The effect of continuous renal replacement therapy on serum BNP, IL-34, hs-CRP and blood gas analysis index in acute myocardial infarction patients with cardiac insufficiency.

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Abstract

Objective: To study the effect of Continuous Renal Replacement Therapy (CRRT) on serum BNP, IL-34, hs-CRP and blood gas analysis index in acute myocardial infarction patients with cardiac insufficiency.

Methods: 80 AMI patients who have received treatment in our hospital during the period from March, 2014 to March, 2016 were selected as our study objects. CRRT was initiated in these patients because of the failure of medical drug therapy. Blood gas analysis index, urea nitrogen, creatinine and heart rhythm index were recorded before and after CRRT and serum BNP, IL-34 and hs-CRP were measured after 12 h, 24 h and 48 h respectively.

Results: CRRT was terminated in 2 patients due to rapid decrease of thrombocyte and in other 2 patients because of visceral perfusion insufficiency, poor peripheral circulation, skin cold clammy and oliguria, additionally, their systolic pressure was less than 90 mmHg. 76 patients who could tolerate CRRT showed stable vital signs and reduced heart failure symptoms. After CRRT, serum BNP, IL-34 and hs-CRP decreased (P<0.05), urea nitrogen, creatinine, heart rate and blood gas analysis index were improved greatly (P<0.05). Four cases died of sudden cardiac death. Other 72 cases were discharged after 23-63 d and followed up for one year. All discharged patients’ NYHA grading was II and III. No deterioration of heart dysfunction was found, no long-term dialysis was required and no unstable angina and myocardial infarction appeared.

Conclusion: CRRT is a relatively safe and effective method for patients with cardiac insufficiency after AMI. It can not only stabilize internal environment, improve cardiac failure and blood gas analysis index in a short time, but also decrease serum BNP, IL-34 and hs-CRP, so as to help patients pass dangerous period and improve the prognosis.

Keywords: Acute myocardial infarction, Cardiac insufficiency, Continuous renal replacement therapy, BNP, IL-34, hs-CRP.

Introduction

In recent years, although the early myocardial reperfusion therapy has decreased the morbidity of Acute Myocardial Infarction (AMI) and Heart Failure (HF), their occurrence rates were still over 45% [1]. AMI patients are usually combined with myocardial ischemia and hypoxia, and decline of cardiac output may cause perfusion insufficiency in different organs and thus causing Multiple Organ Dysfunction Syndrome (MODS). If this cannot be corrected in time, irreversible multiple system organ failure will happen, which in turn increase death rate. Before, the combination of AMI and MODS is a relative contraindication of Percutaneous Coronary Intervention (PCI), however, if infarct-related arteries are not opened in time to regain myocardial contractility, the problem of hypoperfusion in each organ cannot be solved [2]. CRRT is a 24 h or nearly 24 h continuous blood purification [3]. At present, CRRT is one of the treatments of MODS, having positive effect on saving MODS patients and prolonging patients’ survival time [4]. Clinically, a stable renal environment may improve the survival of AMI patients with acute heart failure, indicating that CRRT may potentially to be able to improve the treatment of this disease [5]. Some studies [6] have shown that application of CRRT when medical drug therapy fail to cure congestive heart failure can reduce mortality.

Mounting evidence [7,8] suggests that inflammation plays an important role in the occurrence and development of AMI. AMI that is related to inflammation is marked by the increase...
of serum BNP, IL-34 and hs-CRP, therefore, measuring BNP, IL-34 and hs-CRP at different time points can be very helpful in predicting patients’ prognosis and outcome. Studies [9,10] indicate that the increase of serum BNP, IL-34 and hs-CRP reflects the evolution of AMI acute stage and its related nonspecific inflammatory response. However, the relationship between BNP, IL-34, hs-CRP, cardiac function and prognosis remains to be further studied. This study mainly detected blood gas analysis index, serum BNP, IL-34 and hs-CRP in AMI patients with cardiac insufficiency before and after CRRT. All study objects were followed up for one year to evaluate the treatment effect of CRRT on AMI patients with cardiac insufficiency.

Materials and Methods

General materials

A total of 80 AMI patients who have received treatment in our hospital during the period from March, 2014 to March, 2016 were selected as our study objects. All patients showed a level of creatine kinase, creatine kinase MB fraction, or troponins higher that twice of the upper limit of normal level, and with Killip class ≥ 2 on admission. CRRT was initiated in these patients because of the failure of medical drug therapy. Among all patients, 48 were male and 32 were female, and the age ranged from 47-69 y, with an average age of (63.8 ± 2.4 y). 50 patients had extensive anterior myocardial infarction, 21 had anterior myocardial infarction, and 9 patients had myocardial infarction in inferior wall, posterior wall and right ventricle. Patients’ cardiac function was rated II and III according to Killip grading. All patients were treated with conservative treatment at first: oxygen inhalation was kept at a medium level; myocardial oxygen loss was alleviated by sedation; blood vessels were supported by active drug; preload and after load of heart were relieved by diuretics. Nevertheless, cardiac function was not improved by the above treatment, additionally, blood urea nitrogen (Bun) and serum Creatinine (Cr) apparently increased. In this situation, CRRT was applied. This study was approved by the ethics committee of our institute, and all patients signed informed consent.

Therapy

Conservative treatment: Based on patient’s conditions, all patients were given calcium antagonists, lipid-lowering drugs, aspirin, nitrates and other drugs. Besides that, 0.4 ml of low molecular weight heparin calcium was subcutaneously injected twice a day for 7 d. Cardiac function was assessed by echocardiography.

CRRT therapy: Double channel catheter was put inside subclavian veins or femoral veins. Patients were treated with CVVHDF therapy, which was equipped with Jinbao Machine, matched M60 pipeline and filter AN69 (pan membranes, 2.0 m²). Displacement liquid based on Port formula was added after heating through dilution method, with a flow rate of 1500-2000 ml/h. Meanwhile, 5% of NaHCO₃ was added at constant speed. The blood flow rate was 180200ml/min, the dialysate flow rate was 20-40 ml/min and the ultrafiltration volume was adjusted into 25-32 ml/min according to blood pressure. In the process of CRRT, patients with low blood pressure were given fluid infusion, vasoactive agent support, 5-15 µg/(kg•min) of dopamine and 0•05~0•20 µg/(kg•min) of norepinephrine to keep their blood pressure at 95-100 mmHg. Dialysis was terminated in patients whose systolic pressure was lower than 90 mmHg because of hypoperfusion in important organs, poor peripheral circulation, skin cold clammy, cyanosis, oliguria and mental and neurological symptoms.

Anticoagulation methods: Pipeline and filter were washed by heparin saline according to the settled procedure before dialysis. Different anticoagulation methods were applied in accordance with different conditions: 1. Systemic heparin anticoagulation method: The first dosage of heparin was 10-15 mg, with an addition of 10 mg/h. 2. Low molecular heparin therapy: Bleeding tendency patients were given low molecular heparin. The first dosage was 4000 IU, and 2000-4000 IU were added after 4-6 h. 3. Heparin-free anticoagulation method: patients who had less than 80,000 blood platelets were treated with heparin-free purification. At first, the filter and extracorporeal circulation line were flushed in advance with isotonic saline which contained 0.05 mg/L heparin and were soaked for 15-20 min. Before CRRT, filter and pipeline were washed by isotonic saline. The blood flow volume was kept at 160-180 ml/min and pipelines were washed again by 100 ml-200 ml isotonic saline every 60 min, in the meantime, blood access was closed and ultrafiltration volume was added to remove additional flushing fluid.

Observational index: Vital signs of all patients were closely observed and recorded, including urea nitrogen, creatinine and heart rate index. Serum BNP, IL-34, hs-CRP and blood gas analysis index were all measured before treatment as well as 12 h, 24 h and 48 h after treatment.

Statistical method

Data were analysed by statistical software SPSS 21.0, and measurement data were expressed as x ± s. Intragroup comparisons were performed by two way ANOVA for repeated measures. p<0.05 was considered to be statistical analysis.

Results

CRRT was started when conservative treatment showed no positive effects on cardiac function, or conditions became even worse. CRRT was stopped when vital signs became stable or at least were controlled. After the treatment, CRRT was terminated in 2 patients due to rapid decrease of thrombocyte. After CRRT was stopped, these two patients’ thrombocyte was gradually increased to 8 × 10⁹/L. In the process of CRRT, 17 patients with low blood pressure were given fluid infusion and vasoactive agent support to keep blood pressure at 95-100 mmHg. Dialysis was terminated in 2 patients whose systolic pressure was lower than 90 mmHg because of organ
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76 patients showed stable vital signs, and their heart failure symptoms were obviously alleviated in 12 h after CRRT. Patients could only sit before the treatment, but after CRRT, 64.5% (49 cases) of the patients were able to lie on their back and 35.5% (27 cases) were able to sleep with high pillow. In addition, breathing difficulties and lung rales in patients were greatly reduced. Serum BNP, IL-34 and hs-CRP in 76 patients were measured 12 h, 24 h and 48 h after CRRT, respectively. All the indexes were kept at a relatively low level, showing great improvement comparing to the situation before CRRT (P<0.05, Table 1). Moreover, urea nitrogen, creatinine, heart rate and blood gas analysis index also presented significant improvement (P<0.05, Tables 2 and 3).

Table 1. The comparison of serum BNP, IL-34 and hs-CRP in patients between prior CRRT treatment and post-CRRT treatment.

<table>
<thead>
<tr>
<th>Monitoring indexes</th>
<th>BNP (pg/ml)</th>
<th>IL-34 (pg/ml)</th>
<th>hs-CRP (μg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before treatment</td>
<td>3987.3 ± 67.2</td>
<td>325.7 ± 65.2</td>
<td>13.8 ± 2.4</td>
</tr>
<tr>
<td>12 h treatment</td>
<td>2782.5 ± 74.5</td>
<td>256.1 ± 32.8</td>
<td>10.9 ± 1.7</td>
</tr>
<tr>
<td>24 h treatment</td>
<td>1279.2 ± 54.8</td>
<td>194.3 ± 22.5</td>
<td>8.4 ± 1.2</td>
</tr>
<tr>
<td>48 h treatment</td>
<td>568.4 ± 34.3</td>
<td>123.5 ± 17.4</td>
<td>6.2 ± 0.6</td>
</tr>
<tr>
<td>F</td>
<td>12.093</td>
<td>10.246</td>
<td>11.004</td>
</tr>
<tr>
<td>P</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
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</tbody>
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Table 2. The comparison of urea nitrogen, creatinine and heart rate between prior CRRT treatment and post-CRRT treatment.

<table>
<thead>
<tr>
<th>Monitoring indexes</th>
<th>Urea nitrogen (mmol/L)</th>
<th>Creatinine (μmol/L)</th>
<th>Heart rate (bmp)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before treatment</td>
<td>19.3 ± 4.2</td>
<td>149.8 ± 42.5</td>
<td>113.5 ± 6.7</td>
</tr>
<tr>
<td>12 h treatment</td>
<td>10.2 ± 2.7</td>
<td>118.3 ± 37.5</td>
<td>109.4 ± 5.2</td>
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<tr>
<td>24 h treatment</td>
<td>8.1 ± 2.2</td>
<td>106.2 ± 17.7</td>
<td>97.3 ± 3.5</td>
</tr>
</tbody>
</table>

Table 3. The comparison of blood gas analysis index between prior CRRT treatment and post-CRRT treatment.

<table>
<thead>
<tr>
<th>Monitoring indexes</th>
<th>Blood gas (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before treatment</td>
<td></td>
</tr>
<tr>
<td>7.12 ± 0.12</td>
<td>42.3 ± 4.2</td>
</tr>
<tr>
<td>12 h after treatment</td>
<td></td>
</tr>
<tr>
<td>7.37 ± 0.17</td>
<td>35.7 ± 4.1</td>
</tr>
<tr>
<td>24 h after treatment</td>
<td></td>
</tr>
<tr>
<td>7.35 ± 0.13</td>
<td>36.4 ± 3.5</td>
</tr>
<tr>
<td>48 h after treatment</td>
<td></td>
</tr>
<tr>
<td>7.32 ± 0.15</td>
<td>35.7 ± 2.6</td>
</tr>
<tr>
<td>F</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Discussion

Acute heart failure is a common and severe complication of AMI, which seriously threatens patients’ life, causing cardiac rupture, malignant arrhythmia and sudden death. Renin-angiotensin-aldosterone system can be activated due to low ejection fraction, low cardiac output and renal perfusion insufficiency. And liver blood stasis leads to the decline in aldosterone biodegradability, making the system stay active [11]. For patients who show the above symptoms diuretic is rarely helpful, and the general medical therapy often brings poor treatment effect. CRRT is a 24 h or nearly 24 h continuous blood purification with the advantages of hemodialysis and hemofiltration. Blood hyperfiltration can help remove the excess fluid from plasma, relieve left ventricular preload, reduce lung blood stasis and improve respiratory function, and increase SpO2 level [12,13]. Blood hyperfiltration can not only decrease blood volume, but also block the vicious circle of neuronal regulation and hemodynamics [14]. Even a single hyperfiltration therapy can block the vicious circle, making great improvement in patients after several days or months. CRRT even hyperfiltration is close to kidney’s filtration function towards blood, which can reduce the disturbance towards cardiovascular system, control various high capacity load conditions in a short time and help circulation and restore respiration function. Slowly intermittent and continuous hyperfiltration method can be applied to patients with poor cardiovascular stability. Meanwhile, during hyperfiltration, adjustment of filtration speed can quickly control the central venous pressure and arterial blood pressure. BNP is mainly distributed in the left and right atria. Ventricle has a few BNP and when the tension of ventricular wall increases, overload will break myocardial function, thus stimulating the synthesis of BNP. Therefore, BNP is a specific indicator of ventricular overload [15]. Monitoring BNP level...
can be very helpful in learning the treatment effect and prognosis of AMI patients. It can be more sensitive to screening when AMI patients have inconspicuous clinical symptoms and ultrasonic cardiomgram. AMI always come with cardiac insufficiency in patients, and higher degree of cardiac insufficiency is usually followed by higher plasma BNP level. As we can see, concentration of plasma BNP has superiority to the diagnosis of AMI patients with cardiac insufficiency. As a novel cytokine, IL-34 is a protein dimer composed of 241 amino acids. Under certain conditions, macrophages, endothelial cells, fibroblasts, nerves, liver, epithelial cells and Treg cells can secrete IL-34. In recent years, studies [16] have shown that IL-34 is closely associated with inflammatory disease. Hs-CRP is phasic proteins of systemic inflammatory response and is always found at trace levels. When acute inflammation occurs, concentration of serum hs-CRP increases rapidly and deposits largely inside arterial wall. Combination of hs-CRP and lipoprotein activates complement system and increases inflammatory mediators and oxygen free radicals, leading to arterial vasospasm and damage and plaques shedding [17]. BNP, IL-34 and CRP levels can help make serological guidance in terms of cardiac insufficiency degree, treatment effect and prognosis. 80 AMI patients after PCI who were rated as II and III were selected as our study objects. Those patients were given CRRT because of poor treatment effect of conventional therapy. 76 out of 80 patients have finished their CRRT therapy. After 12 h of CRRT, the heart failure symptoms in the 76 patients have been reduced, patients’ heart rate has gradually slow down, indexes of urea nitrogen and creatinine have improved and BNP, IL-34 and hs-CRP have decreased. Additionally, there is no increase of serum BNP, IL-34 and hs-CRP in patients after stopping CRRT treatment.

In conclusion, CRRT therapy may help AMI patients with cardiac insufficiency to pass dangerous period. Based on our observation, no long-term dialysis treatment is required for safely discharged patients whose cardiac function is improved. The improvement of BNP, IL-34 and hs-CRP brings serological guidance on cardiac insufficiency degree, treatment effect and prognosis. However, the lack of control group in this study makes the experimental data hard to be interpreted. Changes in inflammatory markers may be caused by other factors other than CRRT. Therefore, our study only provided some references for the application for CRRT in the treatment of this disease. Future clinical studies are still needed to confirm those conclusions.

References


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