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RESEARCH ARTICLE

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Efficacy of different hemodialysis methods on dendritic cell marker CD40 and CD80 and platelet activation marker CD62P and P10 in patients with chronic renal failure

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Background: Chronic renal failure (CRF) has become a major public health concern, which increases the risk of stroke and systemic thromboembolism. Therefore, therapeutic strategies are in urgent requirement. This study was conducted for investigating efficacy of hemodialysis (HD), hemodiafiltration (HDF), and hemoperfusion (HP) in patients with CRF and the correlation with the presence of complications following HD therapy.

Methods: The therapeutic effect, living quality, biochemical indicators, and dry weight were detected before and after the treatment regimens. Flow cytometry was conducted to detect expressions of dendritic cell markers (CD40 and CD80) and platelet activation markers (CD62P and P10), and the relationship between their expression and therapeutic effect as well as the association of these expressions with complications was analyzed.

Results: After HD therapy, patients presented with decreased serum creatinine, serum phosphorus, triglyceride, parathyroid hormone, and β_2-MG expression; increased hemoglobin, plasma albumin expressions, and dry weight; and enhanced therapeutic effect and living quality. CD62P and P10 expressions decreased, while CD40 and CD80 expressions increased following HD therapy. The therapeutic effect improved in patients with low expressions of CD40 and CD80 and high expressions of CD62P and P10 following HP treatment and complications were lower after treatment of HDF and HP.

Conclusion: The aforementioned results indicated that CRF patients treated with HP exhibited higher expression of CD40 and CD80 and lower expression of CD62P and P10, suggesting that HP is conferred to have better efficacy than HDF and HD. Therefore, HP may be a promising clinical regimen for treatment of CRF patients.

KEYWORDS

CD40, CD62P, CD80, chronic renal failure, hemodialysis

1 | INTRODUCTION

Chronic renal failure (CRF), also known as chronic kidney disease (CKD), is usually the end-stage of most kidney diseases, which is characterized by a progressive and irreversible decline in the glomerular filtration rate, causing the rise in the levels of serum creatinine and blood uremic nitrogen, accompanied by cardiovascular diseases.[1,2] It has become an important public health concern in China, with increasing prevalence in rural areas with developing economies and other specific geographical regions.[5] Nowadays, various risk factors leading to CRF have been identified, including age, diabetes mellitus, high blood pressure, higher incidence of glomerular conditions,

and obesity.[6] Based on a previous study, the therapeutic approaches have not been successful in the limitation of disease progression in CRF.[7] Hemodialysis (HD) is a well-established and long-standing life-saving treatment for CFR patients.[8]

Dialysis is the filtration of blood through a semipermeable membrane under certain electrochemical concentration gradient.[9] The main purpose of HD is to maintain molecular homeostasis of the extracellular environment, which involves removal of waste products including uremic solutes, and excess sodium and water.[10] Hemodiafiltration (HDF) is the process of diluting whole blood with a physiologic electrolyte solution followed by ultrafiltration across a membrane to convectively remove solutes and excess water.[11] Hemoperfusion (HP) is defined as a therapy that is proficient in purifying blood and eliminating the immune mediator.[12] HDF and HD are distinguished by the pore size in the area of fiber since the hollow fiber of the dialyzers is made by semipermeable membrane.[13] CD40 is a constituent of the receptor superfamily of tumor necrosis factor and is expressed upon antigen-presenting cells, such as dendritic cells, B cells, and monocytes as well as many nonimmune cells and a range of tumors.[14,15] The interaction of CD40 with CD40L can lead to the formation of a prothrombotic and proinflammatory molecule, and CD62P, as p-selectin and a constituent of the platelet α-granule membrane, is expressed on the platelet surface.[16] CD80, as a constituent of immunoglobulin supergene family, is expressed upon dendritic cells[17] and can facilitate tumor immunity by preventing the immune suppression of programmed death ligand 1.[18] The simultaneous blockade of CD80 causes complete inhibition of majority of T cell–mediated responses, either by preventing T-cell activation altogether, or by sequentially inhibiting T cell–dependent recruitment of effector immune responses.[19] P10 is a viroporin that can generate the process of cell fusion.[20] Due to shortage of evidence by studies focusing on the three HD methods in the treatment of CRF and their effects on the protein expression of CD40, CD80, CD62P, and P10, we conducted this study to examine the efficacy of these HD methods on the expression of CD40, CD80, CD62P, and P10 in CRF patients, the clinical outcomes of HDF and the correlation with the presence of complications following treatment.

2 | MATERIALS AND METHODS

2.1 | Ethical statements

This study was performed with the approval of the Ethics Committee of the First Affiliated Hospital of Zhengzhou University, with signed informal consents by all patients.

2.2 | Study subjects

A total of 240 CRF patients between March 2012 and January 2014 in The First Affiliated Hospital of Zhengzhou University (Zhengzhou, Henan, China) that met the diagnostic criteria for CRF in the clinical practice guideline of renal anemia were selected as the study subjects.[21] According to different methods of HD, patients were divided into HD group (n = 80, 36 males and 44 females aging from 31-74 years old [53.0 ± 4.3 years] and mean treatment time of 30 ± 6 months, three times for a week), HDF group (n = 80, 42 males and 38 females aging from 30-72 years old [51.3 ± 4.2 years] and mean treatment time of 31 ± 5 months, two times for a week), and the HP group (n = 80, 36 males and 44 females aging from 33-75 years old [53.4 ± 4.4 years] and mean treatment time 31 ± 4 months, one time for a week). There was no significant difference recorded while comparing the baseline characteristics of the aforementioned groups ($P > 0.05$). Along the treatment duration, 60 healthy volunteers from the First Affiliated Hospital of Zhengzhou University were selected as the control group. The inclusion criteria were as follows: patients aging between 18 and 70 years old who received HD for ≥3 months (two to three times a week, at least 4 hours each time), with urea clearance index (Kt/V) ≥1.2, stable and permanent vascular access and a blood flow velocity ≥200 mL/min. The exclusion criteria were patients using drugs affecting the uric acid metabolism such as Hppisopurind, diuretics, and Tongfengding, or drugs affecting platelet activation such as aspirin and dipyridamole 3 months prior to the treatment; patients suffering from primary hypertension, coronary artery disease, diabetes mellitus, and rheumatic diseases, or had liver, lung, or other diseases.

2.3 | Treatment regimens

All patients from each group underwent HD therapy, using the 4008S dialysis machine (Fresenius, Taunusstein-Neuhof, Germany). Patients in the HD group were treated with cellulose triacetate dialyzer (150G; Nipro, Tokyo, Japan) three times a week for 6 months, 4 hours each time, with the blood flow adjusted to 220-250 mL/min, and a dialysate flow rate of 500 mL/min. A high-flux dialyzer F60 (Fresenius) was adopted for the patients in the HDF group. The area of dialysis membrane was 1.3 m^2, with blood flow adjusted to 220-250 mL/min, and the replacement fluid flow at 70-100 mL/min for a total amount of 18-30 L. Patients in the HDF group underwent one cycle of hemofiltration and two cycles of hemodialysis weekly, for 6 months with adequate anticoagulation. In the HP group, patients were treated with cellulose triacetate dialyzer (150G) in series with resin perfusion apparatus (LivZon Medical Biological Material Co., Ltd., Zhuhai, China) and underwent 1-time HP and 5-times HD every 2 weeks with the blood flow adjusted to 220-250 mL/min, for 6 months. Prior to the treatment, the body weight and blood pressure of the patient were measured and recorded, the dialyzer was properly connected with the pipeline and was operated to preheat and self-test, and the prepared heparin saline was employed for preflushing and circulation in order to exhaust the air in the dialyzer and the pipeline. Thereafter, the vascular access was established first through an arteriovenous puncture, which was followed by an intravenous injection of the first dose of heparin (JianFu Medical Technology Co., Ltd., Guangzhou, China). Afterward, the blood pump started; the blood from the arterial end was derived from the body and returned to the body through the dialyzer. During the

hemodialysis period, different medications and symptomatic treatments, including decompression, the correction for anemia, and ion disorders, were applied depending on the patients' condition.

2.4 | Measurement of indexes

Serum phosphorus, serum calcium (SCa), blood urea nitrogen (BUN), serum creatinine (Scr), plasma albumin (ALB), hemoglobin (HGB), triglyceride (TG), parathyroid hormone (PTH), beta 2-macroglobulin (β2-MG) and the patients' dry weight, white blood cell (WBC), and platelet count were recorded for the patients in all groups before and after 6 months of hemodialysis. The improvement of patients' subjective feelings (including symptoms as fatigue, somnus, appetite, osteodynia, and uremic pruritus) was evaluated through a questionnaire. Self-control method and SF-36 were adopted in order to investigate the indexes including overall health status, somatic pain, function of somatic and emotional role, social function, energy, and psychological health. The types and incidence of complications that arose in patients following hemodialysis were observed and calculated. The online clearances monitor (OCM) 4008S (Fresenius) was used to calculate the urea removal index of KT/V (normal range: 1.2-1.4) automatically according to patients' gender, height, and weight. The efficacy assessments for patients after HD, HDF, and HP therapies were as follows: If the liver and kidney function and routine blood returned to normal, and the clinical outcomes disappeared, it was defined as excellence; if the clinical outcomes significantly improved yet HD therapy was still required, it was defined as effective; if the clinical outcomes exhibited no improvement or got worse, which could sometimes result in death, it was defined as ineffective. The clinicians referred to the double-blind method in light of KT/V index and questionnaire results to assess the therapeutic efficacy of HD, in order to divide the patients into the response group (patients of excellent and effective efficacy) and the nonresponse group (patients of ineffective efficacy).

2.5 | Determination of the expression of CD40, CD80, CD62, and P10

Before and after HD, 5 mL of venous blood was extracted from the patients in each group, followed by the addition of 2% ethylenediaminetetraacetic acid-2Na anticoagulant (3 V Biotechnology Co., Ltd., Weifang, China) and 0.7% NaCl in order to prevent blood coagulation. Mononuclear cells were isolated using a Ficoll-Paque (Biochrom, Berlin, Germany) density gradient centrifugation, seeded into a 6-well plate at a density of 1×10^6 cells/cm^2, and cultured in a 5% CO_2 incubator at 37°C after the addition of Royal Park Memorial Institute 1640 medium containing 10% fetal calf serum (FCS). Four hours later, the nonadherent cells were discarded, while the adherent cells were further cultured with the addition of FM-CSF (100 ng/mL) and IL-4 (50 ng/mL) with daily solution replacement. On the 7th d, TNF-α (100 ng/mL) was added, and the cells (namely mature dendritic cells) were collected on the following day. A total of 3 mL of anticoagulated blood was collected and centrifuged at 500 × *g* to separate the platelet-rich plasma (PRP), with the platelet count adjusted to 300×10^6/mL. Four centrifuge tubes were adopted, first added with 100 μL of PRP, then supplemented with 20 μL of fluorescein isothiocyanate (FITC)-labeled mouse anti-human P-selectin (CD62P-FITC; 11-0628, Ebioscience, San Diego, CA, USA), R-phycoerythrin-labeled anti-human thrombospondin (P10-PE, France), negative control goat anti-mouse monoclonal antibody to immunoglobulin G (IgG)-FITC antibody (555748, BD Biosciences, Franklin Lakes, NJ, USA), and IgG-PE antibody (551436, BD Biosciences), respectively. The solution was then diluted by 200 μL of phosphate buffer saline (PBS), incubated at 4°C for 30 minutes under conditions devoid of light, and centrifuged at 2500 *g*/min and mixed with 400 μL of PBS after discarding the supernatant. Finally, the expressions of CD62P and P10 were measured using a flow cytometer (BD Biosciences).

A total of 2 mL of anticoagulated blood was collected and added into three flow cytometers tubes. Next, each tube was added with 5 μL of CD40-PE (12-0409, Ebioscience, San Diego, CA, USA)/CD14-FITC (ANT-253, Prospec, Rehovot, Israel), CD80-PE (560925, BD Biosciences)/CD14-FITC, and isotype-PE/isotype-FITC, respectively. Two additional tubes were then added with PE and FITC, respectively, diluted by 200 μL of PBS, and mixed with 100 μL of anticoagulated bloods, preserved at 4°C for 30 minutes under conditions devoid of light, and hemolysis was performed using the Q-PREP hemolytic instrument (Beckman Coulter, Inc, Chaska, MN, USA). Afterward, the tubes were centrifuged at 2500 *g*/min and flushed by 400 μL of PBS after discarding the supernatant. Finally, the protein expression was detected using a flow cytometer. All the aforementioned antibodies were purchased from BD Biosciences.[22,23]

2.6 | Statistical analysis

All data were analyzed by SPSS20.0 (IBM, Armonk, NY, USA). Measurement data were expressed by mean ±standard deviation. The experimental data were analyzed with variance analysis of repeated measurements. The data in each group were processed with test of normality and test of homogeneity of variance using Shapiro-Wilk and Levene methods separately. When the data reached normal distribution or homogeneity of variance, Bonferroni test was conducted, if the Kruskal-Wallis failed. Enumeration data were expressed by ratio or percentage and compared using chi-square test, with $P < 0.05$ and $P < 0.01$ implying to significant and exceedingly significant differences, respectively.

3 | RESULTS

3.1 | Comparisons of baseline characteristics of all enrolled study subjects

A total of 240 patients in the HD (44 females and 36 males between the ages of 53.00 ± 4.31 years), HDF (38 females and 42 males between the ages of 51.30 ± 4.24 years), and HP (44 females and 36 males between the ages of 53.40 ± 4.45 years) groups were included in the baseline, with the specific data shown in Table 1. No statistical differences were observed in parameters such as the gender, age,

TABLE 1 Comparison of baseline characteristics between the case and control groups

Subjects	HD group (n = 80)	HDF group (n = 80)	HP group (n = 80)	Control group (n = 60)	*P*	*P**	*P*#
Male	36	42	36	33	0.436	0.635	0.634
Age	53.00 ± 4.31	51.30 ± 4.24	53.40 ± 4.45	52.33 ± 12.52	0.198	0.124	0.290
Weight (kg)	65.23 ± 10.12	64.23 ± 11.02	63.94 ± 10.84	64.82 ± 9.95	0.480	0.234	0.867
Primary pathogenesis							
Chronic glomerulonephritis	24	24	22	0	<0.001	0.648	0.691
Chronic interstitial nephritis	12	14	16	0			
Diabetic nephropathy	14	12	14	0			
Hypertensive renal damage	12	16	18	0			
Lupus nephritis	6	6	6	0			
Others	12	8	4	0			
Medical history of cardiovascular disease	14	16	12	0	<0.001	0.688	0.409
Medical history of diabetes	28	28	26	0	<0.001	>0.999	0.740
Vascular access	76	78	72	0	<0.001	0.409	0.051
Residual urine volume							
≥400 mL/d	11	14	15	12	0.654	0.523	0.532
100~399 mL/d	26	26	30	15			
<100 mL/d	43	40	35	33			
KT/V	1.46 ± 0.21	1.48 ± 0.44	1.44 ± 0.33	1.48 ± 0.26	0.854	0.706	0.458
Standard protein metabolism	1.42 ± 0.70	1.41 ± 0.41	1.42 ± 0.25	1.37 ± 0.82	0.911	0.621	0.791
SCa	2.34 ± 0.21	2.31 ± 0.23	2.33 ± 0.51	2.41 ± 0.25	0.635	0.699	0.791
Serum phosphorus	1.77 ± 0.41	1.75 ± 0.21	1.76 ± 0.47	1.81 ± 0.52	0.899	0.782	0.880
BUN	28.44 ± 1.81	27.98 ± 1.26	28.23 ± 1.19	28.69 ± 1.96	0.170	0.056	0.186

BUN, blood urea nitrogen; HD, hemodialysis; HDF, hemodiafiltration; HP, hemoperfusion; SCa, serum calcium; *P* for the comparison between the case and the control groups; *P** for the comparison between the HD group and HDF group; *P*# for the comparison between the HDF group and HP group.

weight, KT/V, standard protein metabolism, SCa, serum phosphorus, and BUN among all groups (all $P > 0.05$). Although there were no statistical differences in the compositions of primary disease, medical history of cardiovascular disease and diabetes, vascular access, and residual urine volume (≥400 mL/d) in the HD, HDF, and HP groups (all $P > 0.05$) in comparison with the control group the HD, HDF, and HP groups exhibited significant statistical differences in the compositions of primary disease, medical history of cardiovascular disease and diabetes, vascular access, and residual urine volume (all $P < 0.05$).

3.2 | Metabolites are very effectively cleared by HD treatment

No changes were observed in BUN (Figure 1A) and Ca (Figure 1D of CRF patients after 6 months of different dialysis treatments compared with the values prior to the treatment (all $P > 0.05$), while Scr (Figure 1B), serum phosphorus (Figure 1C), TG (Figure 1G), PTH (Figure 1H), β_2-MG (Figure 1I), WBC (Figure 1J), and platelet count (Figure 1K) evidently decreased, and HGB (Figure 1E) and ALB (Figure 1F) markedly increased in each group (all $P < 0.05$); the HDF and HP groups presented with more significant changes than the HD group, with the HP group exhibiting the most significant changes (all $P < 0.05$). There was no significant difference in the impact of different therapeutic efficacy on the change of Scr, WBC, and platelet count ($P > 0.05$). Following HD treatment, the SCr, serum phosphorus, TG, and PTH decreased in CRF patients, which was indicative of effective metabolite removal and that HD therapy played a decisive role in the reduction of metabolic acidosis and maintaining the acid-base balance. The level of β_2-MG also decreased dramatically, reducing its accumulation in vivo and long-term HD complications.

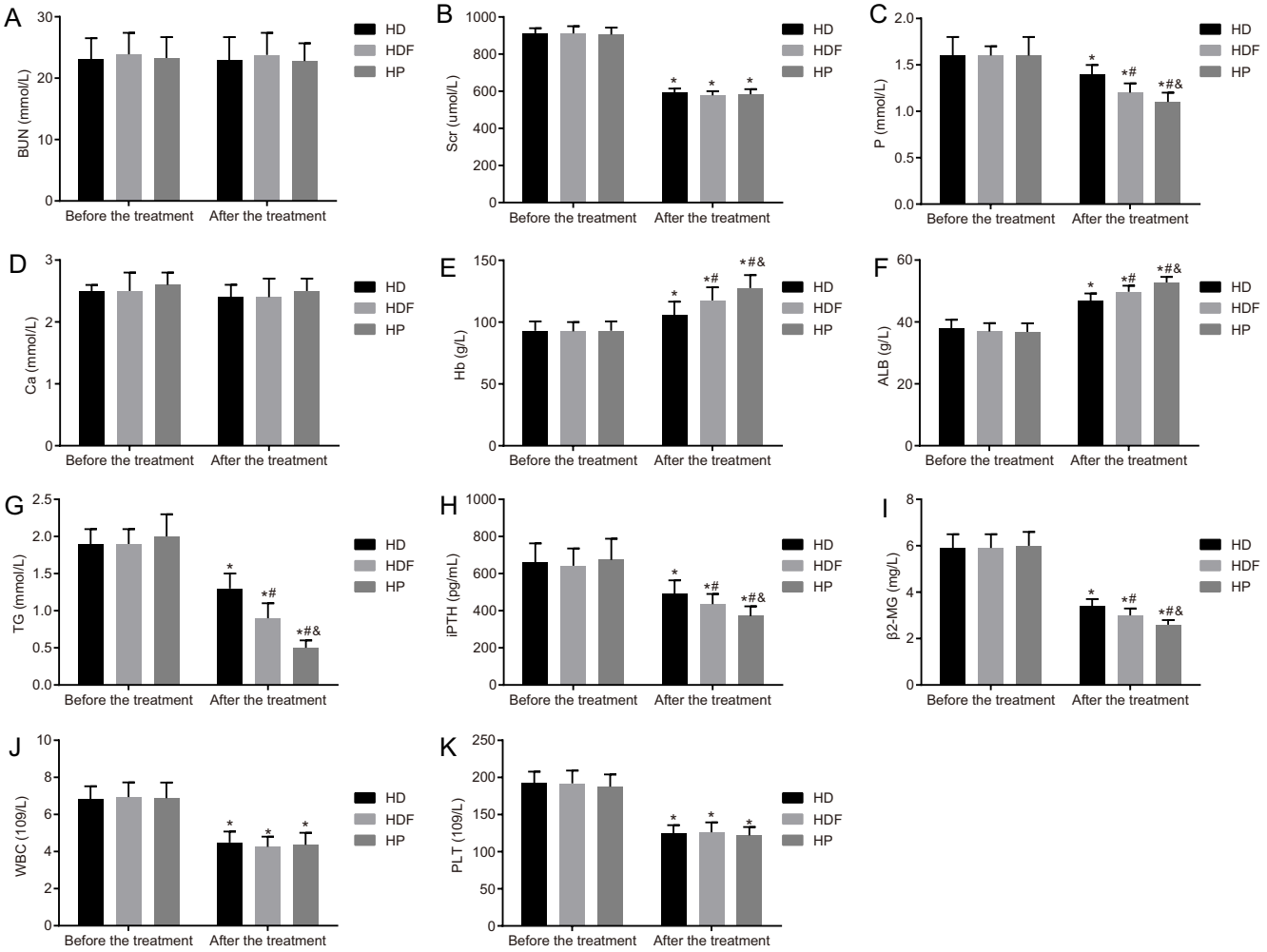

FIGURE 1 The changes in the indexes of patients in each group before and after 6 mo of HD therapy. A-K, the expression of BUN, Scr, P, Ca, Hb, ALB, TG, iPTH, β_2-MG, WBC, and platelet count in each group before and after 6 mo of hemodialysis; ALB, plasma albumin (g/L); BUN, blood urea nitrogen (mmol/L); HD, hemodialysis; HDF, hemodiafiltration; HGB, hemoglobin (g/L); HP, hemoperfusion; PTH, parathyroid hormone (pg/mL); SCa, serum calcium (mmol/L); BUN, blood urea nitrogen (umol/L); Scr, serum creatinine (mmol/L); TG, triglyceride (mmol/L); WBC, white blood cell; β_2-MG, β_2-microglobulin (mg/L); *, $P < 0.05$ vs before treatment; #, $P < 0.05$ vs the HD group after treatment; &, $P < 0.05$ vs the HDF group after treatment

3.3 | The symptoms related to CRF are predominantly improved in patients after HD therapy

The subjective feelings such as fatigue, poor sleep, poor appetite, osteodynia, uremic pruritus, and neuropsychiatric disorders were either significantly reduced or completely abated and the dry weight increased significantly in CRF patients after 6 months of therapy, which was statistically different from the recorded weight before treatment (all $P < 0.05$; Table 2). In comparison with the score before HD, the score of living quality of CRF patients in the HD, HDF, and HP groups noticeably improved (all $P < 0.05$). Following dialysis, the score of living quality of the HDF and HP groups was obviously higher than that of the HD group (all $P < 0.05$), and the score of living quality of the HP group was higher than that of the HDF group ($P < 0.05$; Figure 2). These results suggested that the associated symptoms of CRF patients predominantly improved after HD therapy and that HD therapy in the treatment of CRF has achieved certain therapeutic efficacy.

3.4 | The changes in the expression of CD40, CD80, CD62P, and P10 before and after different methods of HD therapy

As shown in Figure 3, the expression of CD40 and CD80 in monocytes in the blood samples of healthy controls was higher than that of CRF patients before treatment, and it remarkably increased in mononuclear cells in peripheral blood in patients after different HD therapies (all $P < 0.05$). The expression of CD40 and CD80 after HD therapy in the HDF and HP groups was higher than that of the HD group (all $P < 0.05$), while the expression of the HP group was higher than the HDF group ($P < 0.05$). The expression of CD62P and P10 in platelets in the blood samples of healthy controls was lower than that of CRF patients before treatment, and it decreased obviously in peripheral blood platelets in patients following the different regimens of HD therapies (all $P < 0.05$). The expression of CD62P and P10 after HD therapy in

TABLE 2 Comparison of the efficacy of different HD therapies before and after treatment for 6 mo

	HD group			HDF group			HP group		
Subjective feelings	Before treatment	After treatment	*P*	Before treatment	After treatment	*P*	Before treatment	After treatment	*P*
Fatigue	66	16	<0.001	62	20	<0.001	64	24	<0.001
	77.30%	17.69%		77.50%	25.00%		80.00%	30.00%	
Poor sleep	58	24	<0.001	56	30	<0.001	56	36	<0.001
	67.90%	39.23%		70.00%	37.50%		70.00%	45.00%	
Poor appetite	68	28	<0.001	62	34	<0.001	64	42	<0.001
	78.90%	31.54%		77.50%	42.50%		80.00%	52.50%	
Osteodynia	28	0	<0.001	28	0	<0.001	30	0	<0.001
	31.20%			35.00%			37.50%		
Itch of skin	36	12	<0.001	38	10	<0.001	38	8	<0.001
	41.40%	14.62%		47.50%	12.50%		47.50%	10.00%	
Neuropsychiatric disorders	22	2	<0.001	26	2	<0.001	26	0	<0.001
	25.00%	3.85%		32.50%	2.50%		32.50%		
Increase of dry weight	0	34	<0.001	0	40	<0.001	0	50	<0.001
		39.23%			50.00%			62.50%	

HD, hemodialysis; HDF, hemodiafiltration; HP, hemoperfusion.

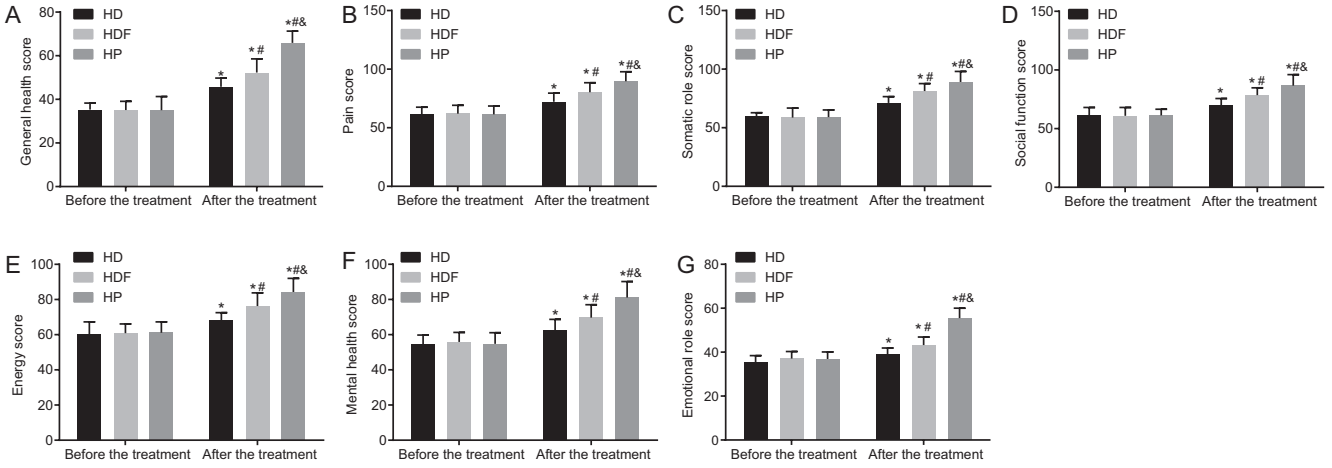

FIGURE 2 Quality of life improved in patients following HD therapy; A-G, comparisons of parameters such as the overall health status, somatic pain, somatic role, social function, energy, psychological health, and emotional role in each group before and after 6 mo of hemodialysis; HD, hemodialysis; HDF, hemodiafiltration; HP, hemoperfusion; *, $P < 0.05$ vs before treatment; #, $P < 0.05$ vs the HD group after treatment; &, $P < 0.05$ vs the HDF group

the HDF and HP groups was lower than that of the HD group (all $P < 0.05$) and that in the HP group was lower than the HDF group ($P < 0.05$).

3.5 | Decreased expression of CD62P and P10 and high expression of CD40 and CD80 are correlated with better therapeutic efficacy

According to the efficacy assessment, patients from each group were subdivided into effective group and ineffective group. There were 50 patients in the effective group and 30 patients in the ineffective group of the HD group, 56 patients in the effective group and 24 patients in the ineffective group of the HDF group and 64 patients in the effective group and 16 patients in the ineffective group of the HP group. A decrease in the expression of CD62P and P10 was observed in the effective group with a high expression in the ineffective group, while CD40 and CD80 showed high expression in the effective group and low expression in the ineffective group in all three groups (all $P < 0.05$; Figure 4). These results highly indicated that the therapeutic efficacy was better in CRF patients with low expression of CD62P and P10 and high expression of CD40 and CD80 after HD therapy.

3.6 | Decreased expression of CD62P and P10 and increased expression of CD40 and CD80 are correlated with lower chances of complications after HD therapy

The relationship between the expression of CD40, CD80, CD62P, P10, and the arising complications of HD therapy was assessed. The results showed that the incidence of these complications reached 45.0% in the patients in the HD group, with 12 cases of hypertension, four cases of heart failure, eight cases of cardiac arrhythmia, four cases of angina pectoris, four cases of itchy skin, and four cases of muscle spasm. In the HDF group, there were four cases of hypertension, zero case of heart failure, four cases of cardiac arrhythmia, zero case of angina pectoris, four cases of itchy skin, and zero case of muscle spasm, with the incidence up to 15.0% after HD therapy. In the HP group, there were four cases of hypertension, zero case of heart failure, zero case of cardiac arrhythmia, zero case of angina pectoris, four cases of itchy skin, and zero case of muscle spasm, with the incidence up to 10.0% after HD therapy. The complication incidence in the HDF and HP groups was lower than that in the HD group, while the complication incidence in the HP group was much lower than that in the HDF group (all $P < 0.05$). On the basis of the analysis on the relationship between the existing complications among the three groups, significant differences were observed in the occurrence and probability of the complications of hypertension, heart failure, arrhythmia, angina pectoris, and muscle spasm among the three groups (Table 3). Patients in all groups were later divided into complicated group and uncomplicated group according to the complications after treatment, with the complicated group presenting with a high expression of CD62P and P10 while a lower expression was observed in the uncomplicated group (all $P < 0.05$). The expressions of CD40 and CD80 were shown to have decreased in the complicated group, while they increased in the uncomplicated group (all $P < 0.05$; Figure 5). Generally, these results revealed that that after HD therapy, a decrease in the expression of CD62P and P10 with a high expression of CD40 and CD80 was evident, along with lowered incidence of complications in CRF patients.

4 | DISCUSSION

Chronic renal failure or CKD is a global epidemic, with clinical manifestations including deregulation of salt and water homeostasis, changes in endocrine functions and renal detoxification capacity, which has a deleterious impact on the overall survival of patients.[27,28] HD has made a remarkable achievement in prolonging

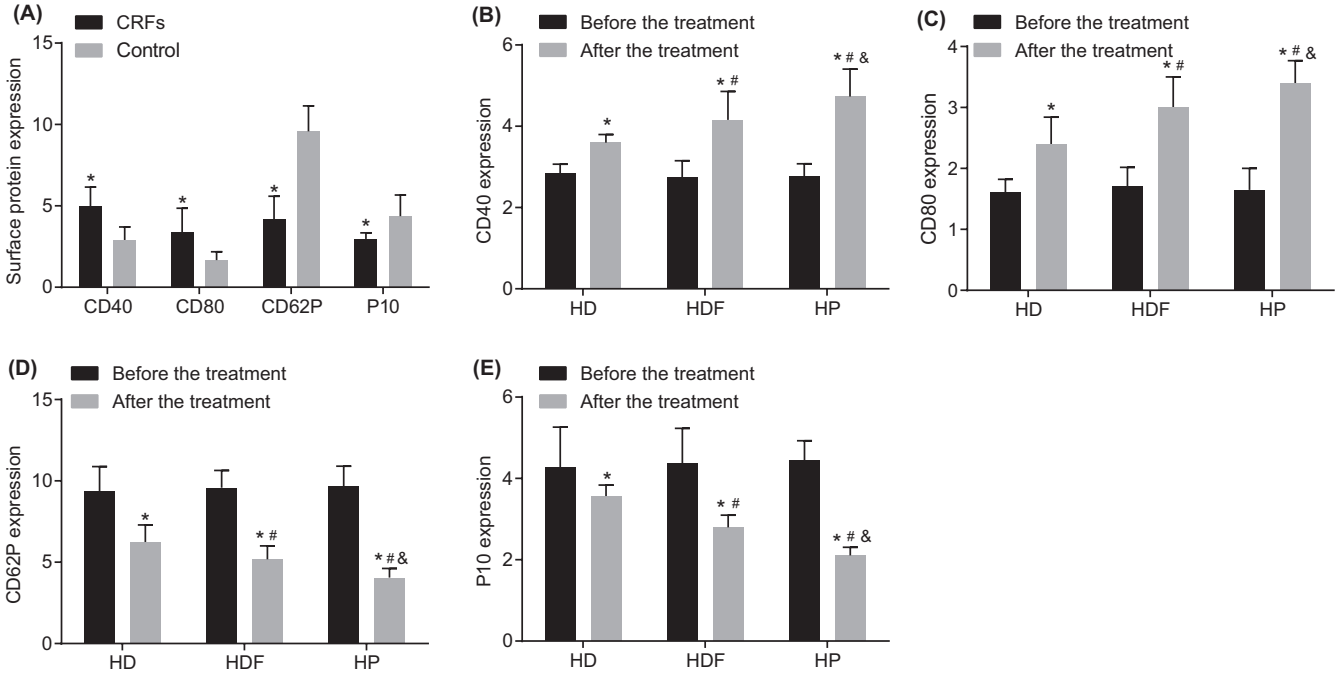

FIGURE 3 After HD therapy, there is a decrease in the expression of CD40 and CD80 and an increase in CD62P and P10 expression. A, the comparison of protein expression (CD40, CD80, CD62P, and P10) between healthy controls and CRF patients; B, the comparison of the protein expression of CD40 in mononuclear cells in peripheral blood in CRF patients before and after different HD treatment; C, the comparison of CD80 protein expression in mononuclear cells in peripheral blood in CRF patients before and after different HD treatment; D, the comparison of the protein expression of CD62P in mononuclear cells in peripheral blood in CRF patients before and after different HD treatment; E, the comparison of the protein expression of P10 in mononuclear cells in peripheral blood in CRF patients before and after different HD treatment; *, $P < 0.05$ vs the control groups or before treatment; #, $P < 0.05$ vs after HD treatment; △, $P < 0.05$ vs after HDF treatment

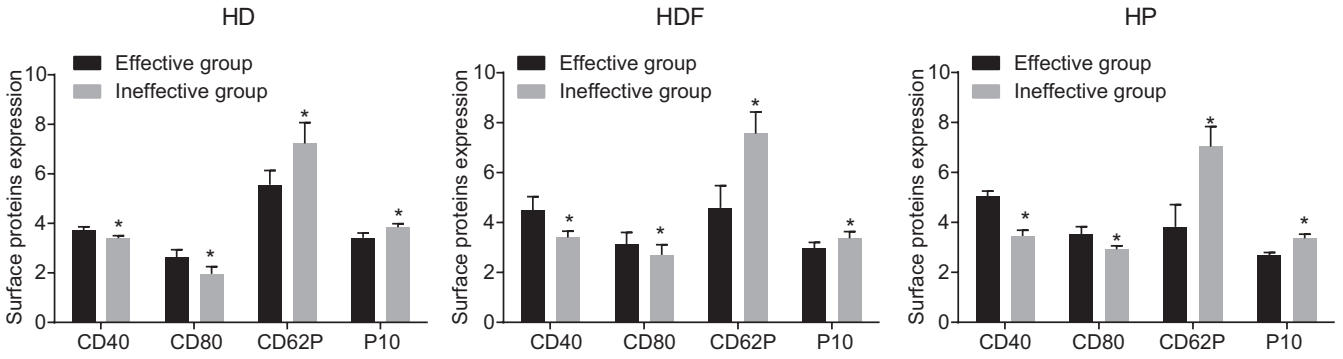

FIGURE 4 Comparison of expression of CD40, CD80, CD62P, and P10 between the effective group and the ineffective group. HD, hemodialysis; HDF, hemodiafiltration; HP, hemoperfusion; *, $P < 0.05$ vs the effective group

the life of more than one million CRF patients with limited or no kidney function.[9] Since different HD methods are known to affect the expression of CD40, CD80, CD62P, and P10 in CRF patients, the present study emphasizes on investigating these effects, the clinical outcomes of HDF, and the correlation with post-HD therapy complications. The results highly indicated that the therapeutic efficacy of HDF and HP is superior to the efficacy of HD in the treatment of CRF, with an existing correlation between the expression of CD40, CD80, CD62P, and P10 and complications arising in patients who underwent HD treatment.

One of the key observations of this study was the obviously decreased levels of Scr, serum phosphorus, TG, PTH, and β2-MG along with evidently increased HGB and ALB levels following 6 months of different procedures of HD therapy in each group. Recent reports have demonstrated a relation between elevated levels of Scr, TG, and serum phosphorus with reduced kidney function.[29,30] Kalantar-Zadeh et al reported that a low level of ALB in CKD patients is associated with malnutrition and higher serum albumin is indicative of a poor prognosis in patients on dialysis.[32] HD therapy, combined with blood perfusion, has been reported to effectively

TABLE 3 Comparisons of the complications after HD therapy in all groups

Groups	Hypertension	Heart failure	Cardiac arrhythmia	Angina pectoris	Itchy skin	Muscle spasm	Complication rate
HD group	12	4	8	4	4	4	0.45
HDF group	4	0	4	0	4	0	15.0%*
HP group	4	0	0	0	4	0	10.0%*,#
P	0.0221	0.0135	0.0037	0.0135	1.00	0.0135	<0.0001

HD, Hemodialysis; HDF, hemodiafiltration; HP, hemoperfusion.
*$P < 0.05$ vs compared with the HD group.
#$P < 0.05$ vs the HDF group.

eliminate PTH and β2-MG.[33] Furthermore, a study by Mcfarlane PA et al also found the HGB level can rise over time in HD patients.[34] Furthermore, the present study also discovered significant change in the aforementioned indexes following HDF and HP treatment compared with HD treatment. A previous study showed that HDF is successful in reducing the β2-MG level and protein carbonyl and in eliminating uremic toxins, thereby improving the adequacy of dialysis in CRF and the quality of life of dialysis patients, making it a more efficacious and effective treatment regimen compared with HD.[35] HP has been reported to be safer and more feasible than other HD therapies when used to treat children, since the tubes and cartridge are all disposable and can eliminate inflammatory mediators efficiently.[12]

The efficacy and living quality in CRF patients following treatment were also assessed and the results showed that there was a great deal of improvement in the subjective feelings including fatigue, poor sleep, poor appetite, osteodynia, uremic pruritus, and neuropsychiatric disorders, an increase in the dry weight, and generally, patients had a better-quality life. The use of high-flux membranes in HDF has been proven to be useful in delaying the long-term complications.[36] In addition to the scarce removal of uremic toxins and protein-bound molecules in low-flux dialysis, the prevalence of long-term complications and poor quality of life in CRF patients are evident; HP treatment leads to better overall survival of patients.[37] There was an increase in the protein expression of CD40 and CD80 and decrease in CD62P and P10 expressions according to our results. The outcome differs in different HD therapies, with more significant outcomes in HDF and HP than in HD. CRF is a chronic condition characterized by inflammation, and hypercoagulability, meaning patients will have increased levels of procoagulant and inflammatory markers.[38] In CRF patients that had undergone HD, a transient decrease in CD40L and CD62P was detected.[39] CD62P, as an indicator of platelet degranulation when expressed on platelet surface, plays a mediate role in the interactions of platelet and leukocyte cells, which can stimulate the production of chemoattractants and growth factors.[16] Targeting CD40 enhances the delivery of tumor antigen and simultaneously stimulates the activation of antigen-presenting cells with CD40-CD40L interaction,[40] which induces the maturation and activation of dendritic cells (DC), thereby promoting immune response.[41] CD80, also known as B7-1, is a transmembrane, which is stimulated by an interaction with allergens and irritants.[42] The maturation of DC induces the upregulation of CD80 expression.[43] P10 is known to be involved in the regulation of angiogenesis, inflammation, and vascular function, and elevated levels of P10 are associated with an adverse outcome in HD patients.[44]

Overall, the findings from our study provided evidence supporting HDF and HP as superior treatment regimens for CRF compared to HD and that the expressions of CD40, CD80, CD62P, and P10 can be correlated with the therapeutic efficacy of HD and improved prognosis. However, due to the limitation of this study in the form of the potential process by which monocytes can be further differentiated into DCs, as well as the expression of activated markers in different groups of DCs, further studies are needed to elucidate the same.

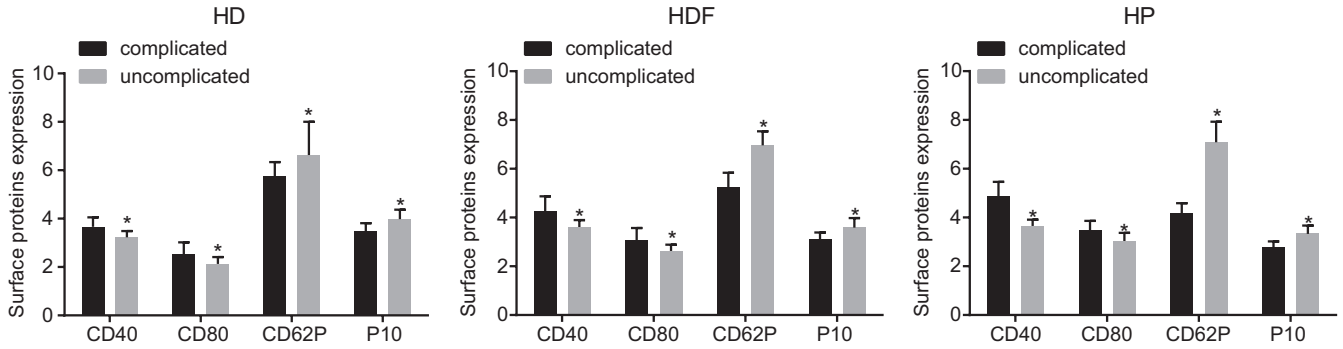

FIGURE 5 The lowered expression of CD40 and CD80 and increased expression of CD62P and P10 are correlated with complications after HD therapy. HD, hemodialysis; HDF, hemodiafiltration; HP, hemoperfusion; *, $P < 0.05$ vs the complicated group

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