Effect of high-flux and low-flux hemodialysis on the side metabolites and cytokines in patients with uremia

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Objective: To study the effect of high-flux and low-flux hemodialysis on the side metabolites and cytokines in patients with uremia. Methods: A total of 50 patients with uremia who accepted high-flux hemodialysis and 140 patients with uremia who accepted low-flux hemodialysis in our hospital between March 2015 and March 2016 were selected and included in high-flux group and low-flux group respectively. Before and after dialysis, serum was collected respectively to determine the levels of side metabolites, calcium-phosphorus metabolism indexes and cytokines. Results: 3 months after dialysis, serum Ca levels of two groups of patients were not significantly different from those before dialysis while BUN, Scr, β2-MG, sTfR, P, PTH and AKP levels were significantly lower than those before dialysis; 3 months after dialysis, serum BUN, Scr and Ca levels of high-flux group were not significantly different from those of low-flux group while β2-MG, sTfR, P, PTH, AKP, TNF-α, IL-1β, IL-6, IL-8 and IL-10 levels were significantly lower than those of low-flux group. Conclusion: Compared with low-flux hemodialysis, high-flux hemodialysis treatment of uremia can more effectively remove middle molecular and macromolecular toxins, correct calcium-phosphorus metabolism disorder and relieve micro-inflammatory state.

1. Introduction

Uremia is the end-stage change of chronic kidney disease, and the chronic kidney disease caused by diabetic nephropathy, hypertensive nephropathy and glomerular disease will eventually progress to end-stage renal failure and requires hemodialysis therapy. Low-flux hemodialysis is the most commonly used method for clinical hemodialysis at present, it removes the by-products of metabolism in the way of pure dispersion, its effect is ideal on removing the macromolecular toxins, but the effect is limited on removing the middle molecular and low molecular toxins, and it can’t effectively correct the calcium-phosphorus metabolism disorders and micro-inflammatory state in the development and change of uremia[1,2].

High-flux hemodialysis is a new way of dialysis developed in recent years, which combines three removing methods: diffusion, convection, and adsorption, and has strong removing effect on macromolecular and middle molecular toxins[3]. In the following study, the effect of high-flux and low-flux hemodialysis on the side metabolites and cytokines in patients with uremia was analyzed.

2. Subjects and methods

2.1 Research subjects

A total 50 patients with uremia who accepted high-flux hemodialysis in our hospital between March 2015 and March 2016 were selected as high-flux group, 140 patients with uremia who accepted low-flux hemodialysis were selected as low-flux group, all patients were clearly diagnosed with chronic renal insufficiency and uremia period, they were in accordance with the hemodialysis
Comparison of serum side metabolite levels between two groups of patients before and after dialysis.

Before dialysis and 3 months after dialysis, 6-8 mL of peripheral blood sample was collected from two groups of patients and centrifuged to separate serum and store it in a -70 °C refrigerator. Automatic biochemical analyzer was used to detect serum creatinine (Scr), blood urea nitrogen (BUN), calcium (Ca) and phosphorus (P) levels, enzyme-linked immunosorbent assay kits were used to determine β2-microglobulin (β2-MG), soluble transferrin receptor (sTfR), parathyroid hormone (PTH), alkaline phosphatase (AKP), tumor necrosis factor-α (TNF-α), interleukin-1β (IL-1β), IL-6, IL-8 and IL-10 levels.

2.3 Serum index detection methods

Before dialysis and 3 months after dialysis, 6-8 mL of peripheral blood sample was collected from two groups of patients and centrifuged to separate serum and store it in a -70 °C refrigerator. Automatic biochemical analyzer was used to detect serum creatinine (Scr), blood urea nitrogen (BUN), calcium (Ca) and phosphorus (P) levels, enzyme-linked immunosorbent assay kits were used to determine β2-microglobulin (β2-MG), soluble transferrin receptor (sTfR), parathyroid hormone (PTH), alkaline phosphatase (AKP), tumor necrosis factor-α (TNF-α), interleukin-1β (IL-1β), IL-6, IL-8 and IL-10 levels.

Comparison of serum side metabolite levels between two groups of patients before and after dialysis.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Dialysis</th>
<th>BUN (mmol/L)</th>
<th>Scr (μmol/L)</th>
<th>β2-MG (μg/mL)</th>
<th>sTfR (μg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High-flux</td>
<td>50</td>
<td>Before dialysis</td>
<td>17.4±2.15</td>
<td>652.4±81.32</td>
<td>62.88±8.15</td>
<td>0.59±0.07</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After dialysis</td>
<td>11.3±1.62*</td>
<td>307.8±42.64*</td>
<td>21.4±2.96*</td>
<td>0.25±0.04*</td>
</tr>
<tr>
<td>Low-flux</td>
<td>140</td>
<td>Before dialysis</td>
<td>18.0±2.18</td>
<td>661.3±78.76</td>
<td>63.5±8.52</td>
<td>0.62±0.08</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After dialysis</td>
<td>10.9±1.93</td>
<td>315.4±42.69*</td>
<td>38.7±5.15*</td>
<td>0.41±0.05*</td>
</tr>
</tbody>
</table>

* compared with same group before dialysis, P<0.05; † compared with low-flux group at the same dialysis time point, P<0.05.

Comparison of serum calcium-phosphorus metabolism indexes between two groups of patients before and after dialysis.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Dialysis</th>
<th>Ca (mmol/L)</th>
<th>P (mmol/L)</th>
<th>PTH (pg/ml)</th>
<th>AKP (U/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High-flux</td>
<td>50</td>
<td>Before dialysis</td>
<td>2.18±0.26</td>
<td>2.44±0.28</td>
<td>479.3±56.12</td>
<td>175.8±22.15</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After dialysis</td>
<td>2.20±0.27</td>
<td>1.62±0.20*</td>
<td>314.6±38.61</td>
<td>130.2±16.74</td>
</tr>
<tr>
<td>Low-flux</td>
<td>140</td>
<td>Before dialysis</td>
<td>2.21±0.32</td>
<td>2.42±0.29</td>
<td>482.4±58.79</td>
<td>177.1±23.15</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After dialysis</td>
<td>2.25±0.24</td>
<td>1.97±0.25*</td>
<td>392.3±46.21</td>
<td>158.6±18.62</td>
</tr>
</tbody>
</table>

* compared with same group before dialysis, P<0.05; † compared with low-flux group at the same dialysis time point, P<0.05.
the changes of side metabolites and cytokines in patients with uremia are no clear reports about the removal of different metabolites after positive value of high-flux hemodialysis for uremic dialysis, but there In recent years, more and more clinical scholars have realized the Hemodialysis is the main way for clinical treatment of uremia, including traditional low-flux hemodialysis and the newly developed high-flux hemodialysis. High-flux hemodialysis and low-flux hemodialysis are different in dialysis membrane permeability, namely the ultrafiltration coefficient \([4,5]\). The ultrafiltration coefficient of low-flux hemodialysis os less than 20 mL/mmHg/h, it mainly removes the solute by means of dispersion, and it has strong scavenging effect on the micromolecular toxins such as creatinine and urea nitrogen that are produced from metabolism in the body. However, the scavenging effect of low-flux hemodialysis on middle molecular toxins and macromolecular toxins is limited, and the accumulation of macromolecular toxins and middle molecular toxins in the body will cause calcium-phosphorus metabolism disorders, micro-inflammatory state, etc., and can also make the body in a continuous nutrient consumption state\([6]\). The ultrafiltration coefficient of high-flux dialysis is more than 20 mL/mmHg/h, it scavenges the solute by means of diffusion, convection and adsorption, and it has strong scavenging effect on macromolecular, middle molecular and micromolecular toxins\([7,8]\). In addition, high-flux hemodialyzer membrane is generally DIAPES membrane, its compatibility with the blood is better than that of traditional low-flux hemodialyzer, and the risk of inflammatory reaction significantly reduces during continuous dialysis\([9]\).

In recent years, more and more clinical scholars have realized the positive value of high-flux hemodialysis for uremic dialysis, but there are no clear reports about the removal of different metabolites after high-flux and low-flux hemodialysis treatment of uremia. In the study, the changes of side metabolites and cytokines in patients with uremia were compared before and after high-flux and low-flux hemodialysis. Scr and BUN are the protein metabolites in the body and belong to micromolecular toxins, and the analysis in the study showed that Scr and BUN levels of both groups of patients significantly decreased after dialysis, and there was no significant difference between groups. This means that both low-flux and high-flux hemodialysis can effectively scavenge the micromolecular toxins and the scavenging effect is equivalent. \(\beta_2\)-MG and sTfR are middle molecular toxins that are mainly produced after cell lysis, the former is from lymphocytes, the latter is from red blood cells\([10,11]\), and the analysis in the study showed that the \(\beta_2\)-MG and sTfR levels of both groups of patients significantly reduced after dialysis and serum \(\beta_2\)-MG and sTfR levels of high-flux patients group were significantly lower than those of low-flux group. This means that high-flux hemodialysis has better scavenging effect on middle molecular toxins than low-flux hemodialysis.

Parathyroid hormone is an important hormone that regulates calcium-phosphorus metabolism and also the representative of macromolecular toxins in the body. In the process of hemodialysis, secondary hyperparathyroidism is a common concurrent change, and the abnormal parathyroid hormone secretion caused by poor parathyroid hormone scavenging and calcium-phosphorus metabolism disorder is associated with the occurrence of secondary hyperparathyroidism in the process of hemodialysis\([12,13]\). Phosphorus belongs to micromolecular toxin, but phosphorus is hydrophilic and cannot be freely diffused through the cell membrane, so the hemodialysis removal on blood phosphorus is closer to the middle molecular toxins, the removal efficiency of low-flux hemodialysis on blood phosphorus is low, so the phosphorus is abnormally accumulated in the body, blood phosphorus content increases, and it activates parathyroid gland and increases the secretion of parathyroid hormone\([14]\). In addition, abnormal blood phosphorus metabolism and parathyroid hormone secretion can enhance the activity of osteoblasts and increase the secretion and release of AKP. In the study, analysis of serum calcium-phosphorus metabolism indexes of two groups of patients showed that serum P, PTH and AKP levels of both groups of patients significantly reduced after dialysis and serum P, PTH and AKP levels of high-flux group were significantly lower than those of low-flux group. It means that high-flux hemodialysis has better scavenging effect on macromolecular toxins than low-flux hemodialysis, and also has better

### Table 3
Comparison of serum cytokine levels between two groups of patients after dialysis (pg/mL).

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>TNF-(\alpha)</th>
<th>IL-1(\beta)</th>
<th>IL-6</th>
<th>IL-8</th>
<th>IL-10</th>
</tr>
</thead>
<tbody>
<tr>
<td>High-flux</td>
<td>50</td>
<td>26.51±3.52</td>
<td>62.49±7.59</td>
<td>11.57±1.58</td>
<td>16.86±2.37</td>
<td>9.37±0.93</td>
</tr>
<tr>
<td>Low-flux</td>
<td>140</td>
<td>44.27±5.59</td>
<td>103.25±15.38</td>
<td>18.39±2.84</td>
<td>37.58±5.27</td>
<td>16.57±1.86</td>
</tr>
<tr>
<td>(T)</td>
<td></td>
<td>9.182</td>
<td>8.784</td>
<td>8.273</td>
<td>13.264</td>
<td>7.659</td>
</tr>
<tr>
<td>(P)</td>
<td></td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

#### 3.3 Serum cytokine levels

3 months after dialysis, analysis of serum cytokines TNF-\(\alpha\), IL-1\(\beta\), IL-6, IL-8 and IL-10 between two groups of patients was as follows: serum TNF-\(\alpha\), IL-1\(\beta\), IL-6, IL-8 and IL-10 levels of high-flux group were significantly lower than those of low-flux group. Differences in serum TNF-\(\alpha\), IL-1\(\beta\), IL-6, IL-8 and IL-10 levels were statistically significant between two groups of patients 3 months after dialysis \((P<0.05)\).

#### 4. Discussion

Hemodialysis is the main way for clinical treatment of uremia, including traditional low-flux hemodialysis and the newly developed high-flux hemodialysis. High-flux hemodialysis and low-flux hemodialysis are different in dialysis membrane permeability, namely the ultrafiltration coefficient\([4,5]\). The ultrafiltration coefficient of low-flux hemodialysis is less than 20 mL/mmHg/h, it mainly removes the solute by means of dispersion, and it has strong scavenging effect on the micromolecular toxins such as creatinine and urea nitrogen that are produced from metabolism in the body. However, the scavenging effect of low-flux hemodialysis on middle molecular toxins and macromolecular toxins is limited, and the accumulation of macromolecular toxins and middle molecular toxins in the body will cause calcium-phosphorus metabolism disorders, micro-inflammatory state, etc., and can also make the body in a continuous nutrient consumption state\([6]\). The ultrafiltration coefficient of high-flux dialysis is more than 20 mL/mmHg/h, it scavenges the solute by means of diffusion, convection and adsorption, and it has strong scavenging effect on macromolecular, middle molecular and micromolecular toxins\([7,8]\). In addition, high-flux hemodialyzer membrane is generally DIAPES membrane, its compatibility with the blood is better than that of traditional low-flux hemodialyzer, and the risk of inflammatory reaction significantly reduces during continuous dialysis\([9]\).
The hemodialysis process is associated with the secretion of inflammatory cytokines, which play an important role in the pathophysiological features of continuous hemodialysis. Low-flux hemodialysis has a weaker activating effect on the micro-inflammatory state compared to high-flux hemodialysis. This is because high-flux hemodialysis membranes have a better biocompatibility, leading to less stimulation of the body and a lighter micro-inflammatory state. Additionally, high-flux dialysis can effectively remove middle molecular and macromolecular toxins, with better correcting effects on calcium-phosphorus metabolism and scavenging effects on toxins harmful to the body. These effects help reduce the inflammatory response during dialysis.

In summary, high-flux hemodialysis has a stronger scavenging effect on middle molecular and macromolecular toxins, a better correcting effect on calcium-phosphorus metabolism disorder, and a weaker activating effect on the micro-inflammatory state compared to low-flux hemodialysis. It is effective in reducing the inflammatory response during the dialysis process.

**References**


