Analysis of thrombelastography in type 2 diabetes patients complicated with angina pectoris of coronary heart disease and its correlation with disease severity

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Objective: To analyze the thrombelastography parameters in type 2 diabetes patients complicated with angina pectoris of coronary heart disease and their correlation with disease severity. Methods: 30 cases of healthy volunteers, 30 cases of patients with simple angina pectoris of coronary heart disease (CHD) and 30 cases of type 2 diabetes patients complicated with angina pectoris of coronary heart disease were selected for study. Thrombelastography parameters R value, K value, $\alpha$ angle and MA value as well as inflammation-associated molecules YKL-40 and NK-kB expression were detected. Results: R values and K values of simple CHD group and diabetes complicated with CHD group were lower than those of control group, and $\alpha$ angle and MA values were higher than those of control group; R values and K values of diabetes complicated with CHD group were lower than those of simple CHD group, and $\alpha$ angle and MA values were higher than those of simple CHD group; R values and K values of 2 branch lesions group and 3 branch lesions group were lower than those of 1 branch lesion group, and $\alpha$ angle and MA values as well as YKL-40 and NK-kB contents were higher than those of 1 branch lesion group; R values and K values of 3 branch lesions group were lower than those of 2 branch lesions group, and $\alpha$ angle and MA value were positively correlated with YKL-40 and NK-kB contents. Conclusions: Thrombelastography parameters in type 2 diabetes patients complicated with angina pectoris of coronary heart disease are significantly abnormal, and R value, K value, $\alpha$ angle and MA value can reflect disease severity and inflammation degree.

1. Introduction

Angina pectoris of coronary heart disease (CHD) is the most common disease of cardiovascular system, and accurately assessing the condition and implementing treatment and intervention can stabilize the condition and prevent disease progression into the acute phase of CHD such as unstable angina and myocardial infarction, etc. Type 2 diabetes is currently known the most specific risk factor of angina pectoris of CHD and diabetic patients have chronically high blood glucose level, thereby participating in coronary artery thrombosis and stenosis process through affecting lipid metabolism, blood coagulation, inflammation and endothelial function, etc[1]. Related studies believe that long-term poor control of blood glucose level will seriously affect the prognosis of patients with angina pectoris of CHD and increase the incidence of serious complications such as myocardial infarction and heart failure, etc[2].
patients complicated with angina pectoris of CHD can provide basis for the development of treatment options. Thrombelastography (TEG) analyzer is a newly developed instrument for the evaluation of coagulation function[3]. In the following research, thrombelastography parameters in type 2 diabetes patients complicated with angina pectoris of CHD and their correlation with disease severity were analyzed.

2. Information and methods

2.1. Case information

Cases were from Outpatient Department, ward and medical center of our hospital from May 2012 to June 2014, and 30 cases of healthy volunteers, 30 cases of patients with simple angina pectoris of CHD and 30 cases of type 2 diabetes patients complicated with angina pectoris of CHD were randomly selected for study. Healthy volunteers were confirmed by medical examination without diabetes or cardiovascular diseases; patients with simple angina pectoris of CHD were diagnosed with stable angina pectoris and excluded of the diagnosis of type 2 diabetes; type 2 diabetes patients complicated with angina pectoris of CHD met the diagnosis of both type 2 diabetes and angina pectoris of CHD.

2.2. Detection of TEG parameters

Fasting peripheral venous blood of subjects was collected, 0.109 mol/L of ACD was added for coagulation and TEG-500 thrombelastography instrument of Haemoscope Company was used to detect thrombus maximum amplitude (MA), blood clotting reaction time (R), kinetics of clot development (K) and blood clot formation rate (α angle).

2.3. Detection of inflammation–associated molecules

Fasting peripheral venous blood of subjects was collected, mononuclear cells were separated and then transferred into flow cytometry reaction tubes, YKL-40 and NK-kb monoclonal antibodies were added respectively, and after 20 min of incubation, flow cytometer was used to analyze YKL-40 and NK-kb expression.

2.4. Statistical processing

SPSS19.0 software was used for the input and statistical processing of detected data, measurement data analysis was by variance analysis and correlation analysis was by Pearson correlation test. P<0.05 indicated that differences had statistical significance.

3. Results

3.1. TEG parameters in simple CHD group and diabetes complicated with CHD group

Variance analysis showed that there were differences in TEG parameters R values, K values, α angle and MA values among three groups; pair-wise comparison by LSD-t test showed that R values and K values of simple CHD group and diabetes complicated with CHD group were lower than those of control group, and α angle and MA values were higher than those of control group; R values and K values of diabetes complicated with CHD group were lower than those of simple CHD group, and α angle and MA values were higher than those of simple CHD group (Table 1).

3.2. TEG parameters in patients with different severity of diabetes complicated with CHD

Variance analysis showed that there were differences in TEG parameters R values, K values, α angle and MA values among patients with different severity of diabetes complicated with CHD; pair-wise comparison by LSD-t test showed that R values and K values of 2 branch lesions group and 3 branch lesions group were lower than those of 1 branch lesion group, and α angle and MA values were higher than those of 1 branch lesion group; R values and K values of 3 branch lesions group were lower than those of 2 branch lesions group, and α angle and MA values were higher than those of 2 branch lesions group (Figure 1).

![Figure 1. TEG parameters in patients with different severity of diabetes complicated with coronary heart disease.](image)

Table 1
Comparison of TEG parameters among three groups.

<table>
<thead>
<tr>
<th>Group</th>
<th>Case No.</th>
<th>TEG parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>R value (min)</td>
</tr>
<tr>
<td>Control group</td>
<td>30</td>
<td>7.48±0.83</td>
</tr>
<tr>
<td>Simple CHD group</td>
<td>30</td>
<td>6.03±0.67</td>
</tr>
<tr>
<td>Diabetes + CHD group</td>
<td>30</td>
<td>5.02±0.58</td>
</tr>
<tr>
<td>F</td>
<td></td>
<td>6.822</td>
</tr>
<tr>
<td>P</td>
<td></td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>
3.3. Inflammation-associated molecules

YKL-40 contents in peripheral blood mononuclear cells of 1 branch lesion group, 2 branch lesions group and 3 branch lesions group were (2.5±0.3)%, (13.0±1.4)% and (23.6±3.1)% respectively and NK-kB contents were (3.3±0.4)%, (33.7±4.1)% and (38.4±4.1)% respectively. Statistical analysis showed that YKL-40 and NK-kB contents of 2 branch lesions group and 3 branch lesions group were higher than those of 1 branch lesion group; YKL-40 and NK-kB contents of 3 branch lesions group were higher than those of 2 branch lesions group (Figure 2).

3.4. Correlation of TEG parameters with inflammation-associated molecules

Pearson correlation test was used to analyze the correlation of TEG parameters R value, K value, α angle and MA value with inflammation-associated molecules YKL-40 and NK-kB, and detailed results were shown in Table 2. R value and K value were negatively correlated with YKL-40 and NK-kB contents in peripheral blood, and α angle and MA value were positively correlated with YKL-40 and NK-kB contents in peripheral blood.

<table>
<thead>
<tr>
<th>Index</th>
<th>Regression coefficient b</th>
<th>Correlation coefficient r</th>
<th>Statistics P</th>
<th>Regression coefficient b</th>
<th>Correlation coefficient r</th>
<th>Statistics P</th>
</tr>
</thead>
<tbody>
<tr>
<td>R value</td>
<td>-0.894</td>
<td>-0.774</td>
<td>&lt;0.05</td>
<td>-1.284</td>
<td>-0.805</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>K value</td>
<td>-1.415</td>
<td>-0.834</td>
<td>&lt;0.05</td>
<td>-1.396</td>
<td>-0.793</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>α angle</td>
<td>0.961</td>
<td>0.781</td>
<td>&lt;0.05</td>
<td>1.145</td>
<td>0.736</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>MA value</td>
<td>1.196</td>
<td>0.703</td>
<td>&lt;0.05</td>
<td>0.882</td>
<td>0.695</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

4. Discussion

TEG analyzer is an instrument monitoring platelet aggregation, blood coagulation, fibrinolysis and a series of dynamic processes[4]. The basis of TEG detection is that in vivo coagulation process will eventually form blood clots and the physical properties of blood clots can reflect whether the body has normal blood coagulation function. Therefore, detecting the formation rate of blood clots as well as the ultimate strength and stability of blood clots can reflect body's coagulation status[5]. The common parameters of TEG examination are as follows[6,7]: R value reflects the starting time of blood coagulation process; K value and α angle reflect formation time and rate of blood clots respectively, and are mainly influenced by platelet function; MA value reflects the blood clot strength and stability, and is mainly influenced by fibrinogen and platelet contents.

Current studies about TEG-associated parameters mainly focus on patients with cerebral infarction and abnormal blood coagulation[8,9], and there is still lack of research about the value of TEG analysis in evaluation of the condition in patients with CHD. Type 2 diabetes is one of the important risk factors of CHD[10]. Related studies believe that the severity of coronary lesions in CHD patients complicated with diabetes is heavier, the prognosis is poorer, and the risk of myocardial infarction and heart failure is higher[11], and causes of the phenomena may be coagulation disorders caused by high blood glucose, disturbance of lipid metabolism, endothelial dysfunction, activation of oxidative stress response and systemic low inflammatory state[12]. Among them, abnormal coagulation is closely related to the occurrence of cardiovascular events.

The research used TEG analyzer to detect blood coagulation function in simple CHD group and diabetes complicated with CHD group, and analysis of results showed that R values and K values of simple CHD group and diabetes complicated with CHD group were lower than those of control group, and α angle and MA values were higher than those of control group, indicating that there was coagulation hyperfunction in both simple CHD patients and diabetes patients complicated with CHD. Further comparison of TEG parameters between simple CHD group and diabetes complicated with CHD group showed that R values and K values of diabetes complicated with CHD group were lower than those of simple CHD group, and α angle and MA values were higher than those of simple CHD group, indicating that coagulation hyperfunction in diabetes patients complicated with CHD was more significant than that in simple CHD patients. Above analysis indicated that coagulation hyperfunction was one of the ways for diabetes to increase the
risk of CHD, and coexisting of diabetes can cause coagulation hyperfunction, manifested as changes of TEG parameters. Based on this, TEG parameters in patients with different severity of diabetes complicated with CHD were analyzed, and results showed that the more the number of coronary artery lesions, the more significant the changes of TEG parameters, manifested as decreased R value and K value as well as increased α angle and MA value. This indicated that abnormality of blood coagulation was associated with the severity of diabetes complicated with CHD, and the more the number of lesions, the more significant the abnormality of blood coagulation.

Inflammation is a common pathological feature of diabetes and CHD, both diseases are chronic and subclinical inflammatory, and variety of inflammation-associated molecules are involved in the inflammation process[13]. Nuclear transcription factor NK-κB is body’s hub to regulate inflammation, is activated when stimulated by high glucose, and increases the generation of a variety of inflammatory mediators[14]. YKL-40, also known as human cartilage diabetes 39, is an inflammatory mediator regulated by NK-κB, is synthesized and secreted by locally recruited mononuclear macrophages and neutrophils, and causes coronary artery stenosis and thrombosis by inducing endothelial dysfunction and promoting vascular smooth muscle proliferation[15,16]. Analysis of inflammation-associated molecule expression in peripheral blood of patients with different severity of diabetes complicated with CHD showed that the more the number of coronary artery lesions, the higher the YKL-40 and NK-κB contents in peripheral blood. Further analysis of the correlation between TEG parameters and inflammation showed that R value and K value were negatively correlated with YKL-40 and NK-κB contents, and α angle and MA value were positively correlated with YKL-40 and NK-κB contents, indicating that TEG parameters could not only reflect disease severity and coagulation hyperfunction degree but also accurately assess inflammation degree.

Based on above discussion, it can be concluded that thrombelastography parameters in type 2 diabetes patients complicated with angina pectoris of CHD are significantly abnormal, and R value, K value, α angle and MA value can reflect disease severity and inflammation degree.

References