Influence of calcitriol treatment on nutritional status, inflammation and oxidative stress of patients undergoing maintenance hemodialysis

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Objective: To analyze influences of calcitriol treatment on nutritional status, inflammation and oxidative stress of patients undergoing maintenance hemodialysis. Methods: A total of 132 patients undergoing maintenance hemodialysis in our hospital were enrolled and randomly divided into observation group and control group. The observation group (n=66 cases) underwent calcitriol treatment, while control group (n=66 cases) underwent routine treatment. Results: (1) After treatment, patients’ TSF, MAC, AMC, Hb levels of the observation group were higher than that of the control group (P<0.05); (2) After treatment, TGF-beta 1, CTGF levels of the observation group was significantly lower than that of the control group (P<0.05), but BMP-7 level was higher than control group (P<0.05). (3) Patients’ MPO, CAT, NO, TAC levels of the observation group were higher than control group (P<0.05). Conclusion: For patients with maintenance hemodialysis, Calcitriol can optimize patients’ nutritional status, reduce systemic inflammatory response, enhance antioxidant capacity.

1. Introduction

For patients with kidney failure, maintenance hemodialysis (MHD) is an effective treatment to prolong their life without operation; however, patients with MHD also commonly experience inflammation and oxidative stress, which in a long term can cause the occurrence of cardiovascular complications and eventually increase the mortality of the patients[1]. It is a necessary treatment on alleviating the inflammation and oxidative stress of the patients to help them to prolong their life. At present, calcitriol is considered to be an effective medicine beneficial for the recovery of the patients’ conditions. This study mainly analyze the influence of calcitriol treatment on nutritional status, inflammation and oxidative stress of the patients with MHD.

2. Materials and methods

2.1. General information

132 cases of chronic renal failure patients, who had been hospitalized from December 2013 to December 2014, were selected as objects of this study and accepted the MHD treatment. All these patients did not have combined acute and chronic infection, malignant tumor and multiple organ failure. They signed the consent form with their family members after being informed of the study processes and then were randomly divided into two groups, the observation group and the control group, with 66 cases in each. The control group, in which there were 34 male and 32 female cases, 35–72 years old, with an average age of (58.29±8.05), accepting the hemodialysis of 6–28 months and (12.54±3.02) on average, was given conventional treatment. In the observation group, there were 35 male and 31 female cases, 36–70 years old, with an average age of (57.61±8.33), accepting the hemodialysis of 5–29 months and (12.16±3.35) on average. This group was given calcitriol treatment. The comparison of the general
information between these two groups did not show statistically significant differences ($P > 0.05$); therefore, they would be of comparability.

2.2. Method of the treatment

The hemodialysis was conducted 3 times/week and 4 h/ time on the two groups. The cases from control group were treated by conventional medication; while apart from the conventional medication, the cases from observational group orally took Calcitriol soft capsules (Qingdao Haier Zhengda Pharmaceutical Co. Ltd, national medicine permission NO. H20030491) 0.5 µg/d, treated for 12 weeks.

2.3. Observation indexes

2.3.1. Nutritional status

Before and after the patients took medication, their triceps skinfold thickness (TSF), mid-arm circumference (MAC), and arm muscle circumference (AMC) were measured. Meanwhile, their peripheral venous blood was drawn to test the hemoglobin (Hb) level.

2.3.2. Inflammation indexes

Before and after taking the medication, the patients had their peripheral venous blood drawn to test the changes of transforming growth factor–β 1 (TGF–β 1), connective tissue growth factor (CTGF) and bone morphogenetic protein–7 (BMP–7) levels.

2.3.3. Oxidative stress level

Before and after the patients took the medication, their peripheral venous blood was drawn to test Myeloperoxidase (MPO), Nitric Oxide (NO), total antioxidant capacity (TAC) etc.

2.4. Statistical analysis

All the data was statistically analyzed by statistical software, SPSS 18.0, and the variable data were analyzed by $t$ test. $P < 0.05$ was considered to have statistically significant difference.

3. Results

3.1. Nutritional status

The comparison of each nutritional status index between two groups before treatment did not show a statistically significant difference ($P > 0.05$). After treatment, the level of each nutritional status index in two groups was evidently higher than that before treatment, meanwhile, the levels of TSF, MAC, AMC and Hb in the observational group were higher than that in the control group, with statistically significant differences ($P < 0.05$), as shown in Table 1.

<table>
<thead>
<tr>
<th>Group</th>
<th>TSF (mm)</th>
<th>MAC (cm)</th>
<th>AMC (cm)</th>
<th>Hb (g/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observational Before treatment</td>
<td>10.23±1.54</td>
<td>25.18±3.76</td>
<td>22.18±2.74</td>
<td>83.18±15.06</td>
</tr>
<tr>
<td>After treatment</td>
<td>13.27±2.09</td>
<td>28.73±4.83</td>
<td>25.27±3.83</td>
<td>119.72±23.92</td>
</tr>
<tr>
<td>Control Before treatment</td>
<td>10.19±1.37</td>
<td>25.63±3.92</td>
<td>22.37±2.91</td>
<td>84.24±13.29</td>
</tr>
<tr>
<td>After treatment</td>
<td>11.52±1.68</td>
<td>26.76±4.13</td>
<td>23.13±3.12</td>
<td>96.73±15.28</td>
</tr>
</tbody>
</table>

3.2. Inflammation indexes

Comparing inflammation index levels between two groups before treatment, the difference had no statistical significance. The levels of TGF–β 1 and CTGF in two groups after treatment were lower than that before treatment, while the level of BMP–7 was higher than that before treatment. Meanwhile, after treatment, the levels of TGF–β 1 and CTGF in the observational group were lower than that in the control group, and the level of BMP–7 was higher than that in the control group. These differences had statistical significance ($P < 0.05$), as shown in the Table 2.

<table>
<thead>
<tr>
<th>Group</th>
<th>TGF–β 1 (ng/L)</th>
<th>CTGF (ng/L)</th>
<th>BMP–7 (ng/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observational Before treatment</td>
<td>1 274.13±186.09</td>
<td>735.28±73.11</td>
<td>83.26±8.23</td>
</tr>
<tr>
<td>After treatment</td>
<td>634.18±83.03</td>
<td>318.13±53.17</td>
<td>231.83±11.03</td>
</tr>
<tr>
<td>Control Before treatment</td>
<td>1 264.27±178.33</td>
<td>719.37±76.09</td>
<td>89.63±7.62</td>
</tr>
<tr>
<td>After treatment</td>
<td>1 024.28±153.29</td>
<td>602.17±67.24</td>
<td>119.72±9.73</td>
</tr>
</tbody>
</table>

3.3. Oxidative stress level

The comparison of oxidative stress level between two groups before treatment had no statistically significant difference ($P > 0.05$). The Oxidative stress levels of two groups after treatment were distinctly higher than that before treatment. At the same time, the levels of MPO, CAT, NO and TAC in the observational group were higher than that in the control group after treatment, with statistically significant differences ($P < 0.05$), as shown in Table 3.

<table>
<thead>
<tr>
<th>Group</th>
<th>MPO (µmol/L)</th>
<th>CAT (U/g Hb)</th>
<th>NO (µmol/L)</th>
<th>TAC (Um/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observational Before treatment</td>
<td>8.62±0.93</td>
<td>98.76±9.73</td>
<td>42.18±7.03</td>
<td>12.17±2.18</td>
</tr>
<tr>
<td>After treatment</td>
<td>15.24±1.73</td>
<td>121.83±14.28</td>
<td>61.28±9.74</td>
<td>28.9±6.93</td>
</tr>
<tr>
<td>Control Before treatment</td>
<td>8.59±0.87</td>
<td>99.17±9.21</td>
<td>43.71±6.89</td>
<td>12.35±2.31</td>
</tr>
<tr>
<td>After treatment</td>
<td>11.33±1.12</td>
<td>106.77±11.05</td>
<td>50.42±8.13</td>
<td>16.38±2.11</td>
</tr>
</tbody>
</table>

4. Discussion

MHD is the primarily non-operative way for patients with end-
stage renal disease (ESRD) to maintain their lives. However, MHD in a long time may cause the disorder of each factor level in patients, stimulate the patients’ inflammation and oxidative stress, and evoke the occurrence of cardiovascular disease, atherosclerosis, etc. This currently has become the main cause of MHD patients’ eventual deaths. During the treatment process of MHD patients, prevalent malnutrition is a risk factor for the increase of the patients’ hospitalization rate, while inflammation and oxidative stress are the crucial elements of increasing the related complications[2,3].

Calcitriol is a active form of vitamin D₃, and possesses the effects of regulating calcium and phosphorus metabolism, rebuilding bones, decreasing the inflammatory mediators’ expression, etc. Calcitriol can boost the absorption of calcium by intestines, and adjust the calcification of bones; and for MHD patients, it is necessary to add exogenous calcitriol so as to balance the body’s calcium and phosphorus metabolism, when the synthesis of endogenous calcitriol remarkably decreases or even completely ceases[4]. Recent research shows that progressive malnutrition is prevalent among MHD patients, with its incidence exceeding 50%, and it is also a complication that is difficult to be rectified for the patients and can influence their final prognosis. The major cause of MHD patients’ malnutrition is insufficient dialysis. This can reduce the protein intake, lead to acidosis and insulin resistance, and finally accelerate protein degradation, resulting in malnutrition; while malnutrition can in turn influence the sufficiency of dialysis and this forms a vicious circle. There are few definite conclusions on Calcitriol’s effects on MHD patients’ malnutrition. TSF, MAC and AMC are the commonly indirect means of judging the patients’ nutritional status; and since 2/3 of human’s fats are stored in the subcutaneous tissue, by measuring the thickness of these fats, people’s conditions of thinness or greasiness can be judged, and fat contents in the whole body and the nutritional status can also be speculated; also, Hb level can directly reflect the nutritional status[6]. The above study demonstrated that each nutritional index level of the two groups after treatment were obviously higher than that before treatment, meanwhile, observational group cases’ TSF, MAC, AMC, Hb levels were higher than the control group’s, which indicated that calcitriol can effectively improve MHD patients’ nutritional status, and that concrete mechanism can be related with the improvement of patients’ micro-inflammation state apart from slowing down the protein degradation.

In the patients’ body, there are slight and continuous activation of inflammatory factors, which means that patients do not have the remarkably clinical infection signs clinical infection signs on the whole body or the localized; however, due to the activation of immunity and inflammation cells in the whole body or the localized, inflammation state of continuously low level is evoked in the patients’ body[7]. At present TGF-β1 is generally acknowledged as the strongest promoting renal interstitial fibrosis factors and it is beneficial to chemokine expression of epithelial cells on renal tubular, aggravating renal tubulointerstitial inflammation; also, it can stimulate the epithelial cells of renal tubular to transdifferentiate into myofibroblasts; moreover, it can inhibit the activity of matrix metalloprotease, plasminogen activator and other many types of extracellular matrix degrading enzymes, and stimulate the activity of metalloprotease tissue inhibitors; on top of that, it can increase the expression of cellular membrane’s integrin, etc. and promote the process of tissue fibrosis[8]. Most scholars’ research thinks that TGF-β1 is a crucial link in the occurrence and development of the patients’ micro-inflammation state and its level is directly correlated with patients’ micro-inflammation level, thus TGF-β1 can be considered as a quantitative index reflecting patients’ systemic inflammation state[9]. CTGF belongs to secreting peptides containing cysteine and possesses the obvious mitogen and chemotaxis, which can be induced into fibrocyte proliferation and extracellular matrix secretion. CTGF and TGF-β1 have the synergistic effects and also play important roles in the continuous process of MHD patients’ micro-inflammation state. BMP-7 has the evidently protective effects on kidneys and through various pathways exerts antagonistic effects on renal injury caused by TGF-β1; meanwhile, BMP-7 can decrease inflammatory factors TGF-β1 – induced inflammatory factors secretion and chemokine level[10]. There has been research showing that the loss of endogenous BMP-7 has close correlation with renal fibrosis, and that the concentration of BMP-7 in serum and nephropathy staging are negatively correlated. The above study results displayed that two groups of patients’ TGF-β1 and CTGF levels after treatment were lower than that before treatment, meanwhile, the observational group’s TGF-β1 and CTGF levels were lower than the control group’s, while its BMP-7 level was higher than the control group’s, which indicated that the application of calcitriol has the positive effects on the improvement of MHD patients’ micro-inflammation state and further facilitate the amelioration of nutritional status.

Micro-inflammation state and oxidative stress reaction are the independent pathological processes, but both of them can still build a reciprocal causation and mutually getting promoted. There has been research proving that MHD patients’ oxidative stress system is activated, and the patients present with enhancing lipid peroxidation, decreasing antioxidant capacity, reducing antioxidant substances, etc. meanwhile, inflammatory factors in the above micro-inflammation state can amplify oxidative stress reaction, which can further stimulate the activation of inflammatory cells and thus form a cascade effect[11]. MPO is an important lysosome containing iron, exists in myeloid cells and is a member of heme peroxidase superfamily. MPO is the function and activation marker of neutrophils and its primary function is to kill microorganism in phagocyte and form free radical with oxidative ability[12,13]. CAT is the marker enzyme of peroxisome and its main function is to
catalyze the decomposition of hydrogen peroxide into water and oxygen, which cannot make it react with oxygen under the action of iron chelate compounds and produce extremely harmful -OH. CAT is a kind of enzyme scavenger, protecting cells from hydrogen peroxide’s toxicity through eliminating the hydrogen peroxide, and it is also one of the organism defense system’s key enzymes and one of the human antioxidant capacity’s important symbols.[14]. NO is able to dilate vessels, resist cell proliferation and regulate mesangial cells’ proliferative reaction on all kinds of inflammatory injury, and plays an important role in human antioxidation autonomous defense system; thus, NO level in human body can represent human body’s antioxidant capacity.[15]. The above study results demonstrated that the two groups’ oxidative stress levels after treatment were distinctly higher than that before treatment; meanwhile, MPO, CAT, NO, TAC levels of the cases in the observational group were higher than that of the cases in the control group, which manifested that calcitriol treatment can abate patients’ systemic oxidative stress reaction and strengthen the body’s antioxidant capacity.

In conclusion, calcitriol can be applied in the treatment of MHD patients, enhance their nutritional status, decrease systemic inflammatory response, and boost antioxidant capacity, worth being disseminated and applied in future clinical practice.

References


