Determination of Serum Homocysteine and Hypersensitive C-reactive Protein and Their Correlation with Premature Coronary Heart Disease

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ABSTRACT

Background: This study aims to investigate the correlation between premature coronary heart disease (pCHD) and both serum homocysteine (Hcy) and hypersensitive C-reactive protein (hs-CRP).

Methods: A total of 170 patients with pCHD were enrolled in this study from June 2014 to April 2016 (including 52 patients with stable angina pectoris [SAP], 70 patients with unstable angina pectoris [UAP], and 48 patients with acute myocardial infarction [AMI]), together with 105 healthy controls (CON) selected at the same period, to observe the changes of Hcy and hs-CRP in CHD patients and those with different types of CHD.

Results: The levels of serum Hcy and hs-CRP in group pCHD were significantly higher than in group CON (< .05). The levels of Hcy and hs-CRP in group AMI were significantly higher than in group UAP and group SAP (< .05). The changes of serum Hcy and hs-CRP were significantly higher in patients with multi-vascular lesions and dual-vascular lesions than in those with single-vascular lesion (< .05).

Conclusion: The levels of serum Hcy and hs-CRP in CHD patients are positively correlated with the severity of CHD, which increase with the increase of lesion count. The combined detection of Hcy and hs-CRP can initially reflect the severity of coronary artery, thus better guiding treatment and predicting prognosis.

INTRODUCTION

Coronary atherosclerotic heart disease (CHD) has increased in recent years, and its onset age tends toward younger people. Atherosclerosis and plaque rupture are its pathological basis. Studies have shown that homocysteine (Hcy) is an independent risk factor for CHD, which has significant atherogenic effects [Schroecksnadel 2010]. Chronic inflammatory response is also involved in the progression of atherosclerosis, and hypersensitive C-reactive protein (hs-CRP) is an important inflammatory factor for atherosclerosis [Devaraj 2009; Libby 2010; Weber 2011]. Animal experiments have shown that Hcy upregulates the expression of hs-CRP in the vascular smooth muscles by oxidative stress and cell proliferation. Hcy and CRP have interactions in atherosclerosis [Pang 2014; Pang 2015]. Clinical trials have shown that the levels of CRP and IL-6 in patients with high hcyemia are significantly higher than in healthy people [Holven 2006], and Hcy is positively correlated with such inflammatory indexes as CRP and complement 4 [Li 2015]. Clinical studies have shown that the combination of Hcy and hs-CRP can better predict the clinical prognosis of acute cerebral infarction than hs-CRP alone [Gong 2013]. Cross-sectional studies have shown that Hcy and hs-CRP can better predict the progression and prognosis of perforator artery (BAD) cerebral infarction [Men 2013]. However, the conclusion of combining Hcy and hs-CR in the same CHD patient is still not entirely consistent. In this study, we analyzed the changes of Hcy and hs-CRP in patients with pCHD and healthy controls, and compared the concentrations of Hcy and hs-CRP in patients with different severities of CHD, aiming to explore the correlation of serum Hcy and hs-CRP with pCHD and to evaluate their clinical values in predicting the severity of CHD.

MATERIALS AND METHODS

Subjects

A total of 170 patients with CHD were enrolled from June 2014 to April 2016, including 52 patients with stable angina pectoris (SAP), 70 patients with unstable angina pectoris (UAP), and 48 patients with acute myocardial infarction (AMI). A total of 105 healthy subjects were selected as the control group during the same period. Exclusion criteria were malignant tumors, autoimmune diseases, acute/chronic infections, trauma, liver/brain/kidney/endocrine/other cardiovascular disease. Subjects were not given folic acid, vitamin B, and drugs that might affect the metabolism of Hcy, such as methotrexate, phenytoin, and theophylline within 2 weeks before admission. The CHD patients were subdivided into group Single (55 patients with single-vascular lesion), group Double (53 patients with dual-vascular lesions), and group Multiple (62 patients with multi-vascular lesions). The comparison of general clinical data showed no significant difference in the age and smoking history between the two groups (P > .05), but the two groups showed statistical significance in diabetes and triglycerides (P < .05) (Table 1). This study was conducted in accordance with the Declaration of Helsinki.
This study was conducted with approval from the Ethics Committee of Zhengzhou University. Written informed consent was obtained from all participants.

**Determination of Hcy and hs-CRP**

3-5 mL of fasting venous blood was collected from each subject, followed by 10-min centrifugation at 3000 r/min to separate the serum, and then completion of detection was done within 2 h. Hcy was tested using the cyclophorase method, and hs-CRP was tested by immunoturbidimetry; all the reagents, calibration fluid, and quality control standards were provided by Beijing Reegen BioTech, and all tests were performed using one Olympus AU2700 automatic biochemical analyzer (Japan), strictly in accordance with the operating instructions or standard operating procedures.

**Evaluation of Severity of CHD Lesions**

Coronary angiography was performed using the Judkins method [Plank 2016]. The coronary artery lesions were observed from the conventional projection view. The angiographic images were analyzed by two experienced cardiovascular physicians for evaluating stenosis in the left main branch, left anterior descending branch, left circumflex branch, right coronary artery, and their primary branches. Angiographic stenosis ≥50% in one, two, or three major coronary arteries was defined as single, dual, or triple lesions.

**Statistical Analysis**

SPSS 17.0 software was used for statistical analysis; the measurement data were expressed as mean ± standard deviation and tested using Student t test; count data were tested using the Pearson chi-square test, with P < .05 considered statistically significant.

**RESULTS**

**Comparison of Hcy and hs-CRP in Group pCHD and Group CON**

The Hcy and hs-CRP levels in group pCHD were significantly higher than in group CON (P < .01; Table 2).

**Comparison of Observation Indexes among Groups with Different CHD**

The Hcy and hs-CRP levels in group AMI and group UAP were significantly higher than in group SAP (P < .05; Table 3).

**Correlation of Severity of CHD with Levels of Hcy and hs-CRP**

Compared with group CON, the Hcy and hs-CRP levels in patients with single, dual, or triple CHD lesions were significantly higher (P < .05). The comparison among the groups with different CHD showed that the Hcy and hs-CRP levels were significantly higher in patients with multi-vascular lesions and dual-vascular lesions than in those with single-vascular lesion (P < .05; Table 4).

**DISCUSSION**

This study shows that the Hcy and hs-CRP levels in group pCHD were significantly higher than in group CON; the levels of Hcy and hs-CRP in group AMI and UAP were higher than in group SAP; and the levels of Hcy and hs-CRP in patients with multi- or dual-vascular lesions were significantly higher than in those with single-vascular lesion, indicating that Hcy is related to the severity of CHD. Clinical studies have shown that serum markers such as Hcy are associated with the severity of CHD lesions [Feng 2016]. Another study showed that the Hcy level in 79.1% of CHD patients was higher than 15.0 µmol/L, but that in only 5% of patients with non-coronary heart disease was it above 15.0 µmol/L. Moreover, 66% of patients with SAP, 81.9% of patients with UAP, and 93.15% of patients with AMI showed Hcy higher than 15.0 µmol/L [Liu 2015]. This may be due to the fact that the higher the Hcy level, the more severe the oxidative stress reaction-resulted vascular endothelial damage and dysfunction [Steed 2011].

CRP is a simple and reliable predictor of CHD, and epidemiological meta-analyses have shown that CRP >3.0 mg/dL increases the risk of CHD by 1.6 times than that of <1.0 mg/
Table 3. Comparison of Hcy and hs-CRP Levels among Groups with Different CHD

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Hcy (ummol/L)</th>
<th>hs-CRP (ml/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAP</td>
<td>52</td>
<td>14.42 ± 3.76</td>
<td>9.32 ± 2.78</td>
</tr>
<tr>
<td>UAP</td>
<td>70</td>
<td>18.32 ± 4.17*</td>
<td>16.54 ± 4.27*</td>
</tr>
<tr>
<td>AMI</td>
<td>48</td>
<td>29.16 ± 6.94*</td>
<td>29.96 ± 8.16*</td>
</tr>
</tbody>
</table>

*Compared with SAP, P < .05.

Table 4. Comparison of Hcy and hs-CRP Levels among Groups with Different CHD

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>HCY (ummol/L)</th>
<th>hs-CRP (ml/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CON</td>
<td>105</td>
<td>8.11 ± 2.42*</td>
<td>2.33 ± 0.49*</td>
</tr>
<tr>
<td>Single</td>
<td>55</td>
<td>21.26 ± 4.38†</td>
<td>10.87 ± 3.26†</td>
</tr>
<tr>
<td>Dual</td>
<td>53</td>
<td>26.87 ± 5.96</td>
<td>21.6 ± 4.58</td>
</tr>
<tr>
<td>Triple</td>
<td>62</td>
<td>27.02 ± 4.17</td>
<td>25.96 ± 7.46</td>
</tr>
</tbody>
</table>

*Compared with Group CON, P < .05.†Compared with Group Single, P < .05.

dL [Buckley 2009]. CRP is significantly elevated in patients with severe UAP and can suggest poor prognosis [Liuzzo 1994; Strang 2014]. Significantly elevated CRP after myocardial infarction is associated with poor prognosis, including heart failure, cardiac death, or heart rupture [Pietilä 1996; Suleiman 2003; Suleiman 2006]. Recent studies have shown that CRP genotypes are related to the incidence of CHD [Hernández-Díaz 2015]. This study shows that CRP is associated with the severity of CHD, and that patients with AMI or UAP have significantly increased CRP levels compared to those with SAP, and CRP levels in patients with triple- and dual-vascular CHD are significantly higher than in those with single-vascular lesion.

Hcy and CRP are both predictors of CHD, and the data in this study show that the combination of Hcy and CRP can more accurately reflect the severity of CHD and coronary artery disease. The levels of Hcy and CRP in group AMI were significantly higher than in those in group SAP, and CRP levels in patients with triple- and dual-vascular CHD were significantly higher than in those with SAP.

REFERENCES


