Some Biomarkers in Acute Myocardial Infarction

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Abstract

Background: Several changes in serum biochemical factors occur in acute myocardial infarction (AMI). Recently alterations in serum levels of homocysteine (Hcy), sialic acid (SA) and high sensitive C-reactive protein (HS-CRP) has been attended as risk factors and index for prediction. This study was aimed to show the alterations in these factors and their relationships in AMI.

Methods: Thirty four patients with AMI were enrolled in this case-control study. Also 51 apparently healthy individuals were selected as control group. Serum was prepared from all subjects in fasting state. Hcy and HS-CRP were measured using ELISA and SA was determined by Erlich method.

Results: Serum levels of Hcy, SA and HS-CRP in AMI patients were 14.35±2.55µmol/l, 73.54±2.82 mg/dl, and 17.32±3.45 mg/l, respectively and in the control group they were 8.31±2.66 µmol/l, 59.82±2.70 mg/dl and 2.77±1.98 mg/l, respectively. Statistical analysis of data showed that serum level of Hcy, SA, and HS-CRP in the patients with AMI was significantly higher than those of control ($p<0.001$). Also significant correlation was observed between Hcy-HS-CRP ($r= 0.63$), SA-Hcy ($r= 0.73$), and SA-CRP ($r= 0.75$) ($p< 0.05$ for all items).

Conclusion: Our findings showed increased level of HS-CRP, SA, and Hcy in AMI patients. Also obtained data indicated a direct and significant correlation between HS-CRP as an inflammation index and Hcy and SA. Hence these two factors can be used as biomarkers in this disease.

Keywords: Myocardial infarction, C-reactive protein, Homocysteine, Sialic acid

Introduction

Relationship between increase of homocysteine and cardiovascular diseases have been studied (1-2). It is shown that this relationship is independent of other risk factors (3). Prospective studies about the assessment of the risk of vascular diseases point to this fact that an increase in homocysteine of blood leads to the increase the possibility of myocardial infarction (4).

It seems that the concentration of serum total sialic acid (TSA) is related to the risk factors of cardiovascular diseases (5). In the people suffering from diabetes the level of TSA increased and also increases risk of cardiovascular diseases was observed in these patients (6). Several studies have shown that TSA is related to cardiovascular diseases and the level of TSA increases in the people afflicted by these diseases (7).

The level of sialic acid as a predictor index in long periods for coronary heart diseases (CHD) (especially for women) that lack any cardiovascular diseases was suggested (8). Another study showed that the level of TSA increases in proportion with the numbers of the coronary artery diseases (attack times) and the concentration of lipid-bound associated sialic acid (LASA) was related to the severity of coronary atherosclerosis especially in patients with two or three times vascular disease (9). There are evidences showing that the mean of TSA in people afflicted with AMI increased significantly compared to the...
control group indicating that TSA is a risk factor for coronary artery diseases (10, 11).

Several epidemiological studies strongly suggest that the CRP with high sensitivity (HS-CRP) can be an independent and valid indicator for heart attack, heart arrest (by obstruction not hemorrhage) and vascular deficiencies (12-13). High CRP response occurs after acute myocardial infarction (AMI) whose severity is related to the extent of myocardial necrosis and in this state the peak CRP is about 48 h after the beginning of myocardial infarction (14). Strong experimental evidence suggested that CRP response not only is a reflection of tissue damage but also can participate in the acute myocardial damage significantly (15-17).

The close relationship of CRP concentrations of blood circulation with severity, extent and aggravate of many different damages and the important of prognosis of these relations lead to the emphasis that CRP is not only a disease marker but also participates in their pathogenesis. Recent clinical findings show that CRP is an independent risk factor for coronary artery diseases (18). In addition, it is shown that HS-CRP can be applied as an indicator of atherosclerosis development (19).

This study was aimed to clarify the alteration in these factors in patients with AMI in Hamadan (west of Iran) and also to study their relationships in this disease.

Materials and Methods

The subjects (n= 34) were chosen from patients with AMI hospitalized in CCU of Ekbatan Hospital (Hamadan, Iran) without of age, sex or any special presupposition. The control group consisted of 51 healthy people who did not have any record of this or other systemic diseases. They filled out a questionnaire, and were similar with cases in terms of age, sex, smoking, cholesterol, and triglyceride. The obtained data were compared using t-test.

Blood was taken from the cases and controls in fasting state. The blood samples from AMI patients were taken in the first 24 h after MI. Serum were separated and transported to the freezer in less than an hour in order to prevent continuing synthesis of homocystein in the red blood cells.

The amount of serum homocysteine was measured by ELISA using AXIS- SHIELD kit (England). TSA was measured by chemical method of Erlich (20), and HS-CRP using quantitative assessment kit from DRG HS ELISA.

Serum lipids were assessed by standard enzymatic and colorimetric methods (Pars-Azmoon diagnosis kits, Iran). Statistical analysis was performed using t-test and peason correlation coefficient. A descriptive level of significance was set at \( P \leq 0.05 \).

Results

The cholesterol, TG and HDL levels in two studied groups and the average of their age are shown in Table 1. These findings indicated that they were matched in term of these factors. The concentration of serum homocysteine in the patients with AMI and the healthy subjects is shown in Table 2, indicating higher Hcy level in AMI patients \( (P< 0.001) \).

In Table 3 sialic acid content of serum in studied groups is shown. There was a significant difference in this factor between the patient with AMI and the healthy group \( (P< 0.001) \). A similar result about the difference between serum levels of HS-CRP in two groups was observed that show higher level of HS-CRP in patients with AMI \( (P< 0.001) \). Also the diagram of serum amount of three factors in people with AMI and control group was illustrated in Fig. 1.

To survey probable association of the studied factors, regression diagrams of factors are shown in the Figs. 2- 4. The results show that there is a direct and significant relationship between Hcy and SA, Hcy and HS-CRP and also SA and HS-CRP (correlation coefficient: 0.73, 0.63, 0.75, respectively, \( P< 0.05 \)).
Table 1: Basic characteristics of AMI patients and control group

<table>
<thead>
<tr>
<th>Factors</th>
<th>Control n=51</th>
<th>AMI n=34</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (M/F)</td>
<td>23/11</td>
<td>35/16</td>
<td>-</td>
</tr>
<tr>
<td>Age*</td>
<td>57±10</td>
<td>60±13</td>
<td>0.1</td>
</tr>
<tr>
<td>Smoking (n)</td>
<td>28</td>
<td>19</td>
<td>-</td>
</tr>
<tr>
<td>Cholesterol* (mg/dl)</td>
<td>32 ± 185</td>
<td>199±49</td>
<td>0.16</td>
</tr>
<tr>
<td>HDL(mg/dl)*</td>
<td>61.2±16.7</td>
<td>58.0±15.3</td>
<td>0.63</td>
</tr>
<tr>
<td>Triglyceride (mg/dl)*</td>
<td>148± 45</td>
<td>117± 42</td>
<td>0.59</td>
</tr>
</tbody>
</table>

* Data are mean ±SD

Table 2: Comparison of serum homocysteine in patients with AMI and control group

<table>
<thead>
<tr>
<th>Factor</th>
<th>Control n=34</th>
<th>AMI n=51</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Homocysteine (µmol/l)</td>
<td>8.31±2.66</td>
<td>14.35±2.55</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sialic acid (mg/dl)</td>
<td>59.82±2.7</td>
<td>73.54±2.84</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HS-CRP (mg/l)</td>
<td>1.98±2.77</td>
<td>17.32±3.54</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Fig. 1: Comparison the means of Hcy, SA, hs-CRP in case and control groups
Fig. 2: Relationship between homocysteine and sialic acid in AMI.

Fig. 3: Relationship between homocysteine and hsCRP in AMI.
Discussion
Apart from the controversy over pathogenesis mechanism and other parameters involved in deficiencies and effective factors on the increase of blood homocysteine, there is a general agreement that homocysteine can be a main factor in the degenerative diseases like atherosclerosis. Homocysteine often causes primary damages on the wall of arteries after which cholesterol and fibrinogen are collected in that place and leads to obstruction of veins. In addition, homocysteine contributes to the LDL oxidation and causes vascular platelets aggregate thereby leads to vascular obstruction. The relationship between basic hyperhomocysteinemia and atherosclerosis complications has been investigated by several authors (21-23). In spite of a strong and independent relationship between blood homocysteine and cardiovascular diseases in many case-control and prospective studies, many prospective studies did not show a considerable relationship between homocysteine and cardiovascular diseases, statistically (24).

Selhub et al. (1995) showed that there was a clear relationship between the increases of carotid obstruction with an increase of serum homocysteine (25). Similar findings to our data were presented by Malinow et al. (13 µmol/l serum homocysteine in case group and 10.5 µmol/l in control group with \( P < 0.001 \)) that indicated a significant relationship between increases of serum homocysteine with premature AMI (26). Evans et al. could not find any significant difference between mean of...
homocysteine and cardiovascular diseases (27). However, a relationship was reported between elevated homocysteine level and increased risk of premature myocardial infarction (28).

It seems that the concentration of total sialic acid (TSA) has a relationship with many risk factors of cardiovascular diseases including high concentration of serum cholesterol and triglyceride, high concentration of apoB-100, low concentration of HDL-C, smoking and physical activity. Therefore, TSA is as a main risk factor in cardiovascular diseases (5). Salomone et al. (1998) showed that development and severity of coronary artery disease (CAD) is not related to serum level of sialic acid (29). In addition, they could not find a significant difference between level of sialic acid in CAD and healthy subjects. They also showed that there was a relationship between serum level of sialic acid and mortality of cardiovascular diseases. This shows other factors are involved in the development and severity of CAD (29). Rostam et al. showed that there was a significant difference in serum levels of sialic acid in patient with atherosclerosis of carotid. They remarked serum sialic acid has relationship with the presence of disease but not with risk factors of disease (30).

Our finding showed that the mean serum sialic acid in patients with AMI was higher than those of control group. We can suggest increase of sialic acid plays a role in AMI. Several epidemiological studies obviously show that CRP with higher sensitivity (HS-CRP) can be a valid and independent index for heart attacks, heart arrests (by obstruction not hemorrhage) and vascular problems. Some studies showed that HC-CRP is higher than normal in people with artery fibrillation (31, 32). A case-control study which was carried out in 22000 male physicians (40-84 yr) indicated that men with the highest HS-CRP quartile (%25 of subjects) with more than 1.2 mg/L had heart attack 3 times and heart arrest 2 times more than men with the lowest quartile (less than 0.56 mg/l) (33). The study of European concerted Action on thrombosis showed that increase in mean of HS-CRP in patients who survived after MI with or without an explicable coronary damage and this will increase more if other parts such as environmental veins are engaged (34).

In a screening study which forecast the long-term risk of cardiovascular it was observed that patients have highest level of HS-CRP are prone to MI risk by 2.6 times (35). Our findings showed higher concentration of HS-CRP in AMI that indicated a probable role in this disease.

Another study shows that in patients with MI, there is a relationship between high level of HS-CRP with presence of complicated angiography damages and need to revascularization (36). A study on the people who had bypass surgery of coronary artery showed that people with high HS-CRP has recurrence of the last surgery after 6 yr in comparison with people with low or normal HS-CRP. In addition, increase of HS-CRP can be a definite biomarker for vasculopathy, heart graft and reject of graft or both of them (37). Also it was shown that many patients with angina pectoris (stable and unstable) have a normal level of proteins of acute phase, this points to the fact that coronary atherosclerosis by its own does not lead to the induction of the acute phase response (38).

It was shown that HS-CRP in circulation does not increase in myocardial ischemia without necrosis; therefore, this is not true that HS-CRP is simply a reflection of myocard ischemia. Furthermore, myocardial necrosis increase circulating HS-CRP distinctively, also the extent of necrosis determines the response of HS-CRP (39).

Conclusively, higher levels of HS-CRP, sialic acid and Hcy in AMI patients indicated that these factors can be used as biomarkers in this disease.
Acknowledgements
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