Effect of Dialytic Frequency on Microinflammation in Patient with Maintenance Hemodialysis
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ABSTRACT

Objective: To study influence of different dialytic frequency on micro-inflammation for the maintenance hemodialysis patients.

Methods: Maintenance hemodialysis 53 patients with chronic kidney disease were divided into 3 groups. Groups A, B, C dialysed 3 times per week, twice per week and 3 times per two weeks, respectively. Total time was one year. Index of micro-inflammation state was measured in all patients before and after one year.

Results: There were significantly difference in index of micro-inflammation state between any two groups.

Conclusions: Patients who dialysis lower than 2 times each week had higher rate of micro-inflammation state. This signed that dialytic frequence was important for maintenance hemodialysis.

Key words: Dialysis frequency, hemodialysis, micro-inflammation state

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West Indian Med J DOI: 10.7727/wimj.2016.441
INTRODUCTION

The prevalence rate of chronic kidney disease (CKD) is about 8% to 9% in people with over the age of forty years (1-2). Trends of CKD has become a significant public health and socio-economic issues. Hemodialysis is one of the main methods for treating patients with CKD (3). The optimal frequency of dialysis is three times a week, but the costs is relatively high. Because of the objective situation, some patients cannot afford the enormous long-term cost of dialysis of three times in a week, so these patients deliberate to reduce the frequency of dialysis, and the cost of dialysis was cut down, but the quality of life of patients also decreases. It is a un-ignored problem to balance the above questions in front of clinical nephrologists and patients.

In the present study, we assessed the impact of the frequency of dialysis on hemodialysis micro-inflammatory state in the patient with CKD and evaluated the optimal frequency of dialysis by combined maintenance hemodialysis patients with the actual situation.

SUBJECTS AND METHODS

CKD patients

A total of 53 patients with CKD were enrolled into the present study from department of nephrology, Zaozhuang Municipal Hospital, Shandong province, China, from July 2014 to April 2015. All enrolled patients was under hemodialysis, and male were 30 cases, female was 23 cases, from 19~78 years and mean age was 51.4 ± 15.3 years. All enrolled subjects accepted regular hemodialysis with glomerular filtration rate (GFR) under < 15ml/min•1.73m².
All enrolled subjects have primary diseases, including chronic glomerulonephritis (18 cases, 31.6%), diabetic nephropathy (12 cases, 21.1%), hypertensive renal damage (9 cases, 15.8%), chronic interstitial nephritis (3 cases, 5.3%), polycystic kidney disease (2 cases, 3.5%) and unknown cause (13 cases, 22.8%). The study protocol was approved by the ethics committee of the hospital, and written informed consent was obtained from all patients after they had reviewed a written summary of the study plan.

All patients were enrolled to the present study with regular hemodialysis and they were in stable condition. In all enrolled cases, glomerular filtration rate (GFR) was less than 15ml/min•1.73m^2 (K/DOQI, stage CKD V) (4). All patients had no history of hepatitis B, hepatitis C, cancer, cough, fever, abdominal pain, diarrhea and surgery trauma, etc. All patients also accepted erythropoietin (EPO), vitamin D3 and antihypertensive drugs.

**Groups**

All selected candidates were divided into three groups according to the frequency of dialysis: Group A: three times a week, 19 cases (11 males and 8 females); Group B: twice a week, 15 cases (8 males, 7 females). Group C: three times every two weeks, 19 cases (11 males, 8 females). Each group is marked as group A1, group B1 and group C1 after one year of dialysis. There were no significantly difference between groups in the course of disease, age and gender. One year later, each group was marked A1, B1 and C1.

The machine for dialysis was Fresenius 4008S and Dialyzer is F6. Sodium bicarbonate dialysis was used, blood flow was 200 ~ 280ml/min and dialysate flow rate was 500ml/min. Every dialysis time was four hours.
**Indicators and methods**

The observed indicators included high-sensitivity C-reactive protein (hs-CRP), interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α). Fasting blood 2ml was were centrifuged and serum was retained to measure hs-CRP by solid phase immunoassay according to the principle of double antibody sandwich method. The type II high-sensitivity C-reactive protein quantitative detection kit was purchased from the Norwegian Axxis-shield company. Extracted serum from clotting venous blood by centrifugation was placed at -20°C cryopreservation to measure IL-6 and TNF-α level by radioimmunoassay. IL-6, TNF-α radioimmunoassay kit was purchased from Beijing boreal company and the SN-695B type γ counter was used. One year later, the same indicators were also measured again, the number of deaths, causes of deaths and withdraw of cases were all recorded.

**Statistical analysis**

SPSS 10.0 for windows statistical analysis software was used. All measurement data was masked as mean ± standard deviation (x̄±s) and t test was applied to compare the data between two groups. Chi-square test (x²) was used to count data. Logistic regression analysis was used to mortality analysis. P <0.05 was statistically significant (bilateral).

**RESULTS**

Microinflammatory Comparison (table 1)

There was no significant difference between different groups in hs-CRP and IL-6 in the baseline in table 1(F=38.61, P=0.401 and F=523.7, P = 0.873), but there was significant
differences (F=172.03, P <0.05 and F=3221.3, P< 0.05 ) among the three groups after one year dialysis in hs-CRP and IL-6, and significant difference was seen between A1 and C1 (t =5.733, P <0.05) in hs-CRP and A1 and C1 (t =3.757 , P<0.05) in IL-6. But there were no difference between B and B1 (t = - 2.103, P=0.057), C and C1 (t = - 2.103, P=0.057) in hs-CRP, in IL-6 for A and A1 (t =0.282, P=0.781), B and B1 (t = - 1.523, P=0.154), C and C1 (t = - 1.475, P=0.171). The results showed that the level of hs-CRP and IL-6 in serum in patients with three times dialysis per week was significantly lower than patients with twice dialysis per week, and the frequency of dialysis was an important factor to affect the level of hs-CRP and IL-6 in serum.

DISCUSSION

Chronic kidney disease (CKD), also known as chronic renal disease, is progressive loss in kidney function over a period of months or years (5). The symptoms of worsening kidney function are not specific, and might include feeling generally unwell and experiencing a reduced appetite. Chronic Kidney Disease (CKD) is a common disease with poor prognosis, seriously deducing the quality of life in patients with CKD, and increasing the burden on society and patient’s family (6-8).

At stage 5 of CKD, renal replacement therapy is usually required, in the form of either hemodialysis (HD), peritoneal dialysis (PD) or a transplant (9). Hemodialysis, also spelled haemodialysis, commonly called kidney dialysis or simply dialysis, is a process of purifying the blood of a person whose kidneys are not working normally. Longterm complications of hemodialysis include amyloidosis, neuropathy and various forms of heart
disease. Increasing the frequency and length of treatments have been shown to improve fluid overload and enlargement of the heart that is commonly seen in such patients. Due to these complications, the prevalence of complementary and alternative medicine use is high among patients undergoing hemodialysis.

Chronic micro-inflammatory state is prevalent in patients with MHD, and the main clinical manifestations are acute phase protein changes and cytokine activation, including hs-CRP, IL-6 and TNF-α, etc (10-12). There is closely relationship between chronic microinflammatory and hardening of the arteries, anemia, malnutrition, erythropoietin resistance and infection. The microinflammatory would deteriorate the kidney injury and influence the outcome of CKD. With deepening of the study on complications and mechanism of chronic kidney disease, there has been growing recognition that there are many links between malnutrition, the residual renal function, micro-inflammatory state, leptin and dialysis adequacy, and all above factors are closely related to the complications, quality of life, and mortality of CKD. In the present study, according to the frequency of dialysis, all enrolled patients were divided into three groups. We measured the high-sensitivity C-reactive protein (hs-CRP), interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α) to evaluate the relationship between microinflammatory and dialysis frequency, and to provide a relatively economical method for improving the quality of life of dialysis patients.

In the present study, the level of hs-CRP, IL-6 and TNF-α were all elevated in serum in three groups, and the results indicated there was microinflammatory state in patients with CKD, as similar to other results. After one year period of dialysis, there was a significant difference between group A1 and C1 in hs-CRP and IL-6, and the results showed that the
microinflammatory state and mortality rate were slightly mitigated in three times once week than twice per week.

The main cause of death in ESRD patients is cardiovascular complications. (13) Repeated, persistent inflammation, oxidative stress, and malnutrition are the risk factors for concurrent cardiovascular disease, as the complication of ESRD. But there is no effective measures to block the vicious circle of inflammatory-malnutrition-atherosclerosis. (14-16) Malnutrition is a major risk factor for death in hemodialysis patients. In the present study, the result indicated that there was a total of eight cases of death, mortality rate of 15.1%, four cases of heart failure, 3 cases of pulmonary infection, 1 case of cerebral hemorrhage in total 53 patients after dialysis one year. There was a significantly difference between group A, group B and group C according to a chi-square test. The result of Logistic regression analysis showed that there was a positive correlation between mortality and improvement of SAG, a negative correlation between mortality and Hb, ALB. There was the highest mortality in group C, because of inadequate dialysis, malnutrition, infection and high incidence of high blood pressure.

Reviews reported that there is interaction between malnutrition, inflammation, and atherosclerosis in patients with end-stage renal failure, leading increased mortality (17-18). But there is currently no effective means of prevention from the vicious circle of inflammatory-malnutrition-atherosclerosis. The levels of hs-CRP and IL-6 were significantly lower in 3 times a week dialysis than twice a week, and it was an important factor in influence patient survival.
CONCLUSION

The present study showed that the frequency of dialysis affected the micro-inflammation and mortality. There was the same mortality in patients with twice dialysis a week and three times in a relative short time, and it need further research in a long period. In this study, less number of cases and the shorter observation time were all others shortcomings to study the relationship between the frequency of dialysis and mortality in patient with CKD.

AUTHORS’ NOTE

Zhao Hu and Tao Peng participated in its design and drafted the manuscript. Feng Li and Jijun Wang collected the clinical data. All authors read and approved the final manuscript.
REFERENCES


Table 1: Comparison of microinflammatory (Mean ± standard deviation)

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>hs-CRP (mg/L)</th>
<th>IL-6(pg/ml)</th>
<th>TNF-α(ng/ml)</th>
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<tbody>
<tr>
<td>A</td>
<td>19</td>
<td>8.77±5.98</td>
<td>123.2±57.9</td>
<td>7.62±2.63</td>
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<tr>
<td>B</td>
<td>15</td>
<td>9.08±5.06</td>
<td>118.4±60.3</td>
<td>6.54±3.74</td>
</tr>
<tr>
<td>C</td>
<td>19</td>
<td>11.41±7.73</td>
<td>129.4±67.0</td>
<td>7.38±3.42</td>
</tr>
<tr>
<td>F</td>
<td></td>
<td>38.61</td>
<td>523.7</td>
<td>22.35</td>
</tr>
<tr>
<td>P</td>
<td></td>
<td>0.401</td>
<td>0.873</td>
<td>0.762</td>
</tr>
<tr>
<td>A1</td>
<td>17</td>
<td>9.34±5.99</td>
<td>113.4±61.2</td>
<td>7.54±3.36</td>
</tr>
<tr>
<td>B1</td>
<td>13</td>
<td>11.9±7.08</td>
<td>130.9±76.4</td>
<td>7.27±3.54</td>
</tr>
<tr>
<td>C1</td>
<td>11</td>
<td>13.9±9.68</td>
<td>135.8±69.8</td>
<td>6.65±3.45</td>
</tr>
<tr>
<td>F</td>
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<td>172.03</td>
<td>3221.3</td>
<td>28.31</td>
</tr>
<tr>
<td>P</td>
<td></td>
<td>0.035</td>
<td>0.015</td>
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Table 2: Outcome of Patients in each group

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<td></td>
<td></td>
<td></td>
<td></td>
<td>HF</td>
</tr>
<tr>
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<td>1</td>
<td>0</td>
</tr>
<tr>
<td>B</td>
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<td>0</td>
<td>1</td>
</tr>
<tr>
<td>C</td>
<td>19</td>
<td>2</td>
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<td>3</td>
</tr>
<tr>
<td>x²</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

QT: quit therapy     KT: kidney transplantation     HF: heart failure
PI: pulmonary infection   CH: cerebral hemorrhage