Effect of levosimendan on heart function and hs-CRP, IL-6, TNF-α levels in elderly patients with acute myocardial infarction complicated heart failure

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Objective: To observe the effect of levosimendan on heart function and hs-CRP, IL-6, TNF-α levels in elderly patients with acute myocardial infarction complicated heart failure.

Methods: A total of 80 elderly patients with acute myocardial infarction complicated heart failure were randomly divided into control group (40 cases) and research group (40 cases), the control group was given the basic treatment, and the research group was given levosimendan on the basis of the control group, after 1 weeks' treatment, to compare the clinical curative effect, LVEDD, LVESD, LVEF, hs-CRP, IL-6, TNF-α. Results: Comparing with the before treatment, the LVEDD, LVESD, hs-CRP, TNF-α, IL-6 in two groups after treatment decreased, and LVEF increased, the difference were statistically significant. Comparing with control group after treatment, the LVEDD, LVESD, hs-CRP, TNF-α, IL-6 in research group after treatment decreased obviously, and LVEF increased obviously, the difference were statistically significant. Conclusion: It has great clinical curative effect that levosimendan treat elderly patients with acute myocardial infarction complicated heart failure, it can ameliorate heart function and inflammation reaction, safe and reliable, and it is worthy of application.

1. Introduction

Acute myocardial infarction (AMI) is myocardial ischemia sharply caused by reduction or interruption of coronary blood-supply, which can lead to myocardial necrosis in the blood-supply area of infarct-related artery. AMI elderly patients combining with more diseases, the disease being relatively complicated, the prognosis being relatively poor, mortality rate being relatively high, seriously impact the patients’ health and life[1]. AMI can cause cardiac dysfunction, sudden cardiac death and reduced quality of life. To improve heart function and quality of life timely has important clinical significance for the treatment of AMI patients[2]. Levosimendan is a newly clinical and positive inotropic drug, which can increase myocardial contractility by calcium sensitizing effect.

This study was aimed to investigate the effect of levosimendan for AMI elderly patients complicated heart failure on heart function and Inflammatory factors such as high-sensitivity C-reactive protein (hs-CRP), interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α). And it also summarize their clinical efficacy.

2. Informations and Methods

2.1 General information

A total of 80 cases of AMI patients with heart failure were selected in the Department of Cardiology of our hospital from January, 2013 to April, 2015 and all patients met the AMI diagnostic criteria which WHO had developed. It included the following inclusion criteria specifically: (1) ages 60 years old, the average (69.40 + 6.82) years old, and to get AMI for the first time; (2) with AMI typical...
clinical symptoms, signs and laboratory tests; (3) New York heart association (NYHA) heart function level I, II, III, and the clinical echocardiography, left ventricular ejection fraction (LVEF) < 40%; (4) ruled out with primary valvular disease, fatal arrhythmia, severe lung disease, shock and hyperkalemia (potassium > 5.5 mmol/L); 5. All patients agreed and signed informed consent. 80 patients who were selected were randomly divided into control group and research group, 40 cases in each group and control group with 25 male patients, 15 female patients, ages were from 62 to 80 years old, the average (70.12±7.26) years old, years getting sick: 3-14, the average (8.76-4.74) years, the average time in treatment was (3.08±1.24) h; NYHA heart function classification: I level has 17 cases, II level has 23 cases; Infarction area: 16 cases with anterior wall infarction, 12 cases with inferior wall infarction, 5 cases with anteroseptal infarction, 4 cases with posterior wall infarction, 3 other cases; 11 cases with diabetes, 23 cases with high blood pressure. Research group with 23 male patients, 17 female patients, ages were from 61 to 78 years old, the average (68.92±6.74) years old, years getting sick: 2-16, the average (9.25±5.17) years, the average time in treatment was (3.20±1.31) h; NYHA heart function classification: I level has 15 cases, II level has 25 cases; Infarction area: 14 cases with anterior wall infarction, 13 cases with inferior wall infarction, 4 cases with anteroseptal infarction, 4 cases with posterior wall infarction, 5 other cases; 22 cases with high blood pressure, 13 cases with diabetes. Two groups of patients showed no significant difference in age, gender, treatment time, infarction and complications and other baseline data (P>0.05). So it was comparable.

2.2 Therapeutic method

After admission control group patients were given treatment on a regular basis according to AMI treatment guidelines, specifically including: rest, limiting salt and water, lipid regulation and stabilization of atheromatous plaque, anticoagulant and antiplatelet aggregation, timely making use of diuretics, cardiotonic and vasodilator to treat and so on. For patients with diabetes mellitus, we would use insulin more to control blood sugar levels, For patients with hypertension, we would lower blood pressure treatment. Research group patients were given treatment of levosimendan (Produced by ChengDu ShengNuo Biopharm Co. Ltd. H20110104) on the basis of the treatment of control group. levosimendan (5 mL 12.5 mg) with 5% glucose injection (500 mL) to mix uniformly, by way of micropump infusion, at first keeping the dose at 12 µg/kg, 10 min later, adding intravenous drip 0.1 µg/(kg.min). Two hours later, adding intravenous drip 0.2 µg/(kg.min),then maintain 24 h. Closely observing the changes of patients during treatment, 1 week after treatment, according to the patient's clinical curative effect and laboratory test results, it depends to give treatment again according to the above ways.

2.3 Efficacy evaluation and detection index

2.3.1 Evaluating standards

After treated one week later in both groups, we determined the efficacy of clinical changes according to the following criteria[3], (1) effective: clinical symptoms improved, LVEF>50%; (2) improvement: clinical symptoms improved, LVEF <50%, which had increased before treatment ; (3) invalid: clinical symptoms and heart function was not improved even worse after treatment. To calculate the total efficiency in terms of effectiveness and improvement.

2.3.2 Detection index

Specialized personnels were responsible for detecting changes of the following indices before treatment and after one week’s treatment in two groups: (1) Determining the left ventricular end systolic diameter (LVESD) and left ventricular end diastolic diameter (LVEDD) using color Doppler imagining (vivid7) produced by US company named GE, and calculating the left ventricular ejection fraction (LVEF). (2) In the morning collecting peripheral venous blood of 5ml from patient on an empty stomach and then injecting 3.2% sodium citrate anticoagulant tubes, centrifuging (3 000 r/min) 15 min later to separate plasma, which would be encapsulated into EP tube (0.5 mL) and be placed in -70 °C refrigerator to preserve. By enzyme-linked immunosorbent assay (ELISA), determinating serum IL-6, TNF-α levels, using CX7 biochemical analyzer (produced by Beckman Coulter, Inc.) determining serum hs-CRP levels, the kits were purchased from Beijing East immunity technology company, operating according to the instruction steps. (3) Security indicators, including blood routine and liver and kidney function.

2.4 Statistical methods

To carry on data analysis using SPSS 19.0 statistical software for data analysis, mean ± standard deviation (Mean ± SD) representing measurement data. using t test and χ² test to compare between groups of measurement data and count data. Their differences were statistically significant (P<0.05)

3. Results

3.1 Comparison of the clinical efficacy after treatment in both groups

After one week’s treatment, patients in the research group, 22 cases were cured, 14 cases improved, 4 cases ineffective, total effective rate was 90.00%; patients in the control group, 12 cases were cured,
17 cases improved, 11 cases ineffective, total effective rate was 72.50%. The total efficiency of the research group was significantly higher than control group (P<0.05).

3.2 Comparison of left ventricular function before and after treatment in both groups

LVEDD, LVESD and LVEF levels in both groups of patients had no significant difference compared with those before treatment (P>0.05); LVEDD and LVESD after treatment were significantly lower than those before treatment, LVEF increased, the difference was statistically significant (P<0.05). After comparison with the control group after treatment, LVEDD and LVESD of the research group significantly reduced, LVEF was significantly increased, the difference was statistically significant (P<0.05). Please look at the table 1.

### 3.3 Comparison of serum hs-CRP, TNF-α, IL-6 levels before and after treatment in both groups

Hs-CRP, TNF-α and IL-6 levels of two groups of patients showed no significant difference before treatment (P>0.05); Hs-CRP, TNF-α and IL-6 after treatment were significantly lower than those before treatment, the difference was statistically significant (P<0.05). After compared with the control group after treatment, hs-CRP, TNF-α and IL-6 of the research group after treatment were significantly decreased, the difference was statistically significant (P<0.05). Please look at the table 2.

### Table 1
Comparison of left ventricular function before and after treatment

<table>
<thead>
<tr>
<th>Index</th>
<th>Control group (n=40)</th>
<th>Research group (n=40)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before treatment</td>
<td>After treatment</td>
</tr>
<tr>
<td>LVEDD (mm)</td>
<td>62.20±6.53</td>
<td>58.40±5.81 *</td>
</tr>
<tr>
<td>LVESD (mm)</td>
<td>50.46±5.32</td>
<td>44.69±4.25 *</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>33.12±5.01</td>
<td>42.12±5.30 *</td>
</tr>
</tbody>
</table>

Ps: Compared with the same group before treatment, *Ps<0.05; Compared with the control group after treatment, #Ps<0.05.

### Table 2
Comparison of serum hs-CRP, TNF-α, IL-6 levels before and after treatment in both groups

<table>
<thead>
<tr>
<th>Index</th>
<th>Control group (n=40)</th>
<th>Research group (n=40)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before treatment</td>
<td>After treatment</td>
</tr>
<tr>
<td>hs-CRP (mg/L)</td>
<td>41.35±6.10</td>
<td>26.58±5.06 *</td>
</tr>
<tr>
<td>TNF-α (ng/L)</td>
<td>27.78±3.74</td>
<td>22.03±3.02 *</td>
</tr>
<tr>
<td>IL-6 (ng/L)</td>
<td>34.61±4.51</td>
<td>27.36±3.95 *</td>
</tr>
</tbody>
</table>

Ps: Compared with the same group before treatment, *Ps<0.05; Compared with the control group after treatment, #Ps<0.05.

### 4. Discussion

AMI is a common disease in the middle-aged and elderly, most of AMI occurred on the basis of coronary artery atherosclerosis, which resulted in persistent myocardial blood supply interruption, causing myocardial necrosis.

AMI can lead to the decrease of myocardial contractility and stroke volume decreased obviously, when the infarct area is more than 20%, pump failure easily appears, threatening the lives of patients[4-6]. After myocardial infarction, inflammatory cells, like monocytes and macrophages, can be activated, and the secretion of cytokines, like IL-6 and TNF-α, can be promoted. IL-6 stimulates the liver to produce hs-CRP, participating in the acute inflammatory response after AMI[7]. Myocardial necrosis and malignant arrhythmia after AMI, can lead to heart failure. The clinical application of cardiac diuretics and vasodilators, their curative effect is limited, the prognosis is not ideal[8,9].

Calcium sensitizer levosimendan is commonly used as a new type of positive inotropic drugs in clinic, which have a better improvement for coronary blood flow, pulmonary circulation and peripheral circulation. Levosimendan can increase the sensitivity of cardiac troponin to Ca²⁺, mainly selectively increasing the sensitivity of systolic Ca²⁺, not affecting cardiac diastolic function and increasing myocardial contractility[10,11]. In addition, levosimendan does not affect the Ca²⁺ level of intracellular, does not consume the energy of Ca²⁺ transport needs, and does not increase myocardial oxygen consumption[12-14]. The study found that levosimendan could increase ATP-sensitive K⁺ channel on the open cardiac sarcolemma, protect against inflammation induced by myocardial ischemia, and reduce cytokine levels effectively, then playing a role in the prevention of myocardial remodeling[15,16]. Oxidative stress, inflammatory factors and myocardial apoptosis play important regulatory roles in myocardial remodeling, which is the pathophysiological basis of the development of heart failure[17-19]. The study found that levosimendan can reduce serum TNF-α, IL-6 lipid peroxide malondialdehyde and apoptosis signal factors of patients with heart failure, playing a role on anti-oxidation, anti-inflammatory and anti-apoptosis[20]. Levosimendan had no significantly adverse effect on cardiac electrophysiology, not causing...
arrrhythmia and in the range of therapeutic doses, not causing adverse reactions like headaches, tachycardia, palpitations and hypotension. The patient tolerance was good. The study found that total efficiency based on levosimendan treatment of elderly patients with AMI complicated by heart failure was significantly higher than that based on regular treatment. LVEDD, LVESD, hs-CRP, TNF-α and IL-6 of research group after treatment was significantly reduced compared with control group, LVEF increasing significantly, which further illustrated that levosimendan can improve cardiac function and inflammation for the elderly patients with AMI complicated by heart failure.

In conclusion, the clinical efficacy of levosimendan treatment in elderly patients with AMI complicated by heart failure was significant. Being able to improve cardiac function and inflammation, safe and reliable, it should be widely applied.

Reference