Effect of low protein diet combined with drug therapy on renal function and oxidation – anti-oxidation balance in patients with diabetic nephropathy

Yan Li1, Qin Zeng2

1. Integrated Department of Endocrinology and Nephrology, the Second People’s Hospital of Deyang City Sichuan Province, Deyang, Sichuan Province, 618000
2. Department of Burn, People’s Hospital of Deyang City Sichuan Province, Deyang, Sichuan Province, 618000

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ABSTRACT

Objective: To study the effect of low protein diet combined with drug therapy on renal function and oxidation – anti-oxidation balance in patients with diabetic nephropathy. Methods: Patients with diabetic nephropathy who were treated in the Second People’s Hospital of Deyang City between July 2014 and March 2017 were collected, retrospectively analyzed and then divided into two groups according to the application of low protein diet intervention or not, observation group received low protein diet combined with drug therapy, and control group accepted routine drug therapy. The contents of renal function indexes, oxidative products and antioxidant indexes in serum as well as the expression of podocyte injury markers in urine were measured before treatment and 3 months after treatment. Results: 3 months after treatment, BUN, Scr, CysC, Hcy, MDA and AOPP contents in serum as well as α-actinin-4, ZO-1, nephrin and podocinde mRNA expression in urine of both groups were lower than those before treatment whereas CAT, SOD and T-AOC contents in serum were higher than those before treatment, and BUN, Scr, CysC, Hcy, MDA and AOPP contents in serum as well as α-actinin-4, ZO-1, nephrin and podocinde mRNA expression in urine of observation group were lower than those of control group whereas CAT, SOD and T-AOC contents in serum were higher than those of control group. Conclusion: Low protein diet combined with drug therapy can improve the renal function and the oxidation - anti-oxidation balance in patients with diabetic nephropathy.

1. Introduction

In recent years, with the aggravated aging of the population in China and the change in residents' diet and lifestyle, the incidence of type 2 diabetes mellitus has bee rising, and the corresponding diabetes complications are also growing. Diabetic nephropathy is a common microvascular complication in patients with type 2 diabetes that will cause the accumulation of adverse metabolites in the body and the increase of protein leakage, and severe cases might progress to end-stage kidney disease and require renal replacement therapy[1,2]. The excessive activation of oxidative stress is an important pathological link in the development and change of diabetic nephropathy, and the mass generation of oxygen free radical can cause damage to glomerular endothelial function and filtration barrier, thus affect the elimination of metabolites via glomeruli and increase the leakage of protein via the glomeruli. In clinical practice, the common drugs for diabetic nephropathy include endothelial protective drugs and Chinese patent medicines, etc., which can reduce the renal burden by supplementing the low-protein diet[3,4]. In the following study, in order to define the value of low protein diet for the treatment of diabetic nephropathy, we specifically analyzed the effect of low protein diet combined with drug therapy on renal function and oxidation - anti-oxidation balance in patients with diabetic nephropathy.
2. Information and methods

2.1 General case information

Patients with diabetic nephropathy who were treated in the Second People’s Hospital of Deyang City between July 2014 and March 2017 were retrospectively analyzed, and the inclusion criteria were as follows: (1) patients were in accordance with the diagnostic standards for diabetic nephropathy CDK 3-4 stage; (2) blood glucose and blood pressure control were up to the standard; (3) clinical data and clinical samples were complete. Exclusion criteria: (1) patients combined with acute complications of diabetes mellitus; (2) patients combined with autoimmune diseases. A total of 136 patients were enrolled in the study and divided into two groups according to the history data and the adoption of low-protein diet. Observation group accepted low-protein diet combined with drug therapy, there were a total of 56 cases, including 31 males and 25 females who were 49-65 years old, and the course of diabetes was 3-11 years; control group received routine drug treatment, including 45 males and 35 females who were 46-66 years, and the course of diabetes was 3-12 years. There was no significant difference in the general data between the two groups ($P>0.05$).

2.2 Therapy

Fasting glucose $< 6.0$ mmol/L and 2 h postprandial blood glucose $<10.0$ mol/L were set as the target to control the blood glucose of both groups, and Bailing Capsule, Losartan Potassium Tablets, Sulodexide Soft Capsules and others were taken orally to improve renal function. On the basis of the above drug treatment, observation group accepted low-protein diet combined with drug therapy; the daily total protein intake was strictly controlled at 0.6 g/kg, and Compound alpha-Ketacid Tablets of 1 tablet /5 kg were taken orally. The clinical indicators of both groups were measured after 3 months of continuous treatment.

2.3 Clinical index detection

2.3.1 Serum index detection

Before treatment and 3 months after treatment, the venous blood was collected to separate serum, and the contents of BUN, Scr, CysC and Hcy were determined according to the operation procedure of the automatic biochemical analyzer; the contents of MDA, AOPP, CAT, SOD and T-AOC were determined according to the operation procedure of the radioimmunoprecipitation kit.

2.3.2 Urine index detection

Before treatment and 3 months after treatment, 10 mL of morning midstream urine was collected, the operation processes of the RNA extraction and reverse transcription kit were followed to separate RNA and synthesize cDNA, and then the fluorescent quantitative PCR kit was adopted to determine alpha-actinin-4, ZO-1, nephrin and podocinde mRNA expression.

2.4 Statistical methods

Software SPSS 20.0 was used for data input, the measurement data between two groups were analyzed by t test and $P<0.05$ indicated that the difference was statistically significant.

3. Results

3.1 Renal function indexes in serum

Comparison of renal function indexes BUN (mmol/L), Scr (μmol/L), CysC (mg/L) and Hcy (mmol/L) contents in serum between the two groups of patients before treatment and 3 months after treatment was as follows: BUN, Scr, CysC and Hcy contents in serum were not significantly different between the two groups of patients before treatment ($P>0.05$) whereas BUN, Scr, CysC and Hcy contents in serum were significantly different after treatment ($P<0.05$), and

![Table 1](image)

Comparison of renal function indexes before and after treatment.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time</th>
<th>BUN</th>
<th>Scr</th>
<th>CysC</th>
<th>Hcy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation group</td>
<td>56</td>
<td>Before treatment</td>
<td>11.3±1.6</td>
<td>154.7±20.3</td>
<td>2.39±0.32</td>
<td>14.9±2.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>7.4±0.9*</td>
<td>105.3±16.4*</td>
<td>1.13±0.16*</td>
<td>8.9±1.1*</td>
</tr>
<tr>
<td>Control group</td>
<td>80</td>
<td>Before treatment</td>
<td>11.8±1.8</td>
<td>155.4±19.4</td>
<td>2.44±0.37</td>
<td>15.2±1.9</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>9.6±1.3*</td>
<td>129.5±16.4*</td>
<td>1.87±0.25*</td>
<td>12.4±1.8*</td>
</tr>
</tbody>
</table>

*: comparison between before and after treatment within group, $P<0.05$; #: comparison between observation group and control group after treatment, $P<0.05$.

![Table 2](image)

Comparison of oxidative products and antioxidant indexes before and after treatment.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time</th>
<th>MDA</th>
<th>AOPP</th>
<th>CAT</th>
<th>SOD</th>
<th>T-AOC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation group</td>
<td>56</td>
<td>Before treatment</td>
<td>15.2±1.8</td>
<td>34.7±5.9</td>
<td>29.5±4.6</td>
<td>62.8±8.3</td>
<td>17.6±2.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>8.9±1.2*</td>
<td>19.3±2.2*</td>
<td>42.9±6.5*</td>
<td>98.4±1.12*</td>
<td>34.1±4.8*</td>
</tr>
<tr>
<td>Control group</td>
<td>80</td>
<td>Before treatment</td>
<td>15.7±1.9</td>
<td>35.2±5.4</td>
<td>30.1±4.2</td>
<td>63.3±9.1</td>
<td>18.1±2.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>11.3±1.5*</td>
<td>24.6±3.2*</td>
<td>36.7±4.6*</td>
<td>76.3±9.6*</td>
<td>25.8±3.4*</td>
</tr>
</tbody>
</table>

*: comparison between before and after treatment within group, $P<0.05$; #: comparison between observation group and control group after treatment, $P<0.05$. 

Software SPSS 20.0 was used for data input, the measurement data between two groups were analyzed by t test and $P<0.05$ indicated that the difference was statistically significant.
BUN, Scr, CysC and Hcy contents in serum of both groups after treatment were lower than those before treatment. BUN, Scr, CysC and Hcy contents in serum were significantly different between before and after treatment (P<0.05), and BUN, Scr, CysC and Hcy contents in serum of both groups after treatment were lower than those before treatment.

### 3.2 Oxidative products and antioxidant indexes in serum

Comparison of oxidative products MDA (μmol/L) and AOPP (μmol/L) as well as antioxidant indexes CAT (U/L), SOD (U/L) and T-AOC (U/L) in serum between the two groups of patients before treatment and 3 months after treatment was as follows: MDA, AOPP, CAT, SOD and T-AOC contents in serum were not significantly different between the two groups of patients before treatment (P>0.05) whereas MDA, AOPP, CAT, SOD and T-AOC contents in serum were significantly different after treatment (P<0.05), and MDA and AOPP contents in serum of observation group after treatment were lower than those of control group whereas CAT, SOD and T-AOC contents were higher than those of control group; MDA, AOPP, CAT, SOD and T-AOC contents in serum of both groups were significantly different between before and after treatment (P<0.05), and MDA and AOPP contents in serum of both groups after treatment were lower than those before treatment whereas CAT, SOD and T-AOC contents were higher than those before treatment.

### 3.3 Podocyte injury markers in urine

Comparison of podocyte injury markers α-actinin-4, ZO-1, nephrin and podocindine mRNA expression in urine between the two groups of patients before treatment and 3 months after treatment was as follows: α-actinin-4, ZO-1, nephrin and podocindine mRNA expression in urine were not significantly different between the two groups of patients before treatment (P>0.05) whereas α-actinin-4, ZO-1, nephrin and podocindine mRNA expression in urine were significantly different after treatment (P<0.05), and α-actinin-4, ZO-1, nephrin and podocindine mRNA expression in urine of observation group after treatment were lower than those of control group. α-actinin-4, ZO-1, nephrin and podocindine mRNA expression in urine of both groups were significantly different between before and after treatment (P<0.05), and α-actinin-4, ZO-1, nephrin and podocindine mRNA expression in urine of both groups after treatment were lower than those before treatment.

### 4. Discussion

Diabetic nephropathy is the most common microvascular complication of diabetes and also a common cause of end-stage renal disease in clinic[5,6]. BUN and Scr are the most common biochemical indicators to assess renal function. Both creatinine and urea are excreted by the kidneys, and renal function damage can affect their excretion and increase the BUN and Scr; CysC and Hcy are the newly developed renal function indexes in recent years, the former can freely cross through the glomerulus and be re-absorbed and degraded in renal tubules, and the latter is an amino acid with microvascular damage effect and can increase the glomerular damage[7,8]. In clinical practice, the common drugs for diabetic nephropathy include Losartan Potassium Tablets, Bailing Capsule and Sulodexide Soft Capsules, etc., and the low protein diet at the same time of drug treatment can alleviate the high filtration and high perfusion status of the glomeruli, and relieve the kidney burden[9,10]. In order to define the value of low protein diet for the treatment of diabetic nephropathy, we first analyzed the changes of renal function before and after the treatment, and the comparison of renal function indexes between the two groups showed that BUN, Scr, CysC and Hcy contents in serum of both groups decreased after treatment, and BUN, Scr, CysC and Hcy contents in serum of observation group after treatment were lower than those of control group. This suggests that the low-protein diet on the basis of conventional drug therapy can improve the renal function of patients with diabetic nephropathy and achieve more accurate results.

The excessive activation of oxidative stress and the destruction of oxidation - anti-oxidation balance are the most important pathological links in the course of diabetic nephropathy. Mass generation of oxygen free radicals is the characteristic of oxidative stress reaction activation, and the strongly oxidizing oxygen free radicals have oxidation reaction with the lipids and proteins in local tissue to cause tissue damage, and meanwhile, generate the corresponding product MDA and AOPP[11,12]. Under physiological conditions, the body may maintain the balance of oxidation - anti-oxidation through anti-oxidation mechanism, antioxidant enzymes SOD and CAT are the important parts of antioxidant system, and they may remove the oxygen free radicals and maintain the local tissue in reduction condition through catalytic deoxidizing reaction; however, the excessively generated oxygen free radicals will exceed the body's antioxidant capacity, cause the continuous consumption of SOD and CAT, and eventually result in the reduction of T-AOC[13,14].

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**Table 3.**

Comparison of podocyte injury markers before and after treatment.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Time</th>
<th>α-actinin-4</th>
<th>ZO-1</th>
<th>nephrin</th>
<th>podocindine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation group</td>
<td>56</td>
<td>Before treatment</td>
<td>1.03±0.14</td>
<td>1.01±0.15</td>
<td>0.98±0.13</td>
<td>1.05±0.17</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>0.67±0.09*</td>
<td>0.58±0.07*</td>
<td>0.64±0.07*</td>
<td>0.52±0.08*</td>
</tr>
<tr>
<td>Control group</td>
<td>80</td>
<td>Before treatment</td>
<td>1.01±0.16</td>
<td>1.03±0.17</td>
<td>0.97±0.14</td>
<td>1.05±0.12</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>0.83±0.11*</td>
<td>0.78±0.10*</td>
<td>0.81±0.12*</td>
<td>0.71±0.08*</td>
</tr>
</tbody>
</table>

*: comparison between before and after treatment within group, P<0.05; #: comparison between observation group and control group after treatment, P<0.05.
The analysis of the change of oxidative products and antioxidant indexes in serum before and after treatment showed that MDA and AOPP contents in serum of both groups decreased whereas CAT, SOD and T-AOC contents increased after treatment, and MDA and AOPP contents in serum of observation group after treatment were lower than those of control group whereas CAT, SOD and T-AOC contents were higher than those of control group. This means that the low protein diet on the basis of conventional drug therapy can protect the renal function and oxidation - anti-oxidation balance in patients with type 2 diabetes and obesity. Therefore, drug treatment combined with low protein diet can improve the oxidative stress damage to the podocytes of patients with diabetic nephropathy and reduce the oxidative stress damage to the podocytes, and it is worthy of clinical recommendation.

References