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Effect of Shenkang injection combined with hemodialysis treatment on renal function, renal anemia and cytokine levels in patients with chronic renal failure

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ABSTRACT

Objective: To study the effect of Shenkang injection combined with hemodialysis treatment on renal function, renal anemia and cytokine levels in patients with chronic renal failure. **Methods:** A total of 68 patients with chronic renal failure who received hemodialysis treatment in our hospital during between October 2013 and February 2016 were selected and randomly divided into two groups, the observation group received Shenkang injection treatment in the process of dialysis, and the control group only received conventional symptomatic and supportive treatment. 8 weeks after treatment, serum was collected to determine the levels of renal function indexes, nutritional status indexes, anemia indexes and cytokines, and urine was collected to determine renal function indexes. **Results:** β 2-MG, UA, Cr, phosphorus, IL-17, IL-23, CTGF, TGF- β 1, FGF-2 and FGF-23 levels in serum as well as NGAL, KIM-1 and RBP levels in urine of observation group were significantly lower than those of control group, and TP, Alb, PA, calcium, Hb, EPO, Fe, TRF and FER levels in serum were significantly higher than those of control group. **Conclusion:** Shenkang injection combined with hemodialysis treatment helps to improve renal function, nutritional status and renal anemia, and reduce the synthesis of inflammation and renal interstitial fibrosis-related cytokines in patients with chronic renal failure.

1. Introduction

Chronic renal failure is chronic progressive renal parenchyma damage induced by various causes, nephron is damaged and reduces, and the renal excretion function and endocrine function are damaged, causing the water-electrolyte and acid-base balance disorders and toxic metabolite accumulation as well as renal anemia and renal malnutrition[1,2]. Hemodialysis is the most common renal replacement therapy for treatment of chronic renal failure, and can effectively remove toxic metabolites in the body and maintain water-electrolyte balance and acid-base balance. Hemodialysis treatment, however, could not completely replace complex renal metabolism and endocrine function and has limited effect on the removal of cytokines and other small-molecule toxins. Long-term dialysis therapy may increase the body's micro-inflammatory response and renal fibrosis, the renal metabolism and endocrine function haven′t been replaced, and therefore, the conditions of renal anemia and renal malnutrition will continue to increase[3,4]. Traditional Chinese medicine theory holds that chronic renal failure belongs to the category of "kidney overstrain" and "edema", hemodialysis treatment can cause vital essence damage, and the use of effective prescriptions to support kidney and fortify qi has positive therapeutic effect. Shenkang injection is the compound preparation of safflower, rhubarb, astragalus membranaceus, salvia miltiorrhiza and other traditional Chinese medicines, and has the effect of supporting kidney and fortifying qi[5]. In the following study, the effect of Shenkang injection combined with hemodialysis treatment on renal function, renal anemia and cytokine levels in patients with chronic renal failure was analyzed.

2. Subjects and methods

2.1. Research subjects

A total of 68 patients with chronic renal failure who received

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hemodialysis treatment in our hospital during between October 2013 and February 2016 were selected for study, and all patients had definite primary renal disease and conformed to the diagnosis of chronic renal failure and indications of hemodialysis treatment. According to random number table, the included patients were divided into observation group and control group (n=34). Observation group received hemodialysis combined with Shenkang injection treatment, including 21 male cases and 13 female cases who were (51.3±7.3) years old and with dialysis time (11.58±1.58) months; control group only received hemodialysis and conventional symptomatic and supportive treatment, including 23 male cases and 11 female cases who were (50.9±7.7) years old and with dialysis time (11.58±1.58) months. The two groups of patients were not significantly different in general information.

2.2. Treatment methods

Both groups received standard hemodialysis therapy, dialysis machine was from German B. Braun Company, dialysis membrane was PES membrane, dialysate was bicarbonate, blood flow during dialysis was 180-220 mL/min, dialysate flow rate was 500 mL/min, time of each dialysis was 4 h and there were three times of dialysis every week. During dialysis, low molecular heparin calcium was used for anticoagulation, quality protein diet was provided, water-electrolyte and acid-base balance were maintained, and the cardiac insufficiency and liver damage were symptomatically treated. On the basis of standard hemodialysis treatment and symptomatic treatment, observation group received Shenkang injection treatment, and the method was as follows: they received treatment after each dialysis, Shenkang injection 40 mL in saline injection 50ml, intravenous drip, 20-30 drops /min.

2.3. Clinical sample collection and preservation methods

8 weeks after treatment, 3-5 mL of fasting venous blood was collected in the morning, let stand for 20 min and then centrifuged for 20 min at 2 000 r/min to collect serum and preserve it in a -70 ℃ ultra-low temperature freezer; 5 mL of midstream urine was collected and centrifuged for 20 min at 2 000 r/min to separate supernatant and preserve it in a -70 ℃ ultra-low temperature freezer.

2.4. Index determination methods

Serum samples were taken, and automatic biochemical analyzer was used to determine hemoglobin (Hb), uric acid (UA), creatinine (Cr), total protein (TP), albumin (Alb), prealbumin (PA), calcium and phosphorus levels; enzyme-linked immunosorbent assay kits were used to determine β 2-microglobulin (β 2-MG), iron (Fe), transferrin (TRF), ferritin (FER) and erythropoietin (EPO), interleukin-17 (IL-17), IL-23, connective tissue growth factor (CTGF), transforming growth factor β 1 (TGF- β 1), fibroblast growth factor (FGF-2) and FGF-23 levels. Urine specimens were taken, and enzyme-linked immunosorbent assay kits were used to determine the levels of kidney injury molecule-1 (KIM-1), neutrophil gelatinase-associated lipocalin (NGAL) and retinol-binding protein (RBP).

2.5. Statistical methods

SPSS 16.0 software was used to input the detected data, measurement data analysis between two groups was by t test and P<0.05 indicated statistical significance in differences.

3. Results

3.1. Renal function indexes in serum and urine

8 weeks after treatment, analysis of renal function indexes β 2-MG, UA and Cr in serum of two groups was as follows: β 2-MG, UA and Cr levels in serum of observation group were significantly lower than those of control group; analysis of renal function indexes NGAL, KIM-1 and RBP in urine was as follows: NGAL, KIM-1 and RBP levels in urine of observation group were significantly lower than those of control group. Differences in β 2-MG, UA and Cr levels in serum as well as NGAL, KIM-1 and RBP levels in urine were statistically significant between two groups (P<0.05).

3.2. Nutritional status–related biochemical indexes

8 weeks after treatment, analysis of protein metabolism indexes TP, Alb and PA in serum of two groups was as follows: TP, Alb and PA levels in serum of observation group were significantly higher than those of control group; analysis of trace elements calcium and

Table 1.
Comparison of renal function indexes in serum and urine between two groups.

Groups	n	Serum indexes			Urine indexes (μg/g)		
		β 2-MG (mg/L)	UA (μmol/L)	Cr (μmol/L)	NGAL	KIM-1	RBP
Observation	34	2.86±0.42	241.22±35.23	145.42±18.65	32.52±5.59	10.15±1.42	17.34±1.95
Control	34	4.03±0.67	325.56±41.58	214.57±27.68	50.14±7.61	14.58±1.94	24.45±4.92
T		6.917	6.582	7.193	7.674	6.039	6.683
P		<0.05	<0.05	<0.05	<0.05	<0.05	<0.05

Table 2.
Comparison of nutritional status-related biochemical indexes in serum between two groups.

Groups	n	Protein indexes (g/L)			Trace elements (mmol/L)	
		TP	Alb	PA	Calcium	Phosphorus
Observation	34	70.46±8.95	42.52±6.59	0.41±0.06	2.45±0.31	1.59±0.18
Control	34	63.15±7.65	35.14±5.96	0.28±0.04	2.05±0.25	1.93±0.25
T		5.968	6.516	7.785	6.273	7.028
P		<0.05	<0.05	<0.05	<0.05	<0.05

phosphorus levels in serum was as follows: calcium level in serum of observation group was significantly higher than that of control group while phosphorus level was significantly lower than that of control group. Differences in TP, Alb and PA as well as calcium and phosphorus levels in serum were statistically significant between two groups (P<0.05).

3.3. Renal anemia–related indexes

8 weeks after treatment, analysis of anemia degree of two groups was as follows: Hb level in serum of observation group was significantly higher than that of control group; analysis of EPO levels in serum was as follows: EPO level in serum of observation group was significantly higher than that of control group; analysis of iron metabolism indexes in serum was as follows: Fe, TRF and FER levels in serum of observation group were significantly higher than those of control group. Differences in Hb, EPO, Fe, TRF and FER levels in serum were statistically significant between two groups (P<0.05).

3.4. Serum cytokines

8 weeks after treatment, analysis of cytokines IL-17, IL-23, CTGF, TGF- β 1, FGF-2 and FGF-23 levels in serum of two groups was as follows: IL-17, IL-23, CTGF, TGF- β 1, FGF-2 and FGF-23 levels in serum of observation group were significantly lower than those of control group. Differences in IL-17, IL-23, CTGF, TGF- β 1, FGF-2 and FGF-23 levels in serum were statistically significant between two groups (P<0.05).

4. Discussion

Shenkang injection is traditional Chinese medicine compound preparation that can improve the renal function[6,7], and in order to define the effect of Shenkang injection intervention during hemodialysis treatment for patients with chronic renal failure, the changes of renal function in both groups were analyzed in the study at first. UA and Cr are the metabolites of purine and proteins in blood circulation respectively, are excreted by the liver, and are the routine blood biochemical molecules that reflect renal function; β 2-MG is a kind of small molecular protein produced by lymphocytes, it is freely filtrated through the glomeruli, reabsorbed by proximal convoluted tubule and then degraded, and β 2-MG in serum can reflect the glomerular filtration function[8,9]. In the study, analysis of the renal function indexes in serum confirmed that β 2-MG, UA and Cr levels in serum of observation group were significantly lower than those of control group. NGAL, KIM-1 and RBP in urine mainly reflect renal tubular function. NGAL and KIM-1 are mainly expressed in the proximal tubule, and RBP is mainly reabsorbed through renal tubule; in the case of renal tubular damage, the above three kinds of molecules are eliminated with the urine[10]. Analysis in the study showed that NGAL, KIM-1 and RBP levels in urine of observation group were significantly lower than those of control group. The above analysis shows that Shenkang injection can improve the glomerular filtration function and renal tubular reabsorption function in patients with chronic renal failure.

Chronic renal failure is chronic wasting disease, and in the process of sustainable disease development, protein, fat and other nutrients in the body are constantly consumed, and patients are in a state of malnutrition. In addition, the hemodialysis treatment not only eliminates toxic metabolites, but will also cause nutrient loss through the dialysate, further aggravating the degree of malnutrition. In the study, analysis of protein consumption level in patients after Shenkang injection treatment showed that TP, Alb and PA levels in serum of observation group were significantly higher than those of control group. This means that Shenkang injection can improve chronic protein consumption during dialysis treatment in patients with chronic renal failure. Chronic renal failure not only causes protein loss, but can also affect calcium-phosphorus metabolism and hematopoietic function, characterized by renal osteodystrophy and renal anemia. High calcium and low phosphorus are the characteristics of calcium-phosphorus metabolism in patients with chronic renal failure, calcium-phosphorus metabolism disorders can cause abnormal bone metabolism and increase the risk of osteoporosis[11,12]. In the study, serum calcium and serum phosphorus were analyzed to reflect the nutritional status of patients, and the results showed that calcium level in serum of observation group was significantly higher than that of control group while phosphorus level was significantly lower than that of control group. That means that Shenkang injection can improve calcium-phosphorus metabolism disorder during dialysis treatment in patients with chronic renal failure. Combined analysis of protein loss and calcium-phosphorus metabolism shows that Shenkang injection can improve the nutritional status during hemodialysis in patients with chronic renal failure.

Table 3.
Comparison of renal anemia-related indexes in serum between two groups.

Groups	n	Hb (g/L)	EPO (ng/mL)	Iron metabolism indexes		
				FE (μmol/L)	FER (ng/mL)	TRF (mg/mL)
Observation	34	103.51±14.42	0.67±0.09	22.68±2.62	221.25±27.79	2.26±0.25
Control	34	92.44±10.27	0.42±0.06	13.41±1.89	196.32±22.52	1.70±0.20
T		6.019	7.584	8.812	5.968	6.792
P		<0.05	<0.05	<0.05	<0.05	<0.05

Table 4.
Comparison of serum cytokine levels between two groups.

Groups	n	IL-17 (pg/mL)	IL-23 (pg/mL)	CTGF (ng/mL)	TGF- β 1 (pg/mL)	FGF-2 (pg/mL)	FGF-23 (ng/mL)
Observation	34	53.95±7.84	103.65±16.75	20.32±4.52	252.39±36.62	57.61±7.86	12.93±2.15
Control	34	79.33±9.14	179.75±22.54	34.15±5.94	346.61±46.84	93.51±10.62	19.14±3.28
T		6.958	8.481	7.981	7.382	9.038	8.371
P		<0.05	<0.05	<0.05	<0.05	<0.05	<0.05

Renal anemia is a special manifestation of malnutrition in patients with chronic renal failure. The determination of hemoglobin levels in the study showed that Hb level in serum of observation group was significantly higher than that of control group. This means that Shenkang injection can improve renal anemia in patients with chronic renal failure. The main causes of renal anemia include the iron loss and insufficient erythropoietin (EPO) synthesis in the body[13]. In the process of hemodialysis, iron in serum can be lost through the dialysate, which causes iron deficiency and iron depletion in the body, and then results in iron-deficiency anemia; chronic renal failure will affect the renal endocrine function, result in decreased EPO synthesis and affect hematopoietic function[14,15]. In the study, analysis of EPO levels and iron metabolism indexes confirmed that EPO as well as Fe, TRF and FER levels in serum of observation group were significantly higher than those of control group. That means that Shenkang injection can increase EPO synthesis during hemodialysis in patients with chronic renal failure, also regulate iron metabolism and reduce iron loss, thus improving anemia status.

Hemodialysis treatment can effectively remove macromolecule toxins in the body, but its removal effect is weaker on small-molecule toxins, especially cytokines. Micro-inflammatory state is a common pathological condition in patients with chronic renal failure during dialysis, dialysis membrane, as a foreign body, will induce micro-inflammation and increase the synthesis of inflammatory cytokines, but hemodialysis is unable to effectively remove the excessively produced inflammatory cytokines in the body, which will cause the accumulation of inflammatory cytokines and enhancement of inflammation. IL-17 and IL-23 are the inflammatory cytokines closely related to micro-inflammatory state during hemodialysis[16], and the analysis in the study showed that IL-17 and IL-23 levels in serum of observation group after treatment were significantly lower than those of control group. In addition to the inflammatory cytokines, there are a variety of cytokines associated with renal fibrosis in patients with chronic renal failure. CTGF, TGF-β1, FGF-2, FGF-23 and various other cytokines can promote fibroblast proliferation and increase collagen synthesis and accumulation, thus causing the glomerular sclerosis and renal interstitial fibrosis[17,18]. In the study, analysis of the levels of above four cytokines confirmed that CTGF, TGF-β1, FGF-2 and FGF-23 levels in serum of observation group after treatment were significantly lower than those of control group. This means that Shenkang injection can reduce the synthesis of inflammation and renal interstitial fibrosis-related cytokines during hemodialysis in patients with chronic renal failure.

To sum up, Shenkang injection combined with hemodialysis treatment helps to improve renal function, nutritional status and renal anemia, and reduce the synthesis of inflammation and renal interstitial fibrosis-related cytokines in patients with chronic renal failure.

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