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Original Article

Comparison of high flux hemodialysis with hemodialysis filtration on pro-inflammatory and oxidative stress related cytokines in uraemic peripheral blood mononuclear cells

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Abstract: Inflammation and oxidative stress are critical pathological factors for uremia in dialysis patients. Hemodialysis is recognized as one of the renal replacement therapeutic methods for uremic patients, which can improve the symptoms and prolong their life. The present study was designed to compare the clinical effects of high flux hemodialysis (HFHD) with hemodialysis filtration (HDF) in the treatment of uremia in end-stage renal disease (ESRD) patients, and to explore the possible underlying mechanisms. A total of 56 uremia patients from March 2009 to April 2013 were recruited and randomly assigned to intervention (n=28) and control (n=28) groups. The control group was received only HDF therapy and the intervention group was subjected to HFHD treatment three times a week for 3 months. After 3 months of treatment, the malondialdehyde, (MDA, 4.8±1.3 VS. 1.7±0.8, P=0.024) and cortisol (Cor, 132.7±16.8 VS. 67.5±19.4, P=0.031) levels in peripheral blood mononuclear cells (PBMCs) of intervention group reduced more, but the glutathione (GSH, 0.1±0.2 VS. 0.3±0.2, P=0.024) and super oxide dismutase (SOD, 0.2±0.1 VS. 0.4±0.6, P=0.031) levels in PBMCs of intervention group decreased less than the control group. In comparison with the control group, the levels of C-reactive protein (CRP, 8.3±2.6 VS. 5.1±1.7, P=0.012), interleukin-6 (IL-6, 145.2±33.5 VS. 95.7±21.6, P=0.010) and tumor necrosis factor-α (TNF-α, 8.4±1.8 VS. 5.3±1.4, P=0.011) in PBMCs of intervention group were significantly decreased. The patients in the intervention group exhibited a better improvement in quality of life than the control group from baseline to 3 months treatment. Our results demonstrate that HFHD can significantly improve the metabolic disorders in blood lipid, calcium and phosphorus, and effectively inhibit the inflammatory mediums and oxidative stress of PBMCs, which may largely contribute to the improvement in quality of life in uremic patients in a short time. A large number of prospective researches are needed to investigate the long term effects of HFHD and HDF on uremic patients.

Keywords: End-stage renal disease, hemodialysis, uremia, peripheral blood mononuclear cells

Introduction

The uremia patients of end-stage renal disease (ESRD) continue to increase around the world [1]. The high prevalence of severe renal diseases aggravates the difficulties of the treatment of uremia. The constrained medical resources are exhausted for therapy of uremia, especially in China [2]. It is accepted that the uremia patients may have a variety of other targeted organs dysfunction. The extreme hyperkalemia, pulmonary edema, ventricular arrhythmia and uremic autonomic neuropath are overwhelming and life-threatening complications in progressively developed uremic symptoms [3]. The malnutrition, pruritus, poor appetite and frequent vomiting substantially impair the patients' quality of life associated with depression, poor sleep, and increased mortality [4].

Inflammation [5] and oxidative stress [6] are demonstrated to be involved in the pathophysiology of chronic kidney disease. The uremia may lead to imbalances in systematic inflammatory reaction and oxidative stress, which may accelerate the renal injury progression [7]. Recent studies indicate that the uremia may promote the left ventricular hypertrophy associ-

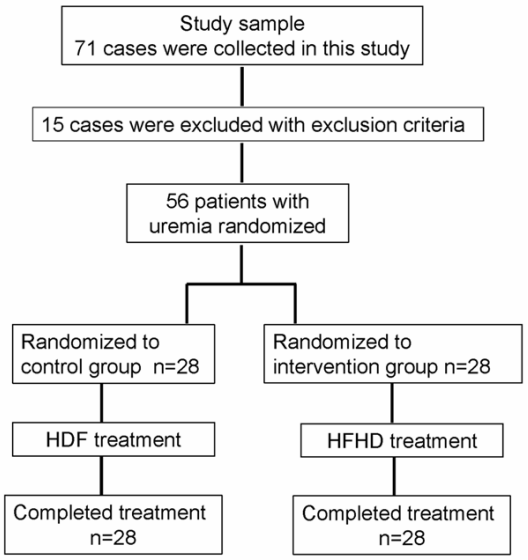

Figure 1. Flowchart of participant screening, randomization, and completion in this study.

ated with changes in serum cytokines [8]. Chronic inflammation is considered as major determinant for inability and mortality in dialysis patients [9]. The anti-inflammation and antioxidant may be beneficial for lowering uremic targeted organs toxicity [10].

Renal transplantation may be the most effective method for treatment of uremia [11]. However, maintenance hemodialysis (HD) has been acknowledged as a common tool for the treatment of uremia diseases, because the donated organs are limited available for transplantation [12]. The maintenance HD is taken as a renal replacement therapy, which may reduce the risk of death and improve the patients' wellbeing in patients with ESRD [13]. High-flux HD (HFHD) and hemodialysis filtration (HDF) are newly developed blood purification technologies for scavenging large and medium molecules with more advantageous effects on hemodynamic stability, and they are emerged to eliminate blood toxins in ESRD patients [14, 15]. However, it is still unclear that whether HFHD could influence pro-inflammatory and oxidative stress related cytokines in uraemic peripheral blood mononuclear cells (PBMCs). In the present study, we evaluated the effects of HFHD or HDF on the pro-inflammatory and oxidative stress related cytokines in PBMCs of uremia patients.

Material and methods

Study design

The 3 months randomized and parallel-group clinical study was conducted at Second People Hospital of Nantong in China. The study protocol was approved by the Ethics Committee of the Second People Hospital of Nantong. The study procedures, risks, benefits, and data management were illustrated in detail before all patients were given an informed consent. The end point of the study was to compare the effects between HFHD and HDF on in uremic patients. All enrolled patients were received conventional standard hemodialysis treatment in our Conventional hemodialysis treatment more than 3 months. No acute infection, surgery and trauma, serious cardiac and pulmonary dysfunction were occurred during the time of conventional standard hemodialysis therapy. The eligibility criteria for this study were diagnosis of ESRD; no contraindications for dialysis; between 20 and 65 years of age; signed consent form; voluntary participation; not having visible infection, not having undergone surgical operations, concomitant medication, or immunosupresive therapy. The patients with the hepatic, immune diseases, severe anemia, cardiopulmonary and uncontrolled psychiatric diseases were excluded for the study. The subjects with active smoking or active inflammation were also excluded.

Patients

A total of 56 patients from March 2009 to April 2013 with uremia were eventually eligible to enroll in the study (**Figure 1**). Fifteen of 71 patients were excluded for the inconformity of eligibility criteria: 1) 2 cases were older than 65 years; 2) 6 cases had vascular, or soft-tissue disorders in their extremities; 3) 4 cases undergone surgical operations on their extremities; 4) 2 cases had cardiopulmonary diseases; 5) one case had not completed the informed consent. The enrolled 56 patients were randomly allocated to two groups with the aid of ClinStat software (http://www.sghms.ac.uk/depts/phs/staff/jmb/jm bsoft.htm). Of the 56 enrolled patients, 28 patients were allocated to the control group receiving HDF treatment, and other 28 cases were allocated to the intervention group receiving HFHD treatment. Patients of two groups were received respective treatments for 3 months, which was conducted from

Table 1. Baseline clinical characteristics of the patients

Characteristics	Control Group (n=28)	Intervention Group (n=28)	t /χ^2	P
Age, years	56.9±17.3	57.1±18.4	0.405	0.687
Sex (male/female)	16/12	18/10	0.299	0.584
BMI, kg/m^2	22.5±1.8	23.6±1.7	0.166	0.869
Ethnicity (Han/Minority)	26/2	27/1	0.352	0.553
Education level				
≤ Middle school	12	11	0.492	0.782
High school	13	15		
≥ College	3	2		
Conventional HD time (months)	18.2±4.9	19.1±5.8	0.438	0.716
Primary disease diagnosis				
Diabetic nephropathy	9	8	0.523	0.914
Chronic glomerulonephritis	12	13		
Hypertensive nephropathy	5	6		
Other primary diseases	2	1		

Note: All values are expressed as mean ± SD or percentage. BMI, body mass index. The baseline biochemical parameters in the intervention and control groups before treatment were analyzed by using paired t tests for normally distributed and signed rank test for skewed parameters. The comparison with categorical variables was analyzed using the Chi square test. The data in baseline clinical characteristics of the patients between groups were compared with χ^2 test or paired-T test.

4 h per session three times per week. A CA-HP170 dialyzer (Baxter, Deerfield, USA) was used for HDF. The surface area of the tri-cellulose acetate (TCA) membrane was 1.4 m^2 and the ultrafiltration coefficient was 10.0 ml/hr/mmHg. A Polyilux 140 H dialyzer (GAMBRO, Lund, Sweden) was used for HFHD. The surface area of the high flux polysulfone membrane was 1.4 m^2 and the ultrafiltration coefficient was 60.0 ml/hr/mmHg.

Evaluation of quality of life

An internationally standard assessment indicator of the Medical Outcomes Study 36-Item Short Form Health Survey (SF-36) was used for elevation of the quality of life as previously described [16, 17]. The scores for physical functioning, general health perceptions, mental health, bodily pain, vitality, social role functioning, and emotional role functioning will be quantified for the basis for analysis.

Collection of PBMCs

The PBMCs peripheral blood cells of were obtained as previously reported [18]. A commercial extraction kit (Tianjin Hao Yang Biological Manufacture Co., Ltd, Tianjing, China) was provided to collect the PBMCs of 20 ml of peripheral blood cells in all cases following the instructions of the manufacturer. The cell pellet was stored and frozen at -80°C. The concentration of PBMCs in the supernatant was quantified with the Bradford assay (BCA; Pierce, Santa Cruz, CA, USA).

Laboratory measurements

Five ml venous blood of patients was collected before treatment and 3 months after treatment. The levels of calcium, phosphorus, albumin (ALB), hemoglobin (Hb), blood urea nitrogen (BUN) and serum creatinine (Scr) were determined with Roche automatic biochemical analyzer in our hospital. Commercial reagent kits provided by the Roche kits of United States was used to measure the β2-microglobulin (β2-MG) and parathyroid hormone (PTH) levels with the electrochemical luminescence immunoassay. The levels of tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6) were detected using ELISA kits (Boster Inc., Wuhan, China). The C-reactive protein (CRP) levels were assayed with the modification of the laser nephelometric technique (Behring Diagnostics, GmbH, Rarburg, Germany). The kits for measurement of malondialdehyde, (MDA), cortisol (Cor), glutathione (GSH), super oxide dismutase (SOD) were purchased from Nanjing Jiancheng Bioengineering Institute (Nanjing, China). The levels of CRP, IL-6, TNF-α, MDA, Cor, GSH and SOD were normalized to the protein expressions in PBMCs of each patient.

Statistical analysis

Results were expressed as mean ± SD or percentage. All the tests were performed using the Statistical Package for the Social Sciences software, version 15.0 (SPSS Inc, Chicago, IL, USA). A single sample K-S test of non parametric test was used to determine the uniformly of parameters. The baseline VAS scores and biochemical parameters in the intervention and

Table 2. Comparisons of laboratory serum data in two groups before and after treatment

	Control Group	Intervention Group	t	P
BUN (mmol/L)				
Before treatment	19.3±7.2	19.6±8.5	0.084	0.933
3 month after treatment	11. 2±5.5*	3.6±1.7*,†	2.764/3.871/6.146	0.040/0.015/<0.001
Scr (μmol/L)				
Before treatment	716.8±172.6	710.7±183.4	0.341	0.734
3 month after treatment	563.5±155.3*	423.5±114.7*,†	2.024/9.125/11.213	0.029/<0.001/<0.001
Calcium (mmol/L)				
Before treatment	1.3±0.5	1.4±0.6	0.601	0.550
3 month after treatment	1.8±0.9*	2.5±1.2*,†	3.297/3.576/4.652	0.022/0.016/0.009
Phosphorus (mmol/L)				
Before treatment	2.8±1.5	2.7±1.6	0.858	0.395
3 month after treatment	1.7±0.8*	0.8±0.4*,†	4.108/14.516/3.145	0.009/<0.001/0.021
PTH (mg/L)				
Before treatment	631.5±232.3	628.5±245.7	1.108	0.273
3 month after treatment	304.5±125.6*	167.3±69.8*,†	3.721/9.887/4.672	0.014/<0.001/0.007
β2-MG (mg/L)				
Before treatment	28.9±9.7	30. 2±11.5	1.571	0.122
3 month after treatment	13.4±5.6*	3.7±0.7*,†	3.469/10.288/4.615	0.018/<0.001/0.006
ALB (g/L)				
Before treatment	18.5±6.3	17.8±7.2	1.788	0.081
3 month after treatment	30.2±11.5*	49.6±16.4*,†	3.213/12.152/8.113	0.024/<0.001/<0.001
Hb (g/L)				
Before treatment	5.7±1.5	5.6±1.7	1.347	0.183
3 month after treatment	9.2±2.1*	12.7±2.4*,†	2.961/11.458/4.478	0.031/<0.001/0.007

Note: All values are expressed as mean ± SD. *P<0.05 compared with that before treatment in each group; †P<0.05 compared to control group by covariance analysis at the same period. Blood urea nitrogen, BUN; serum creatinine, Scr; parathyroid hormone, PTH; β2-microglobulin, β2-MG; albumin, ALB; hemoglobin, Hb. The baseline biochemical parameters in the intervention and control groups before treatment were analyzed by using paired t tests for normally distributed and signed rank test for skewed parameters. Independent t tests were applied to detect the differences in measurement data between two groups after treatment.

control groups before treatment were analyzed by using paired t tests for normally distributed and signed rank test for skewed parameters. Independent t tests were applied to detect the differences in measurement data between two groups after treatment. ANOVA and post-hoc Newman-Keuls tests were used to detect differences in multiple groups. The comparison with categorical variables was analyzed using the Chi square test. P<0.05 was considered as statistically significant.

Results

Characteristics of studied patients in two groups

Totally, 56 out of the 71 uremic patients were enrolled in this study. There were no significant differences in socio-demographic characteristics between two groups at baseline (**Table 1**).

Comparisons of laboratory data in two groups before and after treatment

There was no statistical significance in BUN, Scr, calcium, phosphorus, PTH, β2-MG, ALB and Hb levels between two groups before treatment (**Table 2**). The levels of BUN, Scr, calcium, phosphorus, PTH, β2-MG, ALB and Hb were obviously improved in both two groups at the 3 months follow-up. In comparison of the changes from baseline between the control groups, there was greater improvement in BUN, Scr, calcium, phosphorus, PTH, β2-MG, ALB and Hb levels of intervention group (**Table 2**).

Comparisons of serum lipid metabolism in two groups before and after treatment

There was no statistical significance in TG, CHOL, HDL-C and LDL-C between the control

Table 3. Serum lipid metabolism in two groups before and after treatment

	Control Group	Intervention Group	t	P
TG (mmol/L)				
Before treatment	1.6±0.5	1.7±0.6	1.720	0.091
3 month after treatment	1.3±0.4*	0.9±0.2*,†	3.554/4.518/4.166	0.016/0.006/0.009
CHOL (mmol/L)				
Before treatment	4.5±1.4	4.5±1.3	1.478	0.145
3 month after treatment	3.4±1.5*	2.8±0.8*,†	3.360/11.272/2.713	0.020/<0.001/0.042
HDL-C (mmol/L)				
Before treatment	1.2±0.1	1.2±0.2	1.966	0.054
3 month after treatment	1.3±0.3	1.5±0.4*,†	2.931/15.168	0.033/<0.001
LDL-C (mmol/L)				
Before treatment	2.7±0.5	2.6±0.7	1.243	0.219
3 month after treatment	2.1±0.8*	1.8±0.5*,†	3.149/14.177/2.618	0.025/<0.001/0.047

Note: All values are expressed as mean ± SD. *P<0.05 compared with that before treatment in each group; †P<0.05 compared to control group by covariance analysis at the same period. Tricaylglycerols, TG; cholesterol, CHOL; high density lipoprotein cholesterol, HDL-C; Low density lipoprotein cholesterol, LDL-C. The baseline biochemical parameters in the intervention and control groups before treatment were analyzed by using paired t tests for normally distributed and signed rank test for skewed parameters. Independent t tests were applied to detect the differences in measurement data between two groups after treatment.

Table 4. Oxidative stress related factors of PBMC in two groups before and after treatment

	Control Group	Intervention Group	t	P
MDA (pmol/g)				
Before treatment	7.9±1.8	7.8±2.2	0.870	0.388
3 month after treatment	4.8±1.3*	1.7±0.8*,†	3.958/4.511/3.213	0.011/0.006/0.024
Cor (ng/g)				
Before treatment	180.3±27.6	185.7±34.8	1.201	0.235
3 month after treatment	132.7±16.8*	67.5±19.4*,†	3.469/14.518/2.961	0.018/<0.001/0.031
GSH (U/g)				
Before treatment	0.4±0.3	0.4±0.4	1.565	0.123
3 month after treatment	0.1±0.2*	0.3±0.2*,†	2.720/13.937/3.213	0.042/<0.001/0.024
SOD (U/g)				
Before treatment	0.6±0.4	0.6±0.5	1.018	0.313
3 month after treatment	0.2±0.1*	0.4±0.6*,†	3.469/12.167/2.961	0.018/<0.001/0.031

Note: All values are expressed as mean ± SD. *P<0.05 compared with that before treatment in each group; †P<0.05 compared to control group by covariance analysis at the same period. Malondialdehyde, MDA; cortisol, Cor; glutathione, GSH; super oxide dismutase, SOD. The baseline biochemical parameters in the intervention and control groups before treatment were analyzed by using paired t tests for normally distributed and signed rank test for skewed parameters. Independent t tests were applied to detect the differences in measurement data between two groups after treatment.

group and intervention group before treatment (**Table 3**). The levels of TG, CHOL and LDL-C were significantly decreased in two groups after treatment (**Table 3**). The level of HDL-C was significantly increased in the intervention group. The indicators showed statistically significance in improvement of TG, CHOL, HDL-C and LDL-C in the observation group (**Table 3**).

Comparisons of MDA, Cor, GSH and SOD in two groups before and after treatment

Baseline MDA, Cor, GSH and SOD levels in PBMCs did not differ significantly between the intervention and control groups before treatment (**Table 4**). After 3 months of treatment, the MDA, Cor, GSH and SOD levels in PBMCs

Table 5. Pro-inflammatory related factors of PBMC in two groups before and after treatment

	Control Group	Intervention Group	t	P
CRP (μg/g)				
Before treatment	11.4±4.8	11.7±3.9	1.727	0.090
3 month after treatment	8.3±2.6*	5.1±1.7*,†	2.720/10.713/3.851	0.042/<0.001/0.012
IL-6 (pg/g)				
Before treatment	180.2±45.7	185.7±51.5	1.128	0.264
3 month after treatment	145.2±33.5*	95.7±21.6*,†	3.963/12.428/4.077	0.011/<0.001/0.010
TNF-α (pg/g)				
Before treatment	12.8±2.7	13.1±2.9	1.449	0.153
3 month after treatment	8.4±1.8*	5.3±1.4*,†	4.044/13.157/3.953	0.010/<0.001/0.011

Note: All values are expressed as mean ± SD. *P<0.05 compared with that before treatment in each group; †P<0.05 compared to control group by covariance analysis at the same period. C reactive protein, CRP; interleukin-6, IL-6; tumor necrosis factor-α, TNF-α. The baseline biochemical parameters in the intervention and control groups before treatment were analyzed by using paired t tests for normally distributed and signed rank test for skewed parameters. Independent t tests were applied to detect the differences in measurement data between two groups after treatment.

Table 6. Improvement of complications in two groups after treatment

	Control Group	Intervention Group	χ^2	P
Sleep Improvement	(11/28)	(20/28)*	6.470	0.011
Appetite Improvement	(7/28)	(19/28)*	10.388	0.001
Pruritus Improvement	(12/28)	(22/28)*	7.487	0.006
Arthralgia Improvement	(7/28)	(17/28)*	7.292	0.007
Thirsty Improvement	(13/28)	(23/28)*	7.778	0.006

Note: *P<0.05 compared with control group. The comparisons between categorical variables were analyzed using the Chi square test.

were significantly decreased in both groups (**Table 4**). The MDA and Cor levels in PBMCs of intervention group reduced more, but the GSH and SOD levels in PBMCs of intervention group decreased less than the control group (**Table 4**).

Comparisons of CRP, IL-6 and TNF-α in two groups before and after treatment

The levels of CRP, IL-6 and TNF-α in PBMCs were not significantly different between the control group and intervention group on the enrollment day (**Table 5**). Both of two groups showed obvious reductions in CRP, IL-6 and TNF-α in PBMCs of uremic patients after 3 months of treatment. In comparison with the control group, the levels of CRP, IL-6 and TNF-α in PBMCs of intervention group were significantly decreased and the differences were statistically significant (**Table 5**).

Improvement of complications in two groups after treatment

After treatment of 3 months, the disorders of sleep, appetite, pruritus, arthralgia and thirsty exhibited more improvement in the intervention group compared with the control group (**Table 6**).

Comparison of quality of life in two groups before and after treatment

The evaluating indicators for quality of life were similar to those of the two groups at the baseline (**Table 7**). The physical and mental health scores were obviously improved in both two groups after treatment (**Table 7**). Both two groups showed significant increases in scores for general health, physical functioning, bodily pain, vitality, and mental health after 3 months therapy, but there were no statistically significant differences in the scores for social role functioning and emotional role functioning in the control group (**Table 7**). In addition, patients in the intervention group showed a better improvement in quality of life than the control group from baseline to 3 months treatment (**Table 7**).

Discussion

Traditional hemodialysis is able to clear blood small molecules including BUN and creatinine, but unable to scavenge other large and medi-

Table 7. Quality of life in two groups before and after treatment

	Control Group	Intervention Group	t	P
GH				
Before treatment	25.7±9.7	26.2±10.5	1.377	0.174
3 month after treatment	35.8±11.2*	47.8±12.6*,†	4.050/16.189/3.788	0.010/<0.001/0.013
PF				
Before treatment	48.7±15.4	47.2±13.6	1.906	0.062
3 month after treatment	55.7±16.1*	64.8±17.3*,†	3.308/13.692/3.568	0.021/<0.001/0.016
BP				
Before treatment	50.8±18.2	49.6±17.4	0.713	0.479
3 month after treatment	60.5±20.7*	72.4±21.5*,†	4.040/13.519/3.953	0.010/<0.001/0.011
VT				
Before treatment	30.6±10.5	31.5±9.4	0.117	0.911
3 month after treatment	39.4±11.5*	48.9±12.7*,†	3.851/15.628/4.070	0.012/<0.001/0.010
MH				
Before treatment	48.2±12.7	49.5±13.1	1.731	0.089
3 month after treatment	59.2±14.5*	68.9±15.7*,†	3.851/10.429/3.963	0.012/<0.001/0.011
SRF				
Before treatment	30.7±12.4	32.5±11.7	0.713	0.479
3 month after treatment	32.6±13.1	38.7±12.7*	2.751	0.040
ERF				
Before treatment	50.6±12.7	51.7±13.9	1.554	0.126
3 month after treatment	55.6±13.4	62.6±14.4*	9.562	<0.001

Note: All values are expressed as mean ± SD. *P<0.05 compared with that before treatment in each group; †P<0.05 compared to control group by covariance analysis at the same period. General health, GH; physical functioning, PF; bodily pain, BP; vitality, VT; mental health, MH; social role functioning, SRF; emotional role functioning, ERF. The baseline biochemical parameters in the intervention and control groups before treatment were analyzed by using paired t tests for normally distributed and signed rank test for skewed parameters. Independent t tests were applied to detect the differences in measurement data between two groups after treatment.

um molecular substance such as PTH and β2-MG [19]. HDF and HFHD are developed for scavenging large and medium molecules [20]. HFHD is conducted with a high-flux biocompatible dialyzer [21]. In our present study, we showed that the levels of BUN, Scr, calcium, phosphorus, PTH, β2-MG, ALB and Hb were obviously improved in both two groups at the 3 months follow-up. In comparison of the changes from baseline between the control groups, there was greater improvement in BUN, Scr, calcium, phosphorus, PTH, β2-MG, ALB and Hb levels of intervention group. These results indicated that HFHD may regulate the metabolism disorders in calcium and phosphorus, secondary parathyroid gland hyperthyroidism to improve the renal function in uremia patients.

Improvement of the disorder of lipid metabolism will help to improve the survival rate in HD patients [22]. The maintenance hemodialysis treatment cannot effectively correct lipid metabolism disorders in uremia patients with [23]. The conventional hemodialysis may also increase the abnormal metabolism of blood lipids [23, 24]. Our data displayed that the levels of TG, CHOL and LDL-C were significantly decreased in two groups after treatment. The level of HDL-C was significantly increased in the intervention group. These results suggested that HFHD can improve blood lipid metabolism in dialysis patients, which may reduce cardiovascular complications and prolong the life of uremia patients. It is noted that the levels of albumin and hemoglobin are extremely low, but the tricaylglycerols, cholesterol, low density lipoprotein cholesterol levels are increased in all uremia patients. In this study, the low albumin and hemoglobin levels may be attributed to nephrotic syndrome. The sentences have been added into the main text.

Subclinical inflammation and oxidative stress are key mechanisms responsible for the devel-

opment and progression of uremia [25]. The alterations in immune and inflammation are clinically presents in HD patients [26]. Inflammation is also crucial in the pathogenesis of uremic anemia [27]. The exiting researches indicate the involvement of oxidative stress in the development of uremia in chronic kidney disease [28]. HFHD is found to minimize inflammation and oxidative stress in patients with chronic kidney disease [29]. A recent study demonstrates that combination of hemodialysis and hemoperfusion effectively remove the inflammatory mediums and repress the activation of inflammatory related transcription factors NK-κB of PBMCs in multiple organ dysfunction syndrome patients [29, 30]. It is attractive that plasma myeloperoxidase persistently increased higher during dialysis in regenerated cellulose dialysis membranes than polysulphone membrane, and polysulphone membrane exhibits a better profile as regards oxidative stress [31]. It is also evidenced that haemodialysis with polysulphone but not polyamide membranes significantly changed arterial stiffness due to its high membrane bioincompatibility [32]. Our results showed that in comparison with the control group, the levels of CRP, IL-6 and TNF-α in PBMCs of intervention group were significantly decreased and the differences were statistically significant. The MDA and Cor levels in PBMCs of intervention group reduced more, but the GSH and SOD levels in PBMCs of intervention group decreased less than the control group. These results hinted that HFHD may relieve uremic symptoms and improve the quality of life via inhibition of inflammation and oxidative stress. The surface area of high flux polysulfone membrane at least partially, contributed to a better alleviation of oxidative stress than tri-cellulose acetate in uremic patients.

The uremia are often complicated with heart failure, refractory high blood pressure, anemia, bone metabolism disorders, malnutrition, skin itching, digestive tract disease and psychological obstacles, which seriously affect the quality of life in uremia patients [33]. Recent study indicates that HFHD can significantly improve the survival rate and quality of life of patients with ESRD [34]. In this study, we showed that patients in the intervention group showed a better improvement in quality of life than the control group from baseline to 3 months treatment. These results suggested that the disorders in quality of life or clinical complications were significantly improved by both HFHD and HDF, and HFHD was better than HDF in terms of improvement in complications and quality of life.

HFHD may be an adjuvant therapy for treatment of uremic patients with a better effect in improvement in quality of life, recovery of renal metabolic homeostasis and lipid metabolism in a short time. HFHD may play an important role in the regulation of inflammatory mediators and oxidative stress in PBMCs of uremia patients, which may be critical mechanisms whereby HFHD had a therapeutic effect on the uremia. A large number of prospective researches are needed to investigate the long term effect of HFHD and HDF on uremic patients.

Disclosure of conflict of interest

None.

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