Effects of telmisartan in combined with L-carnitine on the oxidative stress and micro-inflammation status in peritoneal dialysis patients

Jin-Xiu Cheng*, Xing Pan, Cui-Lan Liu, Hua Liu, Sheng-Jun Liu, Ling-Ling Wang

The First Hospital Affiliated to Hebei North University, 075000

Objective: To explore the effects of telmisartan in combined with L-carnitine on the oxidative stress and micro-inflammation status in peritoneal dialysis (PD) patients.

Methods: A total of 80 patients with chronic renal failure (CRF) who were admitted in our hospital from November, 2011 to January, 2014 for PD were included in the study and randomized into the treatment group and the control group. The patients in the two groups were routinely performed with PD. The patients in the treatment group were given L-carnitine oral liquid, 10 mL/time, 3 times/d, and telmisartan, 80 mg/time, 1 time/d. The patients in the control group were given L-carnitine oral liquid, 10 mL/time, 3 times a day. The patients in the two groups were treated for 24 weeks continuously. A volume of 5 mL morning fasting venous blood before and after treatment was extracted, and centrifuged for serum. The levels of hs-CRP, IL-6, IL-8, TNF-α, MDA, and GSH-Px were determined.

Results: After treatment, the levels of hs-CRP, IL-6, IL-8, TNF-α were reduced, and the reduced degree in the treatment group was significantly superior to that in the control group. After treatment, MDA was reduced, GSH-Px was elevated, and the reduced degree and elevated degree in the treatment group were significantly superior to those in the control group.

Conclusions: Telmisartan in combined with L-carnitine can probably become an ideal therapeutic measure for inhibiting the micro-inflammation state and oxidative stress reaction in PD patients, thus reducing the risk of cardiovascular events, which can provide an evidence for the clinical application in the future.

1. Introduction

Chronic renal failure (CRF), a chronic and progressive renal parenchyma damage caused by various reasons, is the terminal stage of chronic renal disease, and usually requires dialysis, as a renal replacement therapy, in order to delay residual renal function (RRF) loss[1]. PD is one of the renal replacement therapy for the treatment of CRF, with advantages of less interference on the immune system, small blood loss, low occurrence rate of hypotension, less opportunity of blood-borne diseases, and dialysis at home[2]. During PD period, a certain micro-inflammation and oxidative stress state exist. With the extending of dialysis time, RRF is constantly reducing, which can directly affect the dialysis effect and living qualities; therefore, interference on the micro-inflammation and oxidative stress is of great significance in protecting RRF[3]. The study is aimed to explore the effects of telmisartan in combined with L-carnitine on the oxidative stress and micro-inflammation status in PD patients.

2. Materials and methods

2.1. General materials

A total of 80 patients with CRF who were admitted in our hospital from November, 2011 to January, 2014 for PD were included in the study, among which 46 were male, and 34 were female; aged from 30 to 70 years old, with an average age of (52.3±6.3) years old; course from 1 to 7 years, with an average course of (4.7±1.1) years; 42 had chronic glomerulonephritis, 20 had primary hypertension, 10 had diabetes, 5 had lupus nephritis, 4 had congenital abnormalities; 15 had hypertension requiring antihypertensive drugs, and 6 had diabetes requiring antidiabetic drugs; 13 had no other systemic disease, and 67 had other systemic diseases.

*Corresponding author: Jin-Xiu Cheng, The First Hospital Affiliated to Hebei North University, 075000.
Tel: 15530392570
E-mail: cjxyfy1980@163.com
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and 18 had diabetic nephropathy. The patients in the two groups were randomized into the treatment group (telmisartan + L-carnitine) and the control group (L-carnitine), with 40 cases in each group. The comparison of the general materials between the two groups was not statistically significant (P>0.05).

2.2. Inclusion and exclusion criteria

Inclusion criteria: (1) those who were in accordance with the diagnostic criteria of CRF uremia[6], and were routinely performed with PD treatment for more than 6 months; (2) those whose RRF was greater than 2 mL/min, SCr clearance rate was 5-9 mL/min, and 24 h urine volume was greater than 200 mL; (3) those who had signed the informed consent. Exclusion criteria: (1) those who were merged with hepatopathy or tumors, and acute and chronic infections; (2) those who had accepted hormone and immunosuppressant treatments; (3) those who were allergic to related drugs.

2.3. Methods

The patients in the two groups were routinely performed with PD. The patients in the treatment group were given L-carnitine oral liquid (Shenyang Daiichi Pharmaceutical Co. Ltd., Approval No. H20113215), 10 mL/time, 3 times/d, and telmisartan (Beijing Wansheng Pharmaceutical Co. Ltd., Approval No. H20060442), 80 mg/time, 1 time/d. The patients in the control group were given L-carnitine oral liquid, 10 mL/time, 3 times a day. The patients in the two groups were treated for 24 weeks continuously.

2.4. Observation indicators

A volume of 5 mL morning fasting venous blood before and after treatment was extracted, and centrifuged for serum. Immunoturbidimetry was used to detect hs-CRP. ELASA was used to detect the levels of IL-6, IL-8, and TNF-α. Spectrophotometry was used to detect MDA and GSH-Px.

2.5. Statistical analysis

SPSS 19.0 software was used for the statistical analysis. The measurement data were expressed as mean ± SD, and t test was used. Chi-square test was used for the enumeration data. P<0.05 was regarded as statistically significant.

3. Results

3.1. Comparison of cytokine levels before and after treatment between the two groups

After treatment, the levels of hs-CRP, IL-6, IL-8, and TNF-α were reduced, and the reduced degree in the treatment group was significantly superior to that in the control group (P<0.05) (Table 1).

3.2. Comparison of the stress reaction before and after treatment between the two groups

After treatment, MDA was reduced, GSH-Px was elevated, and the reduced degree and elevated degree in the treatment group were significantly superior to those in the control group (P<0.05) (Table 2).

4. Discussion

Micro-inflammation state has no clinical signs and symptoms of local or general acute infections, but a low-level inflammation state exists, manifesting in the elevation of serum inflammatory cytokine levels[5]. Micro-inflammation state is one of the important factors for developing anemia, malnutrition, and atherosclerotic cardiovascular diseases, and can determine the severity degree to a certain extent and predict the prognosis of PD patients. At the time of micro-inflammation state, the pro-inflammatory cytokines can activate the immune system, induce mass synthesis of inflammatory cells and release of pro-inflammatory cytokines, activate the lymphocyte excreted factors, and are involved in in vivo inflammatory reaction[6]. In recent years, with the proposal of MIAS, it is realized that micro-inflammation state and atherosclerosis in PD patients are of great significance for the prognosis. Micro-inflammation state is associated with CRF own factors and complications, and PD complications. The metabolites can activate the chronic inflammation state, and is an important risk factor for promoting the development of inflammation[7]. Many researches demonstrate

Table 1
Comparison of cytokine levels before and after treatment between the two groups

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time</th>
<th>hs-CRP (mg/L)</th>
<th>IL-6 (ng/L)</th>
<th>IL-8 (ng/L)</th>
<th>TNF-α (ng/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment</td>
<td>40</td>
<td>Before treatment</td>
<td>9.32±10.25</td>
<td>86.32±13.61</td>
<td>83.57±15.81</td>
<td>45.28±10.57</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>4.87±6.53*#</td>
<td>38.72±15.43*#</td>
<td>33.67±16.51*#</td>
<td>23.67±6.68*#</td>
</tr>
<tr>
<td>Control</td>
<td>40</td>
<td>Before treatment</td>
<td>9.41±9.72</td>
<td>85.37±12.61</td>
<td>82.72±16.47</td>
<td>45.36±10.14</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>7.47±9.68*</td>
<td>59.87±16.48*</td>
<td>65.81±11.26*</td>
<td>34.76±11.45*</td>
</tr>
</tbody>
</table>

*P<0.05, when compared with before treatment; #P<0.05, when compared with the control group.

Table 2
Comparison of the stress reaction before and after treatment between the two groups

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time</th>
<th>MDA (nmol/L)</th>
<th>GSH-Px (μmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment</td>
<td>40</td>
<td>Before treatment</td>
<td>7.76±1.35</td>
<td>78.67±6.87</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>3.67±0.58*#</td>
<td>142.15±11.37*#</td>
</tr>
<tr>
<td>Control</td>
<td>40</td>
<td>Before treatment</td>
<td>7.74±1.43</td>
<td>78.75±7.52</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>6.85±0.45*</td>
<td>95.47±9.34*</td>
</tr>
</tbody>
</table>

*P<0.05, when compared with before treatment; #P<0.05, when compared with the control group.
that micro-inflammation state is prevailing in PD patients, whose mechanism is by activating the mononuclear phagocytic system, and increasing the release of TNF-α, hs-CRP, IL-1, IL-6, IL-8, and other pro-inflammatory cytokines, thus inducing the inflammatory reaction, and is closely associated with the occurrence of cardiovascular events in CRF patients; therefore, interference on the micro-inflammation state in PD patients is key to prevent the complications[8].

hs-CRP is an objective indicator to reflect the micro-inflammation state at an early stage with a high sensitivity, and is involved in the occurrence of inflammatory reaction, immunological recognition, and immune regulation[9]. IL-6 can sensitively reflect the inflammation, is a main regulatory factor of inflammatory cells, can strengthen the inflammatory reaction, which can further accelerate the renal damage, is an independent risk factor for developing end-stage renal disease complicated with cardiovascular and death incidents, is an ideal indicator to diagnose the uremic micro-inflammation state, and is a predictive factor to estimate the prognosis[10]. IL-8 is closely associated with the kidney diseases, is involved in the glomerular immune injury process, and can be served as a marker of inflammation state in CRF patients[11]. TNF-α is an important inflammatory cytokine, whose elevated level suggests an micro-inflammation state existing in PD patients[12]. The increased production of oxygen radical and damaged radical scavenging system function in PD patients can strengthen the oxidative stress, and increase the oxygen radical and related metabolites, which can directly damage the nucleic acid and protein to cause the body damage. In a normal condition, reactive oxygen production and anti-oxidation mechanism keep a balance state, which can maintain the normal function. In PD patients, this normal oxidation balance is destroyed to accelerate the oxygen reactive reaction[13]. MDA is a degradation production of lipid peroxide, and is the most representative indicator to reflect the oxidative stress level, whose content can reflect the lipid peroxide degree[14]. GSH-Px is a kind of protective enzyme and an important antioxidant, can eliminate the toxicity of oxygen radical, and block the lipid peroxidation chain reaction, whose content can reflect the free radical scavenging capability. The reduced GSH-Px activity means that the tissue peroxidation is strengthening[15].

L-carnitine has anti-inflammation and antioxidant properties, can reduce the phosphorylation protein level in the peripheral blood mononuclear cells and the activity of c-Jun amino terminal kinase, inhibit the activation of monocytes and production of pro-inflammatory factors, and restrain the acute-phase reaction induced by PDX[16].

Telmisartan is a kind of Ang II 1 receptor antagonist, can retard Ang II, can combine with the peroxidase proliferation activation receptor 1, regulate the phagocyte function, block C-c chemokine 2b receptor, interfere the monocytes accumulated in the inflammation sites, and regulate the immune system, thus playing an anti-inflammation role[17]. The results in the study showed that after treatment, the levels of hs-CRP, IL-6, IL-8, and TNF-α were reduced, and the reduced degree in the treatment group was significantly superior to that in the control group (P<0.05); after treatment, MDA was reduced, GSH-Px was elevated, and the reduced degree and elevated degree in the treatment group were significantly superior to those in the control group (P<0.05), suggesting that telmisartan in combined with L-carnitine can effectively regulate the oxidative stress and micro-inflammation state in PD patients.

In conclusion, telmisartan in combined with L-carnitine can probably become an ideal therapeutic measure for inhibiting the micro-inflammation state and oxidative stress reaction in PD patients, thus reducing the risk of cardiovascular events, which can provide an evidence for the clinical application in the future.

References