosterone concentration was significantly (p<0.001) decreased in AMI patients whereas cortisol : testosterone ratio were significantly (p<0.001) increased in our study group as compared with normal subjects. Cortisol and testosterone secretion are interrelated. Activation of the hypothalamo-pituitary-adrenal axis not only results in an elevation of adrenal corticosteroids but also inhibits gonadotrophin secretion [22], which will result in a secondary reduction of testosterone concentration in the male. Therefore, decreased testosterone and increased C/T ratio in AMI which corroborates with the other studies, [23-27] is a useful proximal marker of processes that may lead to increased risk of CVD.

Hyperhomocysteinemia, in such AMI patients was found in our study might to be due to alteration of cardiac functions. Homocysteine is a sulphur-containing amino acid that results as an intermediary product of the methionine degradation pathway. The folic acid and vitamin B12 or B6 deficiencies can play a role as cofactors that increase homocysteine levels. Additional studies have shown a negative correlation between homocysteine levels and folic acid and vitamin B12 and B6 plasma levels [28,29]. In this study we cannot estimate serum vitamin B. Several studies have been performed to demonstrate association between homocysteine levels and cardiovascular diseases which corroborates with the work of Gravina-Taddei, Yadav et al [3,31].

Better correlation between the cortisol : testosterone ratio and homocysteine in overall AMI patients was statistically positive (r = 0.899) and significant (p < 0.001) were observed (Figure 1). The correlation coefficient (r) of 0.457 (p > 0.001) between the serum cortisol : testosterone ratio and MBP level was good (Figure 2). These correlations were in agreement with the findings of Smith et al [31].

We can conclude that biochemical screening such as cortisol, testosterone and homocysteine is of paramount importance in all AMI patients. This study suggests that, some methods require which reduces the C/T ratio and homocysteine levels may reduce the risk of AMI. On the other hand, there is an absolute need for large studies designed to answer the question as to whether adrenal dysfunction are associated with increased risk for CVD and whether therapy of these disorders might influence cardiovascular mortality. Further studies should help define the role of genetic polymorphism in increased cortisol, reduced testosterone and homocysteine metabolism enzymes and their role in AMI patients.

References

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