Influence of helicobacter pylori infection on plaque property of patients with coronary heart disease and its correlation with inflammatory response and oxidative stress response

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ABSTRACT

Objective: To study the influence of helicobacter pylori (HP) infection on plaque property of patients with coronary heart disease and its correlation with inflammatory response and oxidative stress response. Methods: Patients who underwent coronary CTA examination and were diagnosed with coronary heart disease in Central Hospital of China National Petroleum Corporation between March 2015 and August 2017 were selected as the research subjects, 14C urea breath test was used to judge the HP infection, coronary CTA examination was used to judge coronary atheromatous plaque properties, and serum specimens were collected to determine inflammatory response indexes and oxidative stress response indexes. Results: The proportion of soft plaques in HP positive patients was significantly higher than that in HP negative patients whereas the proportion of fibrous plaques and calcified plaques were significantly lower than those in HP negative patients; serum SIRT1 and SOD contents of coronary heart disease patients with soft plaques were significantly lower than those of patients with fibrous plaques and calcified plaques whereas MPO, MDA and ET-1, Gal-3, MIP-1α, IL-17 and sICAM1 contents were significantly higher than those of patients with fibrous plaques and calcified plaques; serum SIRT1 and SOD contents of coronary heart disease patients with fibrous plaques were significantly lower than those of patients with calcified plaques whereas MPO, MDA, ET-1, Gal-3, MIP-1α, IL-17 and sICAM1 contents were significantly higher than those of patients with calcified plaques. Serum SIRT1 and SOD contents of patients with HP positive coronary heart disease were significantly lower than those of patients with HP negative coronary heart disease whereas MPO, MDA, ET-1, Gal-3, MIP-1α, IL-17 and sICAM1 contents were significantly higher than those of patients with HP negative coronary heart disease. Conclusion: Helicobacter pylori infection can reduce the plaque stability and activate the inflammatory response and oxidative stress response in patients with coronary heart disease.

1. Introduction

Coronary heart disease is the most common clinical cardiovascular system disease, it is basically characterized by coronary atherosclerotic plaque formation and will further cause myocardial ischemic damage, and serious cases may cause myocardial infarction and induce malignant arrhythmia and heart failure[1]. Coronary atherosclerotic plaque formation process involves many factors and many links, inflammatory response and oxidative stress response are considered as the important pathological changes throughout each link of the development and change of atheromatous plaque[2,3], but the mechanism causing excessive inflammation and oxidative stress activation is still not clear. Helicobacter pylori (HP) infection is a risk factor for a variety of gastrointestinal diseases, more and more studies in recent years have found that HP infection is also involved in endothelial injury and atheromatous plaque formation[4,5], but it is yet to be clarified whether HP infection affects the inflammation and oxidative stress in the process of coronary atherosclerosis. In the following studies, we specifically analyzed the effects of helicobacter pylori infection on the plaque properties of patients with coronary heart disease and its correlation with inflammatory response and oxidative stress response.
2. General information and research methods

2.1 General information of research subjects

Patients who underwent coronary CTA examination and were diagnosed with coronary heart disease in Central Hospital of China National Petroleum Corporation between March 2015 and August 2017 were selected as the research subjects, and all the patients conformed to the indications of coronary CTA and were diagnosed with coronary heart disease according to the results of CTA examination. Patients who were with the history of myocardial infarction and cerebral infarction and those who were combined with current infection and used antibiotics and immune preparations 3 months prior to inclusion were excluded. A total of 78 patients were enrolled, including 42 male cases and 36 female cases that were 51-69 years old.

2.2 Helicobacter pylori infection testing

After fasting for 12 h, the enrolled patients with coronary heart disease received h. pylori infection test, took oral 14C urea breath test capsule, then sat still for 15 min and breathed to the respiration card, H. pylori tester was used to test the respiration card, and the results were referred to judge the h. pylori infection.

2.3 Coronary plaque property evaluation

After fasting for 12 h, the enrolled patients with coronary heart disease received coronary CTA inspections and took metoprolol orally before inspection, the contrast agent was intravenously injected at 4 mL/s rate, the scanning was done after 45 s, the scan images were obtained for reconstruction, coronary plaque Ct value was detected, the plaques with Ct value <60 HU were soft plaques, those with Ct value between 60-130 HU were fibrous plaques and those with Ct value 130 HU were calcified plaque.

2.4 Serum index detection

Before coronary CTA examination, 3-5 mL of cubital venous blood was collected, let stand for the natural coagulation and then centrifuged to separate the serum, the enzyme-linked immunosorbent assay kit was used to determine Gal-3, MIP-1α, IL-17, sICAM1, SIRT and ET-1, and radioimmunoassay kits were used to determine SOD, MPO and MDA contents.

2.5 Statistical methods

SPSS 20.0 software was used to input data, the count data between two groups were by chi-square test and the measurement data were by t test, the measurement data among three groups were by variance analysis and P<0.05 meant that the differences were statistically significant.

3. Results

3.1 Effect of HP infection on plaque properties

There were 35 cases of HP positive patients, including 14 cases with soft plaque, 12 cases with fibrous plaque and 9 cases with calcified plaque; there were 43 cases of HP negative patients, including 7 cases with soft plaque, 20 cases with fibrous plaque and 16 cases with calcified plaque. After chi-square test, the proportion of soft plaques in HP positive patients was significantly higher than that in HP negative patients whereas the proportion of fibrous plaques and calcified plaques were significantly lower than those in HP negative patients.

3.2 Inflammatory response indexes in coronary heart disease patients with different plaque properties and their correlation with HP infection

Analysis of serum inflammatory response indexes Gal-3 (pg/mL), MIP-1α (pg/mL), IL-17 (pg/mL) and sICAM1 (ng/mL) among coronary heart disease patients with different plaque properties was as follows: serum Gal-3, MIP-1α, IL-17 and sICAM1 contents of coronary heart disease patients with soft plaques were significantly higher than those of patients with fibrous plaques and calcified plaques; serum Gal-3, MIP-1α, IL-17 and sICAM1 contents of coronary heart disease patients with fibrous plaques were significantly higher than those of patients with calcified plaques. Analysis of the correlation of serum inflammatory response indexes Gal-3, MIP-1α, IL-17 and sICAM1 with HP infection in patients with coronary heart disease was as follows: serum Gal-3, MIP-1α, IL-17 and sICAM1 contents of patients with HP positive coronary heart disease were significantly higher than those of patients with HP negative coronary heart disease.

<table>
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<tr>
<th>Table 1.</th>
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<tr>
<td>Comparison of serum inflammatory response indexes among coronary heart disease patients with different plaque properties</td>
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<td>Plaque property</td>
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<tr>
<td>Soft plaque</td>
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<td>Fibrous plaque</td>
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<td>Calcified plaque</td>
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*: compared with calcified plaque, P<0.05; †: compared with fibrous plaque, P<0.05.

<table>
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<th>Table 2.</th>
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<td>Correlation between serum inflammatory response indexes and HP infection in patients with coronary heart disease.</td>
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<td>HP infection</td>
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<td>HP positive</td>
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3.3 Oxidative stress response indexes in coronary heart disease patients with different plaque properties and their correlation with HP infection

Analysis of serum oxidative stress response indexes SIRT1 (ng/mL), SOD (U/mL), MPO (U/mL), MDA (μmol/L) and ET-1 (pg/mL) among coronary heart disease patients with different plaque properties was as follows: serum SIRT1 and SOD contents of coronary heart disease patients with soft plaques were significantly lower than those of patients with fibrous plaques and calcified plaques whereas MPO, MDA and ET-1 contents were significantly higher than those of patients with fibrous plaques and calcified plaques; serum SIRT1 and SOD contents of coronary heart disease patients with fibrous plaques were significantly lower than those of patients with calcified plaques whereas MPO, MDA and ET-1 contents were significantly higher than those of patients with calcified plaques. Analysis of the correlation of serum oxidative stress response indexes SIRT1, SOD, MPO, MDA and ET-1 with HP infection in patients with coronary heart disease was as follows: serum SIRT1 and SOD contents of patients with HP positive coronary heart disease were significantly lower than those of patients with HP negative coronary heart disease whereas MPO, MDA and ET-1 contents were significantly higher than those of patients with HP negative coronary heart disease whereas MPO, MDA and ET-1 contents were significantly higher than those of patients with HP positive coronary heart disease. This indicates that HP infection can significantly affect the nature of atheromatous plaque, reduce the plaque stability and promote the development of coronary heart disease in patients with CHD.

The activation of inflammatory response in the local endarterium can recruit macrophages and devour ox-LDL to form foam cells and then participate in the formation of atheromatous plaque. Gal-3 is an inflammatory mediator with strong pro-inflammatory activity, which can not only promote the macrophages to devour ox-LDL and form foam cells, but can also accelerate the degradation of plaque fibrous cap and reduce plaque stability[12,13]; MIP-1 is a kind of chemokine that can make multiple inflammatory cells activated and infiltrate in the atheromatous plaque, promote the inflammation amplification and accelerate the atheromatous plaque process[14]; IL-17 is a cytokine produced by Th17 cells, which has pro-inflammatory activity and chemotactic activity, and can promote the atheromatous plaque development and its property change[15]; sICAM1 is a kind of adhesion molecule that can mediate the adhesion of inflammatory cells within the plaque and activate the inflammatory response[16]. Analysis of the changes in the above inflammatory response indicators in the serum of coronary heart disease patients with different plaque properties in the study showed that the more unstable the plaque properties, the higher the serum Gal-3, MIP-1α, IL-17 and sICAM1 contents. This indicates that the activation of inflammatory response and the secretion of inflammatory mediators are closely related to the changes in the properties of coronary atheromatous plaque. In order to further clarify whether HP infection affected the inflammation in the process of atheromatous plaque property change, the inflammation indexes in the serum of patients with HP positive coronary heart disease was as follows: serum SIRT1 and SOD contents of patients with HP positive coronary heart disease were significantly lower than those of patients with HP negative coronary heart disease whereas MPO, MDA and ET-1 contents were significantly higher than those of patients with HP negative coronary heart disease whereas MPO, MDA and ET-1 contents were significantly higher than those of patients with HP positive coronary heart disease. This indicates that HP infection can significantly affect the nature of atheromatous plaque, reduce the plaque stability and promote the development of coronary heart disease in patients with CHD.

4. Discussion

Coronary heart disease is a common clinical cardiovascular system disease, atherosclerosis is its pathological physiological characteristic, and atheromatous plaque formation process involves inflammation, oxidative stress and many other pathological links[6,7]. HP infection is a newly discovered risk factor for cardiovascular and cerebrovascular events, persistent infection of HP can participate in the formation and development of arterial atheromatous plaque through multiple pathological links: (1) the HP infection can directly act on vascular endothelium and cause endothelial function damage, which makes the platelets, inflammatory cells and so on accumulate in local area with endothelial injury and form atheromatous plaque[8,9]; (2) HP infection can stimulate the smooth muscle cell proliferation, cause the arterial lumen stenosis and aggravate the severity of atheromatous plaque[10]; (3) HP infection can affect the blood lipid metabolism in vivo and promote LDL-C to deposit in endarterium and form atheromatous plaque[11]. In recent years, the occurrence of coronary heart disease and HP infection have received more and more attention, the risk of coronary heart disease increases in patients with HP infection, but it is still not clear about the relationship between coronary atherosclerotic plaque property changes and HP infection. In the study, in order to define the influence of HP infection on the changes in the progression of coronary heart disease, the coronary atherosclerotic plaque properties in patients with HP infection were analyzed, and the results showed that the proportion of soft plaque was higher whereas the proportion of fibrous plaque and calcified plaque were lower in patients with HP positive coronary heart disease. This indicates that HP infection can significantly affect the nature of atheromatous plaque, reduce the plaque stability and promote the development of coronary heart disease in patients with CHD.

Table 3.
Comparison of serum oxidative stress response indexes among coronary heart disease patients with different plaque properties.

<table>
<thead>
<tr>
<th>Plaque property</th>
<th>n</th>
<th>SIRT1 (ng/mL)</th>
<th>SOD (U/mL)</th>
<th>MPO (U/mL)</th>
<th>MDA (μmol/L)</th>
<th>ET-1 (pg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soft plaque</td>
<td>21</td>
<td>0.31±0.04</td>
<td>58.64±7.61</td>
<td>23.48±4.82</td>
<td>10.28±1.47</td>
<td>139.52±17.58</td>
</tr>
<tr>
<td>Fibrous plaque</td>
<td>32</td>
<td>0.45±0.07</td>
<td>79.65±10.24</td>
<td>17.27±2.06</td>
<td>7.18±0.94</td>
<td>98.34±11.27</td>
</tr>
<tr>
<td>Calcified plaque</td>
<td>25</td>
<td>0.70±0.10</td>
<td>98.34±11.25</td>
<td>11.25±1.84</td>
<td>5.76±0.78</td>
<td>75.66±9.57</td>
</tr>
</tbody>
</table>

*: compared with calcified plaque, P<0.05; †: compared with fibrous plaque, P<0.05.

Table 4.
Correlation between serum oxidative stress response indexes and HP infection in patients with coronary heart disease.

<table>
<thead>
<tr>
<th>HP infection</th>
<th>n</th>
<th>SIRT1 (ng/mL)</th>
<th>SOD (U/mL)</th>
<th>MPO (U/mL)</th>
<th>MDA (μmol/L)</th>
<th>ET-1 (pg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HP positive</td>
<td>35</td>
<td>0.28±0.04</td>
<td>51.25±6.48</td>
<td>25.02±4.98</td>
<td>11.89±1.73</td>
<td>147.61±19.39</td>
</tr>
<tr>
<td>HP negative</td>
<td>45</td>
<td>0.74±0.11</td>
<td>107.58±12.85</td>
<td>9.58±1.37</td>
<td>5.12±0.71</td>
<td>70.24±9.25</td>
</tr>
<tr>
<td>t</td>
<td>17.589</td>
<td>11.385</td>
<td>14.589</td>
<td>12.093</td>
<td>11.127</td>
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<tr>
<td>P</td>
<td>&lt;0.05</td>
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</table>
with HP infection coronary heart disease were analyzed in the study, and the results showed that serum Gal-3, MIP-1α, IL-17 and sICAM1 contents were higher in patients with HP positive coronary heart disease. This indicates that HP infection can significantly increase the secretion of inflammatory mediators and activate the inflammatory response in patients with coronary heart disease, and then affect the stability of the plaque through the changes in inflammatory response.

The formation and property change of atheromatous plaque also involve the damage of endothelial structure and function, and overactivation of oxidative stress is an important link in endothelial injury. MPO is an important catalytic enzyme in the body that catalyzes oxygen free radical generation and mediate oxidative stress reaction activation, and high expression of MPO can increase the production of oxygen free radicals and act on endothelial cells, which can on the one hand, cause the increased formation of lipid oxidation product MDA, and on the other hand, cause the increased formation of endothelial damage marker ET-1[17,18]. SIRT1 and SOD are the antioxidants with protective effect in the process of endothelial oxidative damage, the former can antagonize NF-κB activation, and the latter can remove oxygen free radicals, and thus cause the reduced production of oxygen free radicals and the latter can remove oxygen free radicals by reduction reaction[19,20]. Analysis of the changes in above oxidative stress indicators in serum of coronary heart disease patients with different plaque properties in the study showed that the more unstable the plaque properties, the lower the serum antioxidants SIRT1 and SOD contents, the higher the oxidation products MPO, MDA and ET-1 contents. This indicates that the activation of oxidative stress response and the oxidative damage of endothelial cells are closely related to the changes in the properties of the coronary atheromatous plaque. In order to further clarify whether HP infection affected the oxidative stress reaction in the process of atheromatous plaque property change, the serum oxidative stress indicators in patients with HP infection coronary heart disease were analyzed in the study, and the results showed that serum SIRT1 and SOD contents were lower whereas MPO, MDA and ET-1 contents were higher in patients with HP positive coronary heart disease. This indicates that HP infection can significantly activate the oxidative stress response and cause the endothelial cell injury in patients with coronary heart disease, and then affect the stability of plaque through the changes in oxidative stress response. HP infection can reduce the plaque stability in patients with coronary heart disease; increasing the inflammatory mediator secretion and oxygen free radical generation and activating the inflammatory response and oxidative stress response are the relevant pathological links of HP infection to affect plaque stability.

References