ORIGINAL ARTICLE

Effect of Dialysis Frequency on Microinflammation in Patients with Maintenance Haemodialysis

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ABSTRACT

Objective: *To study the influence of different dialysis frequency on microinflammation for the maintenance haemodialysis patients.*

Methods: *Fifty-three maintenance haemodialysis patients with chronic kidney disease were divided into three groups. Groups A, B and C dialysed three times per week, twice per week and three times per 2 weeks, respectively. Total time was 1 year. The index of microinflammation state was measured in all patients before and after 1 year.*

Results: *There were significant differences in the index of microinflammation state between any two groups.*

Conclusion: *Patients who dialysed less than two times each week had a higher rate of microinflammation state. This showed that dialysis frequency was important for maintenance haemodialysis.*

Keywords: Dialysis frequency, haemodialysis, microinflammation state.

INTRODUCTION

The prevalence rate of chronic kidney disease (CKD) is about 8% to 9% in persons over the age of 40 years (1, 2). Trends in CKD have become a significant public health and socio-economic issue. Haemodialysis 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 are relatively high. Some patients cannot afford the enormous long-term cost of dialysis three times per week, so these patients deliberated to reduce the frequency of dialysis, and the cost of dialysis was cut down, but the quality of life of patients also decreased. It is an unignored problem to balance the above situation in front of clinical nephrologists and patients.

In the present study, we assessed the impact of the frequency of dialysis on the haemodialysis microinflammatory state in patients with CKD and evaluated the optimal frequency of dialysis by comparing ideal maintenance haemodialysis patients with other frequencies of dialysis.

SUBJECTS AND METHODS

Patients with CKD

A total of 53 patients with CKD were enrolled into the present study from the Department of Nephrology, Zaozhuang Municipal Hospital, Shandong Province, China, from July 2014 to April 2015. All enrolled patients were under haemodialysis—30 male cases, 23 female cases, from 19 to 78 years, and mean age was 51.4 ± 15.3 years. All enrolled subjects accepted regular haemodialysis with glomerular filtration rate (GFR) under < 15 ml/min/1.73 m^2.

All of the enrolled subjects had 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 causes (13 cases, 22.8%). The study protocol was approved by the ethics committee of the hospital, and written informed consent was

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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 haemodialysis, and they were in stable condition. In all enrolled cases, GFR was less than 15 ml/min/1.73 m^2 (Kidney Disease Outcome Quality Initiative, stage CKD V) (4). All patients had no history of hepatitis B, hepatitis C, cancer, cough, fever, abdominal pain, diarrhoea, and surgery trauma. All patients also accepted erythropoietin, 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 2 weeks, 19 cases (11 males, 8 females). Each group is marked as group A1, group B1 and group C1, after 1 year of dialysis. There were no significant differences between groups in the course of the disease, age and gender.

The machine for dialysis was Fresenius 4008S and Dialyzer is F6. Sodium bicarbonate dialysis was used, blood flow was 200 to 280 ml/min and dialysate flow rate was 500 ml/min. Every dialysis time was 4 hours.

Indicators and methods

The observed indicators included high-sensitivity C-reactive protein (hs-CRP), interleukin-6 (IL-6) and tumour necrosis factor-α (TNF-α). Fasting blood (2 ml) was 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 hsCRP quantitative detection kit was purchased from the Norwegian Axis-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 and 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, and the number of deaths, causes of deaths and withdrawal of cases were all recorded.

Statistical analysis

SPSS 10.0 for windows statistical analysis software was used. All measurement data were marked as mean ± standard deviation (± s), and the *t*-test was applied to compare the data between two groups. Chi-square test (x^2) was used to analyse data. Logistic regression analysis was used for mortality analysis. $p < 0.05$ was statistically significant (bilateral).

RESULTS

Microinflammatory comparison

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 1 year of dialysis in hs-CRP and IL-6, and significant differences were 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. However, there were no differences between B and B1 ($t = –2.103$, $p = 0.057$), and C and C1 ($t = –2.103$, $p = 0.057$) in hs-CRP, and in IL-6 for A and A1 ($t = 0.282$, $p = 0.781$), B and B1 ($t = –1.523$, $p = 0.154$), and 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 a three-times-per-week dialysis was significantly lower than patients with two-times-per-week dialysis, and the frequency of dialysis was an important factor to affect the level of hs-CRP and IL-6 in serum.

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

Group	n	hs-CRP (mg/L)	IL-6 (pg/ml)	TNF-α (ng/ml)
A	19	8.77 ± 5.98	123.2 ± 57.9	7.62 ± 2.63
B	15	9.08 ± 5.06	118.4 ± 60.3	6.54 ± 3.74
C	19	11.41 ± 7.73	129.4 ± 67.0	7.38 ± 3.42
F	38.61		523.7	22.35
p	0.401		0.873	0.762
A1	17	9.34 ± 5.99	113.4 ± 61.2	7.54 ± 3.36
B1	13	11.9 ± 7.08	130.9 ± 76.4	7.27 ± 3.54
C1	11	13.9 ± 9.68	135.8 ± 69.8	6.65 ± 3.45
F	172.03		3221.3	28.31
p	0.035		0.015	0.546

hs-CRP = high-sensitivity C-reactive protein; IL-6 = interleukin-6; TNF-α = tumour necrosis factor-α.

DISCUSSION

Chronic kidney disease, 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 is a common disease with poor prognosis, seriously deducing the quality of life in patients, and increasing the burden on society and the patient`s family (6–8).

At CKD stage V, renal replacement therapy is usually required, in the form of either haemodialysis, peritoneal dialysis or a transplant (9). Haemodialysis, commonly called kidney dialysis or simply dialysis, is a process of purifying the blood of a person whose kidneys are not working normally. Long-term complications of haemodialysis 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 haemodialysis.

Chronic microinflammatory state is prevalent in patients with maintenance hemodialysis, and the main clinical manifestations are acute-phase protein changes and cytokine activation, including hs-CRP, IL-6 and TNF-α (10–12). There is a close relationship between chronic microinflammation and hardening of the arteries, anaemia, malnutrition, erythropoietin resistance and infection. The microinflammation would deteriorate the kidney injury and influence the outcome of CKD. As the research on the complications and mechanisms of CKD deepens, there has been growing recognition that there are many links between malnutrition, the residual renal function, microinflammatory state, leptin and dialysis adequacy, and all of the 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 hs-CRP, (IL-6 and TNF-α) to evaluate the relationship between microinflammation and dialysis frequency, and to provide a relatively economical method for improving the quality of life of dialysis patients.

In the present study, the levels of hs-CRP, IL-6 and TNF-α were all elevated in serum in the three groups, and the results indicated that there was a microinflammatory state in patients with CKD, similar to other results. After a 1-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 per week than twice per week.

The main cause of death in end-stage renal disease (ESRD) patients is cardiovascular complications (13). Repeated persistent inflammation, oxidative stress and malnutrition are the risk factors for concurrent cardiovascular disease, as a complication of ESRD. However, there are no effective measures to block the vicious circle of inflammation-malnutrition-atherosclerosis (14–16). Malnutrition is a major risk factor for death in haemodialysis patients. In the present study, the result indicated that there were a total of eight cases of death, mortality rate of 15.1%, four cases of heart failure, three cases of pulmonary infection, and one case of cerebral haemorrhage in a total of 53 patients after dialysis for 1 year. There was a significant 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 the improvement of SAG, and a negative correlation between mortality and Hb and serum albumin. There was the highest mortality in group C, because of inadequate dialysis, malnutrition, infection and the 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 to increased mortality (17, 18). However, there is currently no effective means of prevention from the vicious circle of inflammation-malnutrition-atherosclerosis. The levels of hs-CRP and IL-6 were significantly lower in three-times-a-week dialysis than in twice-per-week, and it was an important factor in influencing patient survival.

CONCLUSION

The present study showed that the frequency of dialysis affected the microinflammation and mortality. There was the same mortality in patients with twice-a-week dialysis and three-times-a-week dialysis in a relatively short time, and this needs further research over a long period. In this study, a smaller number of cases and shorter observation time are needed to study the relationship between the frequency of dialysis and mortality in patients with CKD.

AUTHORS' NOTE

ZH and TP participated in its design and drafted the manuscript. FL and JW collected the clinical data. All authors read and approved the final manuscript.

REFERENCES

1. Villar E, Zaoui P. Diabetes and chronic kidney disease: lessons from renal epidemiology. Nephrol Ther 2010; **6:** 585–90.
2. Norris KC, Nicholas SB. Strategies for controlling blood pressure and reducing cardiovascular disease risk in patients with chronic kidney disease. Ethn Dis 2015; **25:** 515–20.
3. Gamondi C, Galli N, Schönholzer C, Marone C, Zwahlen H, Gabutti L et al. Frequency and severity of pain and symptom distress among

patients with chronic kidney disease receiving dialysis. Swiss Med Wkly 2013; **143:** w13750.
4. National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Am J Kidney Dis 2002; **39 (2 Suppl 1):** S1–266.
5. Perico N, Remuzzi G. Prevention programs for chronic kidney disease in low-income countries. Intern Emerg Med 2016; **11:** 385–9.
6. Ahlawat R, Tiwari P, D'Cruz S, Singhal R. Prevalence of chronic kidney disease in India: a systematic review and meta-analysis of observational studies. Value Health 2015; **18:** A509.
7. Slinin Y, Greer N, Ishani A, MacDonald R, Olson C, Rutks I et al. Timing of dialysis initiation, duration and frequency of hemodialysis sessions, and membrane flux: a systematic review for a KDOQI clinical practice guideline. Am J Kidney Dis 2015; **66:** 823–36.
8. Demoulin N, Jadoul M. Elderly chronic kidney disease stage 5 patients: a difficult balance between benefits and risks. Nephrol Ther 2012; **8:** 497–8.
9. Sanguankeo A, Upala S, Cheungpasitporn W, Ungprasert P, Knight EL. Effects of statins on renal outcome in chronic kidney disease patients: a systematic review and meta-analysis. PLoS One 2015; **10:** e0132970.
10. Zhang Z, Chen J, Sun Z, Chen C, Xue J, Liu X et al.. Effects of high-flux haemodialysis on FGF-23 and microinflammatory state in end-stage renal diseases patients. Zhonghua Yi Xue Za Zhi. 2015; **95:** 2074–8.
11. Memoli B, Salerno S, Procino A, Postiglione L, Morelli S, Sirico ML et al. A translational approach to microinflammation in end-stage renal disease: molecular effects of low levels of interleukin-6. Clin Sci (Lond) May; **119:** 163–74.
12. Carlsson AC, Carrero JJ, Stenvinkel P, Bottai M, Barany P, Larsson A et al. High levels of soluble tumor necrosis factor receptors 1 and 2 and their association with mortality in patients undergoing hemodialysis. Cardiorenal Med 2015; **5:** 89–95.
13. Peng T, Hu Z, Wu L, Li D, Yang X. Correlation between endothelial dysfunction and left ventricular remodeling in patients with chronic kidney disease. Kidney Blood Press Res 2014; **39:** 420–6.
14. Meyrier A. Atherosclerosis and the kidney. Nephrol Ther 2005; **1:** 183–202.
15. Anand N, Chandrasekaran SC, Alam MN. The malnutrition inflammation complex syndrome—the missing factor in the perio-chronic kidney disease interlink. J Clin Diagn Res. 2013; **7:** 763–7.
16. Mazur-Laskowska M, Bała-Błądzińska A, Zegartowska P, Dumnicka P, Ząbek-Adamska A, Kapusta M et al. Serum pregnancy-associated plasma protein A correlates with inflammation and malnutrition in patients treated with maintenance hemodialysis. Folia Med Cracov 2015: **55:** 37–47.
17. Yadav AK, Banerjee D, Lal A, Jha V. Vitamin D deficiency, CD4+CD28 null cells and accelerated atherosclerosis in chronic kidney disease. Nephrology (Carlton) 2012; **17:** 575–81.
18. de Oliveira Júnior WV, Sabino Ade P, Figueiredo RC, Rios DR. Inflammation and poor response to treatment with erythropoietin in chronic kidney disease. J Bras Nefrol 2015; **37:** 255–63.