Effect of levocarnitine + coenzyme Q10 adjuvant therapy on vasoactive molecules, endothelial injury and oxidative stress in patients with chronic heart failure

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Objective: To study the effect of levocarnitine + coenzyme Q10 adjuvant therapy on vasoactive molecules, endothelial injury and oxidative stress in patients with chronic heart failure.

Methods: A total of 90 patients with chronic heart failure who were treated in the hospital between December 2014 and December 2016 were collected and divided into control group and observation group by random number table method, 45 cases in each group. Control group received conventional therapy, and observation group received levocarnitine + coenzyme Q10 adjuvant therapy on the basis of conventional therapy. The differences in vasoactive molecule, endothelial injury and oxidative stress levels were compared between the two groups before and after treatment.

Results: Before treatment, the differences in vasoactive molecule, endothelial injury and oxidative stress levels were not statistically significant between the two groups of patients. After treatment, serum vasoactive molecules ET-1, Ang II and TXB2 contents of observation group were lower than those of control group while NO content was higher than that of control group; endothelial function indexes FMD level was higher than that of control group; serum oxidative stress indexes SOD and T-AOC contents were higher than those of control group while MDA and ROS contents were lower than those of control group.

Conclusion: Levocarnitine + coenzyme Q10 adjuvant therapy can optimize the vascular activity, and reduce the endothelial injury and systemic oxidative stress response in patients with chronic heart failure.

1. Introduction

Chronic heart failure (CHF) is a clinical common fatal heart disease, patients are with systemic congestion and multiple organ dysfunction as the ventricular pumping function gradually declines, and early active treatment helps delay the illness and optimize the patients’ final outcome\(^{[1,2]}\). Cardiotonic, diuresis and vascular dilation are the basic therapies for chronic heart failure, they can alleviate the illness to a certain extent, but have limitations in reversing the progress of the disease, and many scholars recommend joining drugs with other mechanisms of action as combination therapy. Levocarnitine is the necessary material in energy metabolism of mammals, the main function is to promote lipid metabolism and provide energy for cells, it is mainly distributed in the heart muscle and skeletal muscle tissue under physiological conditions, but levocarnitine is relatively short in patients with chronic heart failure\(^{[3,4]}\). Coenzyme Q10 is a kind of fat-soluble antioxidant, which is with higher content in the heart, liver and kidney, and can help the cell self-repair\(^{[5,6]}\). In this research, levocarnitine + coenzyme Q10 were both used as adjuvant drugs and added in the overall treatment of patients with CHF, and the influence of combination therapy on patients' vascular activity was explored, endothelial injury and oxidative stress, now reported as follows.

2. Information and methods

2.1 Inclusion and exclusion criteria

Inclusion criteria; (1) meeting the diagnostic criteria for CHF; (2) cooperating with the whole treatment and with complete clinical data. Exclusion criteria: (1) history of levocarnitine and coenzyme...
Q10 allergy; (2) combined with systemic infectious diseases; (3) combined with severe liver and renal insufficiency; (4) combined with malignant tumor diseases.

2.2 Case information

A total of 90 patients with CHF who were treated in the hospital between December 2014 and December 2016 were selected, and the families of the patients signed informed consent. Random number table method was used to divide the enrolled patients into control group and observation group, 45 cases in each group. Control group included 24 men and 21 women that were 49-78 years old; observation group included 23 men and 22 women that were 48-76 years old. The differences in the gender and age distribution were not statistically significant between the two groups (P>0.05), and the hospital ethics committee approved the study.

2.3 Therapy

Control group received conventional therapy for CHF, including digitalis for cardiotonic, angiotensin converting enzyme inhibitor for lowering blood pressure, furosemide for diuresis, and nitroglycerin for vascular dilation. Observation group, on the basis of conventional therapy, received levocarnitine + coenzyme Q10 adjuvant therapy, specifically as follows: levocarnitine injection (Jiangsu Sihuan Biological Pharmaceutical Co., Ltd., approved by H20061135) 250 mL intravenous drip for 14 d; Coenzyme Q10 sodium chloride injection (Southwest Pharmaceutical Co., Ltd., approved by H20113536) 2 g in 100 mL saline, intravenous drip, 1 time/d, for 14 d of continuous treatment. Coenzyme Q10 sodium chloride injection (Southwest Pharmaceutical Co., Ltd., approved by H20061135) 250 mL, intravenous drip, 1 time/d, for 14 d of continuous treatment.

2.4 Observation indexes

Before and after treatment, 5.0 mL of fasting cubital venous blood was extracted from the two groups of patients, treated with anticoagulant and then centrifuged at low speed to get the upper serum, which was stored in a cryopreserved environment. Enzyme-linked immunosorbent assay (ELISA) was used to detect the levels of serum vasoactive molecules, including endothelin-1 (ET-1), nitric oxide (NO), angiotensin II (Ang II) and thromboxane 2 (TXB2). Color Doppler diasonograph was used to measure endothelial function index levels, including brachial artery blood vessel diameter at quiescent condition (D0) and brachial artery blood vessel diameter after reactive hyperemia (D1), vascular dilatation function index levels, including brachial artery blood vessel diameter (FMD) = (D1-D0)/D0 100. ELISA was used to detect the serum contents of oxidative stress indexes, including superoxide dismutase (SOD), total antioxidant capacity (T-AOC), malondialdehyde (MDA) and reactive oxygen species (ROS).

2.5 Statistical processing

Statistical software was SPSS 24.0, vasoactive molecules, endothelial function indexes and oxidative stress indexes belonged measurement data, were in terms of mean ± standard deviation and were analyzed by t test and statistic P<0.05 was the standard of statistical significance in differences.

3. Results

3.1 Vasoactive molecules

Before treatment and 14 d after treatment, comparison of serum vasoactive molecules ET-1 (pg/mL), NO (μmol/L), Ang II (pg/mL) and TXB2 (pg/mL) between two groups of patients was as follows: serum ET-1, NO, Ang II and TXB2 contents were not significantly different between the two groups of patients before treatment; 14 d after treatment, serum ET-1, Ang II and TXB2 contents of both groups were significantly lower than those before treatment while NO contents were significantly higher than those before treatment, and serum ET-1, Ang II and TXB2 contents of observation group 14 d after treatment were lower than those of control group while NO content was higher than that of control group.

3.2 Endothelial function indexes

Comparison of endothelial function indexes D0 (mm), D1 (mm) and FMD levels between two groups of patients before and after treatment was as follows: before treatment, D0, D1 and FMD levels were not significantly different between the two groups of patients (P>0.05); after treatment, FMD levels of both groups were higher than those before treatment (P<0.05) while D0 and D1 levels were not statistically different from those before treatment (P>0.05), and FMD level of observation group was higher than that of control group (P<0.05) while D0 and D1 levels were not statistically different from those of control group (P>0.05), shown in Table 2.

Table 1.
Comparison of serum vasoactive molecule contents between two groups of patients before and after treatment.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>ET-1 Before treatment</th>
<th>ET-1 After treatment</th>
<th>NO Before treatment</th>
<th>NO After treatment</th>
<th>Ang II Before treatment</th>
<th>Ang II After treatment</th>
<th>TXB2 Before treatment</th>
<th>TXB2 After treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>45</td>
<td>95.72±10.69</td>
<td>83.74±9.42</td>
<td>95.53±10.27</td>
<td>84.61±6.27</td>
<td>63.71±7.84</td>
<td>67.92±8.53</td>
<td>51.63±6.49</td>
<td>39.62±4.51</td>
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<tr>
<td>T</td>
<td></td>
<td>0.173</td>
<td>0.258</td>
<td>83.74±9.42</td>
<td>84.61±6.27</td>
<td>67.92±8.53</td>
<td>51.63±6.49</td>
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<td>P</td>
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<td>&gt;0.05</td>
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</tbody>
</table>

Note: comparison of indexes within group before and after treatment, *P<0.05.
Comparison of endothelial function index levels between two groups of patients before and after treatment.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Before treatment</th>
<th>After treatment</th>
<th>Before treatment</th>
<th>After treatment</th>
<th>Before treatment</th>
<th>After treatment</th>
<th>Before treatment</th>
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</tr>
</thead>
<tbody>
<tr>
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<td>62.74±0.98</td>
<td>88.72±9.14</td>
<td>6.83±0.75</td>
<td>6.34±0.73</td>
<td>3.09±0.36</td>
<td>3.37±0.17</td>
<td>591.27±68.53</td>
<td>378.64±46.27</td>
</tr>
<tr>
<td>Observation group</td>
<td>45</td>
<td>63.28±7.19</td>
<td>71.53±8.76</td>
<td>6.83±0.79</td>
<td>6.39±0.75</td>
<td>5.17±0.64</td>
<td>5.91±0.91</td>
<td>591.27±68.53</td>
<td>378.64±46.27</td>
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<tr>
<td>D0</td>
<td></td>
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<td>FMD</td>
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</tbody>
</table>

Note: comparison of indexes within group before and after treatment, *P<0.05.

Comparison of serum oxidative stress index contents between two groups of patients before and after treatment.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Before treatment</th>
<th>After treatment</th>
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</tbody>
</table>

Note: comparison of indexes within group before and after treatment, *P<0.05.

3.3 Oxidative stress indexes

Before treatment and 14 d after treatment, comparison of serum oxidative stress indexes SOD (U/L), T-AOC (U/mL), MDA (mol/L) and ROS (μmol/L) between two groups of patients was as follows: serum SOD, T-AOC, MDA and ROS contents were not significantly different between the two groups of patients before treatment; 14d after treatment, serum SOD and T-AOC contents of both groups were significantly higher than those before treatment while MDA and ROS contents were significantly lower than those before treatment, and serum SOD and T-AOC contents of observation group 14d after treatment were higher than those of control group while MDA and ROS contents were lower than those of control group.

4. Discussion

CHF pathogenesis is relatively complex, and the myocardial cell energy intake/utilization obstacle is the recognized cause, which can cause mitochondrial oxidative stress damage and cell membrane integrity destruction in myocardial cells, and eventually lead to the decrease of the overall cardiac pumping capacity and blood circulation disorder[7-9]. Conventional cardiotonic, blood pressure lowering, vascular dilation, diuresis and other therapies for CHF do not involve the improvement on myocardial energy supply, hence many scholars have recommended joining targeted drugs for optimizing myocardial energy supply and intake to expand curative effect. Levocarnitine can promote aerobic oxidation of fatty acid long-chain structure and increase the energy supply of the myocardium so as to ultimately improve the myocardial energy metabolism and reduce the attack of oxygen free radical on the myocardial membrane[10,11]. Coenzyme Q10 can effectively improve the electron transfer process of oxidation respiratory chain, eventually improve the myocardial oxygen utilization, reduce the damage to myocardial cells by oxygen free radicals produced during anaerobic metabolism, and also help the self repair of myocardial cell membrane[12,13]. In this study, levocarnitine and coenzyme Q10 were used in the treatment of CHF patients in order to clarify the role of the therapy in optimizing the disease.

There is common persistent hypertension in patients with CHF, it leads to the increased cardiac afterload and pumping resistance, the abnormal expression of many vasoactive factors is involved in this process, and it can also objectively reflect the CHF severity. Both ET-1 and Ang II have powerful vasoconstrictive effect, and they are unusually highly expressed in CHF patients[14,15]. TXB2 is also a vasoconstrictive factor, which is produced by platelets and antagonizes the vasodilatory effect of prostaglandins. NO is a typical vasodilatory factor, its expression maintains dynamic balance with that of vasoconstrictive factor in physiological state, and the blood vessels are overshrunk when NO secretion decreases or consumption increases[16,17]. In this study, the differences in serum contents of above vasoactive molecules were first compared between two groups of patients, and it was found that compared with those before treatment, serum ET-1, Ang II and TXB2 contents of both groups decreased while NO contents increased after treatment, indicating that both therapies can optimize the expression of vasoactive molecules in the body; further compared with those of control group, serum ET-1, Ang II and TXB2 contents of observation group were lower while NO content was higher after treatment, confirming that levocarnitine + coenzyme Q10 adjuvant therapy can effectively balance the expression of vasoactive molecules and inhibit the excessive vasoconstrictive state.

Endothelial injury is a direct cause of the abnormal vasoactive molecule expression, and also one of the important mechanisms leading to the aggravation of CHF condition, and measuring the endothelial injury extent and change trend can effectively determine CHF outcome[18]. The brachial artery FMD is the most common index to evaluate endothelial function of the body, and the ultrasonic measurement is noninvasive, accurate and so on[19]. There is common FMD level decline in patients with CHF, it indicates the decline of vascular elasticity, differences in FMD levels were compared between two groups of patients in this study, and it was found that compared with those before treatment, FMD levels in...
both groups increased after treatment; further compared with those of control group, FMD level of observation group was higher after treatment, showing that levocarnitine + coenzyme Q10 adjuvant therapy can effectively optimize the vascular endothelial function and increase the vascular elasticity in patients with CHF, it is consistent with the change in vasoactive molecule expression in the study, and both are the direct performance of CHF improvement.

The specific mechanism of the optimized vasoactive molecule expression and the relieved vascular endothelial injury in CHF patients is directly related to the pharmacological properties of levocarnitine and coenzyme Q10. levocarnitine and coenzyme Q10 can both regulate lipid metabolism, reduce the damage to myocardial cells by oxygen free radicals, increase myocardial energy supply, and so on, and it is speculated that they have remarkable effect in reducing oxidative stress reaction[20-22]. In this study, the differences in serum contents of oxidative stress indexes were compared between two groups of patients, and it was found that compared with those before treatment, serum anti-oxidation molecules SOD and T-AOC contents of both groups of patients increased while oxidation molecules MDA and ROS contents decreased after treatment; further compared with those of control group, serum anti-oxidation molecules SOD and T-AOC contents of observation group were higher while oxidation molecules MDA and ROS contents were lower after treatment, confirming that levocarnitine + coenzyme Q10 adjuvant therapy can effectively inhibit the excessive oxidative stress reaction of CHF patients, and it is also the internal mechanism for it to optimize the vascular active and reduce endothelial injury in the study.

It is thus clear that levocarnitine + coenzyme Q10 adjuvant therapy can effectively optimize the vasoactive molecule expression and reduce the vascular endothelial injury in patients with CHF, the realization of its functions relies mainly on the inhibitory effect of the drugs on oxidative stress, and this is consistent with its pharmacological effects.

References


