

## Original Article

# Effects of different dialysis methods on calcium and phosphorus metabolism, oxidative stress and microinflammation in patients with ESRD

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Received June 25, 2020; Accepted July 21, 2020; Epub October 15, 2020; Published October 30, 2020

**Abstract:** Objective: To investigate the effects of peritoneal dialysis and hemodialysis on calcium and phosphorus metabolism, oxidative stress, and microinflammation in patients with end-stage renal disease (ESRD). Methods: Patients (n=84) treated with sustained hemodialysis were divided into two groups according to the random number grouping method. Patients (n=42) with peritoneal dialysis (PD) were selected as the observation group and patients (n=42) with hemodialysis (HD) were selected as the control group. Six months after the treatment, serum creatinine, urea nitrogen, urea clearance index (Kt/V), hemoglobin, serum albumin, serum calcium, serum phosphorus, parathyroid hormone (iPTH), inflammatory factors and oxidative stress factors were observed before and after dialysis. Results: After treatment, blood urea nitrogen, serum creatinine and urea clearance index in the control group were lower than those in the observation group while hemoglobin and serum albumin were higher than those in the observation group (all  $P < 0.05$ ). There was no significant difference in serum calcium, phosphorus and parathyroid hormone between the two groups after treatment. After treatment, interleukin-6 (IL-6), C-reactive protein (CRP), tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), malondialdehyde (MDA), and advanced oxidation protein products (AOPP) were lower, and superoxide dismutase (SOD) was higher in the observation group than in the control group (all  $P < 0.05$ ). The incidence of complications of infection and hypoproteinemia in the observation group was higher than that in the control group, while the incidence of refractory hypertension, arrhythmia and congestive heart failure in the observation group was lower than that in the control group ( $P < 0.05$ ). Conclusion: There are respective advantages of peritoneal dialysis and hemodialysis. Hemodialysis can effectively remove toxins and improve the nutritional status of patients, while peritoneal dialysis can improve microinflammation and oxidative stress. These two methods can be used according to the condition of patients.

**Keywords:** End-stage renal disease, hemodialysis, peritoneal dialysis, calcium and phosphate metabolism, oxidative stress, microinflammation

## Introduction

With the improvement of economic and living standards, the intake of protein in the body increases and the number of patients with chronic kidney disease (CKD) caused by increasing renal burden is also increasing year by year. The prevalence rate is now as high as 11% [1]. With the increase in the incidence, the number of people with end-stage renal disease (ESRD) increases. When the disease progresses to ESRD, there may be a variety of complications, the most significant of which are the disorder of electrolytes, retention of toxins, ane-

mia and so on [2-4]. Clinically, the main treatment of ESRD is sustained dialysis or renal transplantation, in which sustained dialysis includes hemodialysis (HD) and peritoneal dialysis (PD) [5]. More than 2 million people in the world need ESRD replacement therapy every year. HD is the main approach to treat ESRD in China [6].

In recent years, it has been found that the increase of cardiovascular events in patients treated with HD may be related to hemodynamic fluctuations during dialysis [7]. PD is a process that uses the patient's peritoneum as

the dialysis membrane to exchange the dialysate with solute, electrolyte and water in the blood to achieve the purpose of dialysis [8, 9]. At present, the therapeutic effect of PD and HD is still controversial [10, 11].

A clinical study has found that the disorder of calcium and phosphorus metabolism is the most common and prominent symptom in patients with ESRD [12] and the statement of oxidative stress (OS) exists in patients with ESRD. OS is caused by the increase of oxygen free radicals in tissues or cells and the decrease of accumulated scavenging ability in vivo leads to oxidative stress in vivo. Oxidative stress is more obvious in patients with HD, while late protein oxidation products (AOPP), malondialdehyde (MDA) and superoxide dismutase (SOD) are important indexes of OS [13]. In this state of oxidative stress, a variety of inflammatory factors such as interleukin-6 (IL-6), C-reactive protein (CRP) and tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) can be secreted, which aggravate the micro-inflammatory state in vivo [14]. Based on this study, the effects of PD and HD on the efficacy, calcium and phosphorus metabolism, oxidative stress and micro-inflammatory state of the two groups were observed.

### Materials and methods

#### General data

Patients (n=84) with end-stage renal disease were selected from March 2016 to March 2019 in The First Affiliated Hospital of Hainan Medical University and randomly divided into two groups. Patients (n=42) with PD were selected as the observation group and patients (n=42) with HD as the control group. Patients were aged from 40 to 80 years old, with an average age of  $62.5 \pm 8.2$  years. All the patients above signed the informed consent form and this study was approved by the Ethics Committee.

#### Inclusion and exclusion criteria

Inclusion criteria: Patient with end-stage renal disease refer to the diagnostic criteria of end-stage kidney disease in the 14th edition of Internal Medicine; the age is over 18 years old.

Exclusion criteria: Patients with recent infection; patients with severe malnutrition, tumors, and other diseases; patients with mental disorders or cerebrovascular diseases; patients who

took glucocorticoids or immunosuppressant's shortly.

#### Methods

Basic treatment: The patients in the two groups were given the treatment of reducing blood pressure, correcting acid-base balance, and maintaining electrolyte balance. The diet was given high-quality low-protein, low-salt, low-fat and low-phosphorus diet.

The control group was treated with HD in addition to the basic treatment regimen, using a hemodialysis machine (Fresenius 4008 s, Germany) and a low-flux hollow fiber dialyzer (Fresenius FX10, Germany). The dialysate flow rate was 500 mL/min, blood flow was 200 mL/min, blood flow was 200-250 mL/min, dialysis time every 4 h, regular dialysis 3 times a week for 6 months.

The observation group was treated with PD based on the basic treatment plan. The patients in the observation group were treated with a Y-type dialysis device (American Baxter company), Tenckhof catheter (American Baxter company), and dialysate (American Baxter company), the dialysate 2 L each time, 4 times a day. Continuous ambulatory peritoneal dialysis was given for 6 months.

#### Outcome measures

*Primary outcome measures:* 1) The curative effect of dialysis: The venous blood of elbow was drawn at 8 a.m. before the dialysis and 6 months after the treatment. The blood creatinine, urea nitrogen, urea clearance index (Kt/V), hemoglobin, and serum albumin were measured by Beckman's automatic biochemical analyzer (Germany, Beckman). 2) The metabolism index of calcium and phosphorus: Before dialysis and 6 months after treatment, serum calcium and phosphorus were measured by Beckman automatic biochemical analyzer, and parathyroid hormone (iPTH) was determined by serum enzyme-linked immunosorbent assay (kit purchased from Beijing Tianyu Hengtai Technology Co., Ltd.). 3) Inflammatory factor: Inflammatory factors including IL-6 (kit from China, Shanghai enzyme-linked biology, item No. ml059930), CRP (kit from China, Shanghai enzyme-linked biology, item No. ml057570) and tumor necrosis TNF- $\alpha$  (kit from China, Shanghai enzyme-linked biology, item No. ml077385) were detected by serum

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**Table 1.** The comparison of general data and baseline data

Projects	Observation group (n=42)	Control group (n=42)	$\chi^2/t$	P
Gender (male/female)	27/15	29/13	0.214	0.643
Age	57.6±14.2	57.9±13.6	0.099	0.922
Systolic pressure (mmHg)	153.28±7.31	152.75±8.12	0.754	0.314
Diastolic pressure (mmHg)	88.54±7.23	89.37±7.65	0.511	0.611
Triglyceride (mmol/L)	1.75±0.65	1.79±0.68	0.276	0.784
Total cholesterol (mmol/L)	5.58±0.78	5.61±0.76	0.178	0.859
High-density lipoprotein (mmol/L)	1.09±0.33	1.12±0.34	0.410	0.683
Low density lipoprotein (mmol/L)	3.85±0.89	3.89±0.73	0.225	0.822
Hemoglobin (g/L)	102.52±10.46	103.45±9.73	0.422	0.674
Serum albumin (g/L)	35.78±4.76	35.81±4.86	0.028	0.977
Body mass index (kg/m <sup>2</sup> )	17.84±2.98	17.75±2.67	0.146	0.884
Blood sugar (mmol/L)	5.93±1.27	5.87±1.34	0.211	0.834
Urea nitrogen before dialysis (mmol/L)	27.83±8.89	27.65±8.65	0.094	0.925
Serum creatinine before dialysis (μmol/L)	692.86±218.55	687.85±224.95	0.104	0.918
Causes			0.606	0.988
Diabetic nephropathy	15 (35.71%)	16 (38.10%)		
Chronic glomerulonephritis	12 (28.57%)	13 (30.95%)		
Hypertensive nephropathy	8 (19.05%)	8 (19.05%)		
Renal tubulo-interstitial lesion	2 (4.76%)	2 (4.76%)		
Obstructive nephropathy	2 (4.76%)	1 (2.38%)		
Polycystic kidney and others	3 (7.14%)	2 (4.76%)		

enzyme-linked immunosorbent assay (ELISA) before and 6 months after treatment. 4) Oxidative stress factors: Oxidative stress factors including malondialdehyde (MDA) (kit from China, Shanghai enzyme-linked biology, item No. ml058027), SOD (kit from China, Shanghai enzyme-linked biology, item No. ml0763-28) and AOPP (kit comes from enzyme-linked organisms in Shanghai, China, item No. ml02-4017) were detected by serum ELISA before dialysis and 6 months after treatment.

*Secondary outcome measures:* Complications: Including infection, hypoproteinemia, refractory hypertension, arrhythmia, congestive heart failure, and so on were recorded during dialysis.

### *Statistical index*

The data were analyzed by SPSS 17.0. Continuous variables were expressed by mean ± standard deviation ( $\bar{x} \pm sd$ ), which accorded with normal distribution and homogeneity of variance. A paired t-test was used before and after treatment. Independent t-test was used for comparison between groups, the rank-sum

test was used to disaccord with normal distribution and homogeneity of variance. The counting data were expressed as n/% and were tested by the Pearson chi-square test. The difference was statistically significant ( $P < 0.05$ ).

### **Results**

#### *Comparison of general data and baseline data*

There was no significant difference in general data and baseline data between the two groups ( $P > 0.05$ ). See **Table 1**.

#### *Comparison of renal function, hemoglobin and serum albumin before and after dialysis*

The blood urea nitrogen, serum creatinine and urea clearance index were improved after treatment ( $P < 0.05$ ). There was no difference in the level of hemoglobin and serum albumin in the observation group before and after the treatment, but the hemoglobin and serum albumin in the control group was higher after treatment than those before treatment ( $P < 0.05$ ). After treatment, the blood urea nitrogen, serum cre-

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**Table 2.** Comparison of renal function, hemoglobin and serum albumin before and after dialysis

Projects	Urea nitrogen (mmol/L)	Serum creatinine (μmol/L)	Urea clearance index (mL/min)	Hemoglobin (g/L)	Serum albumin (g/L)
Before the treatment					
Observation group	27.83±8.89	692.86±218.55	1.55±0.32	102.52±10.46	35.78±4.76
Control group	27.65±8.65	687.85±224.95	1.51±0.36	103.45±9.73	35.81±4.86
t	0.094	0.104	5.38	0.422	0.028
P	0.925	0.918	0.592	0.674	0.977
After the treatment					
Observation group	14.82±4.74 <sup>a</sup>	427.21±65.58 <sup>a</sup>	1.43±0.35 <sup>a</sup>	100.05±9.03	36.27±5.00
Control group	10.81±4.01 <sup>a</sup>	367.44±58.65 <sup>a</sup>	1.28±0.34 <sup>a</sup>	104.10±7.33 <sup>a</sup>	39.66±4.94 <sup>a</sup>
t	4.091	2.891	1.992	2.205	3.052
P	<0.001	0.005	0.049	0.031	0.003

Note: Compared with the same group before treatment, <sup>a</sup>P<0.05.

**Table 3.** Comparison of serum calcium, phosphorus and parathyroid hormone before and after dialysis

Projects	Serum calcium (mmol/L)	Serum Phosphorus (mmol/L)	Parathyroid (pg/mL)
Before the treatment			
Observation group	2.23±0.22	2.12±0.20	356.48±136.05
Control group	2.22±0.21	2.13±0.23	360.96±144.40
t	0.213	0.213	0.146
P	0.832	0.832	0.884
After the treatment			
Observation group	2.37±0.17 <sup>a</sup>	1.64±0.11 <sup>a</sup>	298.90±107.02 <sup>a</sup>
Control group	2.32±0.19 <sup>a</sup>	1.65±0.14 <sup>a</sup>	300.62±129.34 <sup>a</sup>
t	1.271	0.346	0.066
P	0.207	0.717	0.947

Note: Compared with the same group before treatment, <sup>a</sup>P<0.05.

**Table 4.** Comparison of inflammatory indexes before and after treatment

Projects	CRP (mg/L)	IL-6 (ng/L)	TNF-α (ng/L)
Before the treatment			
Observation group	23.71±2.84	188.12±1.31	55.29±7.31
Control group	23.94±3.52	188.55±1.38	56.48±6.34
t	0.298	1.437	0.757
P	0.766	0.155	0.451
After the treatment			
Observation group	7.81±2.28 <sup>a</sup>	121.19±5.31 <sup>a</sup>	22.42±1.89 <sup>a</sup>
Control group	13.82±2.28 <sup>a</sup>	154.87±5.56 <sup>a</sup>	33.74±2.27 <sup>a</sup>
t	9.709	27.716	24.469
P	<0.001	<0.001	<0.001

Notes: Compared with that of the same group before treatment, <sup>a</sup>P<0.05. IL-6: Interleukine-6; CRP: C-reactive protein; TNF-α: tumor necrosis factor-α.

group, while hemoglobin and serum albumin were higher than those in the observation group (all P<0.05). See **Table 2**.

*Comparison of serum calcium, phosphorus and parathyroid hormone before and after dialysis*

Serum calcium was higher than that before treatment, while serum phosphorus and parathyroid hormone were lower than those before treatment (P<0.05). However, there was no significant difference in serum calcium, phosphorus and parathyroid hormone between the two groups after treatment (P>0.05). See **Table 3**.

*Comparison of inflammatory factors before and after dialysis*

The levels of CRP, IL-6 and TNF-α in both groups after treatment were significantly lower than those before treatment. The levels of CRP, IL-6 and TNF-α in the observation group after treatment were lower than those in the control group (P<0.001). See **Table 4**.

atinine and urea clearance index in the control group were lower than those in the observation

group (P<0.001). See **Table 4**.

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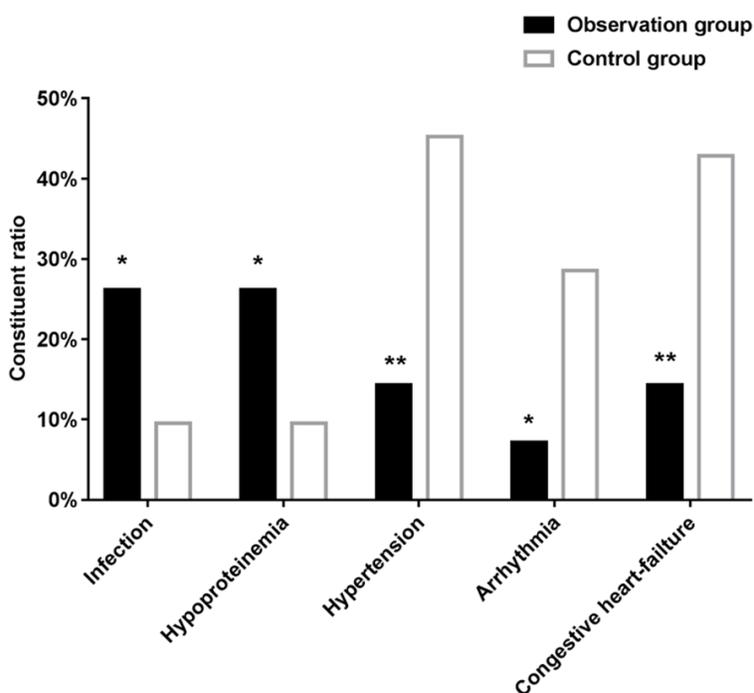
**Table 5.** Comparison of oxidative stress indexes before and after treatment

Projects	MDA (mg/L)	SOD (ng/L)	AOPP (ng/L)
Before the treatment			
Observation group	8.98±1.74	80.18±21.69	76.39±20.29
Control group	8.79±1.87	80.69±22.98	75.98±21.36
t	0.482	0.105	0.090
P	0.631	0.917	0.928
After the treatment			
Observation group	6.54±1.59 <sup>a</sup>	103.78±26.34 <sup>a</sup>	55.98±16.78 <sup>a</sup>
Control group	8.01±1.56 <sup>a</sup>	91.34±16.78 <sup>a</sup>	69.62±20.26 <sup>a</sup>
t	4.277	4.026	3.987
P	<0.001	<0.001	<0.001

Notes: Compared with the same group before treatment, <sup>a</sup>P<0.05. MDA: Malondialdehyde; SOD: Superoxide dismutase; AOPP: Late protein oxidation products.

**Table 6.** Comparison of complications during treatment

Complications	Observation group (n=42)	Control group (n=42)	$\chi^2$	P
Infection	11 (26.19%)	4 (9.52%)	3.977	0.045
Hypoproteinemia	11 (26.19%)	4 (9.52%)	3.977	0.045
Refractory hypertension	6 (14.29%)	19 (45.24%)	9.624	0.002
Arrhythmia	3 (7.14%)	12 (28.57%)	6.547	0.010
Congestive heart failure	6 (14.29%)	18 (42.86%)	8.400	0.004



**Figure 1.** Comparison of complications during treatment. Compared with the control group, \*P<0.05, \*\*P<0.01.

### Comparison of oxidative stress indexes before and after dialysis

MDA, SOD and AOPP of the two groups decreased after treatment (P<0.001). MDA, SOD and AOPP of the observation group after treatment were lower than those of the control group (P<0.05). See **Table 5**.

### Comparison of complications during treatment

It was found that the incidence of complications of infection and hypoproteinemia in the observation group was higher than that in the control group. However, the incidence of refractory hypertension, arrhythmia and congestive heart failure was lower than that in the control group (P<0.05). See **Table 6** and **Figure 1**.

### Discussion

ESRD is the final state of a variety of kidney diseases [15]. At present, HD is still the main treatment of ESRD in our country. With the development of technology, PD is more and more widely used in clinics [16, 17]. In the past, a comparative study of the two methods found that HD dialysis is more effective, while PD plays a positive role in the control of blood pressure and the protection of residual renal function. The two dialysis methods have their advantages [18]. In this study, it was found that the blood urea nitrogen, serum creatinine and urea clearance index in the control group treated with HD were lower than those in the observation group treated

with PD, suggesting that HD was more effective in dialysis. Another study found that protein-energy consumption after PD treatment was more significant than that of HD [19]. This study also found that hemoglobin and serum albumin in HD groups were higher than those in the PD group. In terms of regulation of the disorder of calcium and phosphorus metabolism, both PD and HD patients can regulate the disorder of calcium and phosphorus metabolism, and there is no difference between them. Similar results were obtained in this study, which may be related to the fact that calcium and phosphorus are small molecular substances [20].

The Micro-inflammatory reactions can cause inflammatory injury, lead to the deposition of extracellular matrix in the kidney, and lead to renal fibrosis. Previous studies have found that PD can effectively eliminate inflammatory factors while improving renal function and thus the micro-inflammatory state in patients. However, during the treatment of HD, it is easy to show incompatibility phenomenon after the contact between blood and dialysis membrane. Dialysis line may promote the release of inflammatory factors, which leads to the aggravation of micro-inflammatory state in vivo, while PD treatment has less release of inflammatory factors [21]. In this study, it was found that the clearance of CRP, IL-6 and TNF- $\alpha$  in the PD treatment group was relatively more complete than that in the HD treatment group, suggesting that PD treatment can reduce the state of microinflammation in patients with ESRD.

Due to the existence of oxidative stress in patients with ESRD, a variety of inflammatory factors can be secreted under this state of oxidative stress, aggravating the state of microinflammation in the body [14]. Previous studies have found that PD is less likely to produce oxidative stress than HD, thus reducing the production of inflammatory factors [22]. In this study, it was found that the clearance of AOPP, MDA and increase of SOD in PD treatment groups were better than that in the HD treatment group, suggesting that PD treatment can improve the state of oxidative stress in ESRD patients.

In terms of complications, studies have shown that protein and energy consumption is a common complication in dialysis patients and it is

more obvious in PD patients. Peritoneal infection often occurs due to improper operation because PD is mostly operated at home [23]. Patients with large hemodynamic fluctuations during HD lead to an increase in cardiovascular events, while PD dialysis mode has little effect on hemodynamics [7]. In this study, it was found that the incidence of infection and hypoproteinemia complications in the PD group was higher than that in HD, while the lower incidence of refractory hypertension, arrhythmia and congestive heart failure in HD group might be related to the above factors.

However, the sample size of this study is small, so we can further expand the sample size for multicenter randomized controlled trials. Since the follow-up time is short, we can also further prolong the follow-up time and observe the clinical efficacy of the PD regimen.

To sum up, peritoneal dialysis and hemodialysis have their advantages. Hemodialysis can effectively remove toxins to improve the nutritional status of patients, while peritoneal dialysis can improve microinflammation and oxidative stress, which can be used according to the condition of patients.

### Disclosure of conflict of interest

None.

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