Laboratory Research

Effect of Puerarin on the myocardial perfusion and ventricular wall motion in patients with acute coronary syndrome

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Objective The purpose of the present study was to investigate the effect of Puerarin (Pur) on the myocardial perfusion and ventricular wall motion in patients with acute coronary syndrome (ACS).

Methods Thirty-seven patients with ACS were randomly divided into two groups: conventional group (n=17, 11 men and 6 women, with a range of age from 32 to 80 years, and with a mean age 60.9±4.9 years) and Pur group (n=20, 12 men, 8 women, with a range of age from 40 to 76 years, and with a mean age 62.7±3.5 years). Course of treatment for all patients was 10 days. Real-time myocardial contrast echocardiography (RT-MCE) was applied to two groups before and after the therapy to evaluate myocardial microcirculation and ventricular wall motion by observing the change of myocardial perfusion index (MPI) and ventricular wall motion index (VWMI).

Results The level of MPI increased and VWMI decreased after 10 days of the therapy, which is significant difference between the Pur group and conventional group (P<0.05).

Conclusions Puerarin can increase the level of MPI and decrease the level of VWMI in patients with ACS. Myocardial microcirculation perfusion and ventricular wall motion could be improved probably in patients with ACS treated by Puerarin. (J Geriatr Cardiol 2008; 5: )

Key Words acute coronary syndrome; myocardial perfusion index; ventricular wall motion index; Puerarin

Patients and methods

Patients Thirty seven patients with ACS, including unstable angina pectoris (UAP) and acute myocardial infarction (AMI) patients, are hospitalized in Department of Cardiology, the affiliated hospital of Xuzhou Medical College from October, 2006 to March, 2007. On admission, thirty-seven patients with ACS were randomly divided into two groups: conventional treatment group and Pur treatment group. There were 17 patients in the conventional treatment group, including 11 men and 6 women. The range of age in this group was from 32 to 80 years, with a mean age of 60.9±4.9 years. The patients in this group were given the major medication including enteric-coated aspirin, low molecular heparin, statins, Β-adrenoceptor blockers, angiotensin-converting enzyme inhibitor, and nitrates and so on. There were 20 patients in the Pur treatment group, including 12 men and 8 women, and the range of age of this group was from 40 to 76 years, with a mean age of 62.7±3.5 years. Major medication used in this group including conventional treatment plus Pur 500mg intravenously every day. Pur was provided by Zhenda-Tianqin Corp. of Nanjing. Time course of treatment for all patients was 10 days. There had no significant difference existing in age and sex of patients between two groups (P>0.05). Diagnosis of AMI was according to diagnostic criteria coming from World Health Organization.
(WHO) in 1979, and diagnosis of UAP was according to diagnostic criteria coming from American College of Cardiology/American Heart Association (AHA/ACC) in 2002. At the same time, serious hepatic and renal disease, serious heart failure, malignant tumor, recent trauma and operation, hyperthermia, pregnancy, acute infection and rheumatic fever were excluded. General information of all selected patients was present in Table 1. No significant difference between age, sex, smoking, and hypertension was found between two groups (P > 0.05).

Table 1 Clinical characteristic of subjects

<table>
<thead>
<tr>
<th></th>
<th>Routine treatment</th>
<th>Pur treatment</th>
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</thead>
<tbody>
<tr>
<td>Age(Years)</td>
<td>60.9 ±6.4.9</td>
<td>62.7 ±3.5</td>
</tr>
<tr>
<td>Female/male</td>
<td>6/11</td>
<td>8/12</td>
</tr>
<tr>
<td>AMI/UAP</td>
<td>2/15</td>
<td>3/17</td>
</tr>
<tr>
<td>Smoking</td>
<td>6</td>
<td>9</td>
</tr>
<tr>
<td>Family history of CAD</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>10</td>
<td>12</td>
</tr>
<tr>
<td>Dysglycemia</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>Hypertension</td>
<td>10</td>
<td>13</td>
</tr>
</tbody>
</table>

Machine and machine settings

RT-MCE was performed in all patients by using the ultrasonoscope (HP5500 American Hewlett Packard Company). The frequency of the transducer (S3) was 1.0-3.0 MHZ. The mechanical index was 0.1. The emission frequency/receive frequency of the transducer was 1.8/3.6 MHZ. The real-time opacification mode of MCE and “ANGIO” energy display mode was chosen. The frame frequency was 14/S and the chroma gain was adjusted to 50%. The rest of machine settings were default values of the machine. The machine settings were kept constant throughout the study.

RT-MCE study

SonoVue, produced by the Italian Bracco Company, were utilized as contrast medium in patients. The dose of SonoVue was 59 mg per bottle. Before utilization, SonoVue were dissolved with Sodium Chloride (5ml) and oscillated according to the instruction. All patients for the study underwent infusion of SonoVue at 1ml/min with the venous duct (20 g) through the antecubital vein. After infusion of SonoVue (5ml), the douche was completed to the pipe with Sodium Chloride (5ml). When the myocardium was filled by enough constrast medium, flash echocardiography at a high mechanical index (1.6) was performed to destroy microbubbles in the myocardium and to observe replenishment at a high mechanical index (0.1). End-systolic frames up to 15 cardiac cycles after microbubble destruction were digitally captured in the 3 apical views (apical 4-, 2-, and 3-chamber views). All captured images were collected to cline loop and written to Magnetic Optic Disc for off-line analysis.

Image analysis

A semiquantitative scoring system and the American Society of Echocardiography 16-segment LV model were used to analyze images. Myocardial contrast echocardiography score (MCES) was defined as: 1=homogenous opacification, 0.5= reduced or heterogeneous opacification, and 0=minimal or absent contrast opacification. Ventricular wall motion sore (VWMS) was obtained from the proportionality (score for all segments/number of segments). The more MPI and the less VWMI was, the better myocardial perfusion and wall motion was. Conversely, the less MPI and the more VWMI was, the worse myocardial perfusion and wall motion was. Wall motion and MCE images were analyzed separately by two independent doctors of Department of Echocardiography who were blinded to clinical, angiographic, and other respective imaging data.

Statistical analysis

Mean±SD was used to describe the quantitative data. The paired t test was used to analysis the difference between before and after treatment in the same group. The group comparisons were made with the unpaired t test. The enumeration data were expressed as the rate. The group comparisons of rate were made with the χ²-test. Linear correlation analysis for the relation between two variances was used. A probability value was lower than 0.05 was considered statistically significant.

Results

RT-MCE was performed to 37 patients before and after therapy. After treatment, VWMI depressed significantly compared with the pretherapy in two groups, but MPI increased significantly (P < 0.05). Compared with the conventional group, VWMI depressed and MPI increased in Pur group. The results of RT-MCE were showed in Table 2 and Figure 1.
Discussion

Pur is the main effective constituent of the isoflavone in pueraria which belong to the kudzu group in the pulse family. The chemical name of Pur is 4, 7-dihydroxy radical-8-α-d-glucosyl-isoflavone, molecular formula is C_{21}H_{20}O_{9} and molecular weight is 416. One Japanese scholar found that Pur could expand coronary arteries and had anti-inflammatory effects in 1992. At present, many studies have suggested that Pur could expand coronary arteries and had anti-inflammatory effects in 1992. At present, many studies have suggested that Pur could inhibit the effect of the oxyradical actively, protect the blood vessel endothelium, protect myocardial cells, dilated coronary arteries, relieve the coronary artery spasm, and facilitate the formation of collateral circulation.\(^3,6\) Pur have the inhibitory effect to the platelet aggregation induced by adenosine diphosphate (ADP) in human and animals. It can increase the levels of prostacyclin (PGI) and high density lipoprotein (HDL), reduce thromboxane A2 (TXA2), relieve the coronary artery spasm, and inhibit the platelet aggregation by repairing endothelial cells, resulting in preventing the progression of disease in patients with ACS.\(^7\) From studies in vitro, Li et al confirmed that Pur could inhibit the expression and the activity of matrix metalloproteinase-9 (MMP-9) and secretion of TF by monocyte-derived macrophages (HMDM), stabilize the plaque, and improve the vulnerability of blood to a certain extent.\(^7\) Myocardial cells have autorhythmicity, conductivity, excitability and contractility. Maintaining the function of myocardial cells has the very important significance to improve the wall motion and the cardiac function. Guaranteeing the blood supply of myocardial cells is a key to maintaining myocardial cells function. In the present study, we observed that the perfusion of myocardial microcirculation and the wall systolic function improved obviously after the 10-day-course treatment (Puerarin injection 500mg per day). We presumed that the improvement of the myocardial microcirculation perfusion and the wall systolic function were due to protection of the integrity of blood vessel endothelium, dilation of blood vessels, antioxidation and protection of myocardial cells.

Studies for myocardial microcirculation are limited because of the complexity of microcirculation physiological mechanism and the restriction of intervention means. MCE can reinforce myocardium reecho by injecting acoustic
contrast. It is a new technology to evaluate the myocardial microcirculation. With the improvement of the acoustic contrast and the ultrasonic imaging method, the sensitivity and the specificity of MCE evaluating the myocardial microcirculation raise significantly. The application of RT-MCE is extensive in recent years. The ventricular wall motion can be observed simultaneously when the myocardial perfusion is observed in RT-MCE. Janardhanan et al. reported that MCE was superior to coronary arteriography (CAG) in judging the stenosis of vessels and the size or the range of collateral circulation. Some researchers discovered that the speed and the quantity of myocardial blood flow was lower in patients with Syndrome X than the normal individuals when they used RT-MCE to evaluate the myocardial microcirculation. The utilization of MCE in estimating the myocardial microcirculation perfusion and ventricular wall motion with RT-MCE by calculating MPI and VWMI, and gain a relativity ideal consequence.

RT-MCE was finished successfully in all patients in this study. During RT-MCE, headache, skin rash, palmus and other adverse effects were not observed in patients. The red swelling of the skin, the paraesthesia, and the pruritus were not observed in injection sites. We considered that the application of SonoVue for RT-MCE was relatively safe.

The preliminary findings in the present study displayed that RT-MCE in evaluating the effect of Pur on the myocardial microcirculation perfusion and ventricular wall motion in patients with ACS was simpler and more convenient than CAG. Patients had not injured when RT-MCE was applied to them. The findings would provide the base on the application of Pur and open up the new thinking for the therapy to patients with ACS. It would be a good choice that integrated traditional and western medicine to treat patients with ACS. However, quantitative analysis was not utilized in this study and there were some limitations by using semiquantitative analysis. The relationship between MPI and VWMI and the prognosis of patients with ACS will be investigated in the further research.

Acknowledgement

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References