## Journal of Experimental and Clinical Application of Chinese Medicine

CLINICAL RESEARCH

# The Treatment Efficacy of Buyang Huashi Quzhuo Prescription Combined with CBP on Renal Function, Microcirculation and Inflammatory Response in Patients with Acute Renal Injury

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#### Keywords

Buyang Huashi Quzhuo prescription,
Continue blood purification, Acute renal
injury, Renal function, Microcirculation

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Received: 5 February 2021; Accepted: 8 March 2021; Published online: 29 March 2021

Journal of Experimental and Clinical
Application of Chinese Medicine 2021;
2(2): 88-95

#### Abstract

Objective To explore the treatment efficacy of Buyang Huashi Quzhuo prescription combined with continue blood purification (CBP) in patients with acute renal injury of gi deficiency of spleen and kidney and the accumulation of turbidity-stasis syndrome, and the effect on renal function, microcirculation and inflammatory response of patients. Methods A total of 100 patients with acute renal injury of qi deficiency of spleen and kidney and the accumulation of turbidity-stasis syndrome in our hospital from Jan. 2018 to Jan. 2021 were selected and divided into control group and observation group by using the random number table method. The control group was treated with CBP, and the observation group was treated with Buyang Huashi Quzhuo prescription on the basis of the control group. The clinical efficacy, acute physiology and chronic health evaluation score (APACHE II), renal function, microcirculation and the levels of inflammatory factors of the both groups were compared before and after treatment. Results The total effective rate in the observation group was obviously higher than that in the control group. The APACHE II score, and the levels of serum creatinine, urea nitrogen as well as urinary albumin excretion rate, 24 h urinary protein quantification, β<sub>2</sub>-microglobulin, interleukin-6, interleukin-8 and C-reactive protein of both groups after treatment were obviously decreased in comparison with those before treatment, and those in observation group were obviously lower than those in the control group. Conclusion The clinical efficacy of Buyang Huashi Quzhuo prescription combined with CBP in the treatment of patients with acute renal injury of qi deficiency of spleen and kidney and the accumulation of turbidity-stasis syndrome is significant, and it can improve the renal function as well as microcirculation of patients and reduce the inflammatory response of body.

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#### Introduction

Acute renal injury is a clinical syndrome characterized by a rapid decline in glomerular filtration rate which resulted in accumulation of metabolic waste products, electrolyte disorder, abnormal drug metabolism, etc.[1]. At present, the main methods used to treat acute kidney injury are liquid therapy, antihypertensive drugs, diuretics, kidney replacement therapy and so on<sup>[2]</sup>. As an indispensable rescue measure for critically ill patients, continuous blood purification (CBP) refers to a blood purification method that continuously and slowly removes toxins in the blood, corrects electrolyte disorders, and removes water retention. However, continuous anticoagulation will increase the risk of systemic bleeding, and the therapeutic effect can not reach the expected level, so other auxiliary measures are needed to make up for its drawbacks [3]. Traditional Chinese medicine therapy has a long history and is widely used in clinical treatment of acute kidney injury. Buyang Huashi Quzhuo prescription is composed of a variety of traditional Chinese medicines, which can be decocted into decoction to play a role in drug therapy and effectively promote the recovery of patients by decocting them into decoction. In this study, Buyang Huashi Quzhuo prescription combined with CBP was used to treat patients with acute renal injury of spleen

and kidney qi deficiency as well as the accumulation of turbidity-stasis syndrome, and its clinical curative effect and influence on patients' renal function, microcirculation and inflammatory reaction were discussed, which provided a reference for the clinical treatment of patients with acute kidney injury of spleen-kidney qi deficiency as well as the accumulation of turbidity-stasis syndrome. The research results are reported as follows.

#### Data and methods

#### **General information**

100 patients with acute kidney injury were selected due to deficiency of spleen and kidney qi in our hospital from January 2018 to January 2021. According to the random number table method, we randomly divided these patients into control group (n=50) and observation group (n=50), provided that there was no significant difference (*P*>0.05) between the two groups in general information including gender, age, etiology and staging of the kidney disease improving global outcomes (KDIDO), which was comparable, as shown in Table 1. This study was approved by the medical ethics committee of our hospital, and all patients voluntarily participated and signed written informed consent.

Table 1. Comparison of general information between the two groups

	C	Gender			Etiology					Staging of KDIDO		
Group	Case		Female	Age	Medicine	Abdominal infection	-	_	Post-renal obstruction	_	Stage 2	Stage 3
The									5	14	22	16
observation	50	26	24	50.23±5.85	16	13	9	7				
group												
The									8	15	20	15
control gro	50	27	23	52.21±6.22	14	10	10	8				
up												
$t^{/\chi}2/Z$		0.	040	-1.640			1.336				-0.250	)
P		0.	841	0.104			0.855				0.803	

#### Inclusion and exclusion criteria

#### **Inclusion criteria**

Patients whose symptoms were strictly consistent with the diagnostic criteria of *KDIGO Clinical Practice Guideline for Acute Kidney Injury*<sup>[4]</sup>; patients whose symptoms were strictly consistent with the diagnostic criteria of qi deficiency of spleen and kidney as well as the accumulation of turbidity-stasis syndrome in the *Guiding Principles of Clinical Research of New Chinese Medicine*<sup>[5]</sup>; patients treated with CBP.

#### **Exclusion criteria**

The following categories of people were excluded from our study: patients with other kidney diseases such as chronic renal failure and chronic kidney injury; patients who are allergic to traditional Chinese medicine; patients with malignant tumors; people with abnormal coagulation function; people with immune system diseases; people with a previous history of kidney transplantation.

#### Treatment methods

#### The control group

The control group was treated with CBP: the double-lumen catheter was indwelled in the right internal jugular vein as well as femoral vein of patient to successfully establish the extracorporeal circulation, All patients were treated with continuous high volume venous-venous haemofiltration for 12 hours (h). During the blood purification treatment, the input blood flow was set at  $150{\sim}200$  mL/min and the input speed was set at  $2.0 \sim 3.0$  L/h. According to the patient's loading capacity, we adjusted the ultrafiltration volume, the range of which was  $30 \sim 50$  L/d. The whole treatment lasted for 1 week.

#### The observation group

On the basis of the control group, the observation group was treated with Buyang Huashi Quzhuo prescription whose basic ingredients include Buyang Huashi Quzhuo prescription were composed of 45 g astragalus, 25 g poria cocos, 25 g alisma, 20 g semen plantaginis, 20 g rhizoma acori graminei, 20 g herba epimedium, 15 g magnolia officinalis, 15 g radix

curcumae, 15 g fructus lipuidambaris, 15 g ligusticum chuanxiong, 15 g rhizoma curculiginis, 15 g fried rhizoma dioscoreae, 10 g rhizoma sparganii, 5 g rhubarb. In addition, 15 g semen ziziphi spinosae and 30 g concha margaritifera were added for patients who suffered from insomnia and dreaminess; 15 g achyranthes bidentata and 12 g eucommia ulmoides were added for patients who suffered from soreness weakness of waist and knee; 30 g cortex dictamni radicis and 15 g bombyx batryticatus were added as the main ingredients to patients with pruritus; 20 g ginger and 15 g pinellia ternata were added to patients with obvious nausea and vomiting. Moreover, the above Chinese herbal medicines were decocted with water to yield a final volume 100 ml, and one dose was divided into two parts to be taken in one day (morning and evening). In addition, two courses of treatment were performed continuously, with 14 days as one course of treatment.

#### **Observation indicators**

(1) Clinical curative effect and APACHE II score: ① clinical curative effect<sup>[6]</sup>: cure: experimental examination showed that creatinine clearance rate (Ccr) was increased or serum creatinine (Scr) was decreased by  $\geq 30\%$ ; effective: the clinical symptoms and signs of patients were significantly improved, and the experimental examination clearly manifested that Ccr was increased or Scr was decreased by 20% ~ 30%; ineffective: the clinical symptoms and signs of the patients had not improved or deteriorated obviously, and the experimental examination manifested that the Ccr or Scr had little change; the total effective rate of treatment = (cure+effective) cases/total cases  $\times 100\%$ . ②APACHE II score<sup>[7]</sup>: the total score was 71 points including 0-60 points for acute physiology, 0-6 points for age and 2-5 points for chronic health. Furthermore, the higher the total score, the more severe the patient's condition.

(2) Renal function: before and after the treatment, 3 ml venous fasting blood was drawn from two groups of patients in the morning. Then the supernatant was taken after centrifugation. Furthermore, the levels of Scr and blood urea nitrogen (BUN) were detected

with a usage of an automatic biochemical analyzer (Wuhan Shengshida Medical Equipment Co., Ltd., model: BS - 300).

- (3) Microcirculation: from the morning of the first day to the morning of the next day, the urine of two groups of patients was collected. Next, the 24-h uridine triphosphate (24h-UTP) was measured by urine protein precipitation and biuret method, and the urinary albumin excretion rate (UAER) was calculated, with UAER=24h-UTP/24 h. Besides, the level of  $\beta$ 2-microglobulin ( $\beta$ 2-MG) was detected by immunoturbidimetry with a kit which was purchased from Shanghai Xinfan Biotechnology Co., Ltd., and the test was carried out in strict accordance with manufacturer's protocol.
- (4) Inflammatory factors: before and after the treatment, 3 ml venous fasting blood was drawn from patients in the two groups in the morning, and then the supernatant was taken after centrifugation. Besides, interleukin-6 (IL-6), interleukin-8 (IL-8) and C-reactionprotein (CRP) levels were detected by enzyme-linked immunosorbent assay. All the kits were purchased from Shanghai Zhongqiao Xinzhou Biotechnology Co., Ltd., and the above indexes were tested strictly according to the manufacturer's protocol.

#### Statistical methods

SPSS 20.0 was used for statistical analysis. The counting data were compared by  $\chi^2$  test, rank sum test

was used for analyzing rank data, mean  $\pm$  standard deviation ( $\bar{x}\pm s$ ) was used for analyzing measurement data, and t test was used for comparison. In addition, P-values less than 0.05 were deemed as statistically significant.

#### Results

## Comparisons of clinical efficacy and APACHE II between the two groups

The total effective rate in observation group was significantly higher than that in control group (P<0.05). Before treatment, there was no significant difference in APACHE II score between the two groups (P>0.05). Compared with pre-treatment data, APACHE II score of patients belonging to these two groups were significantly reduced after treatment (P<0.05), and APACHE II score in observation group was significantly lower than that in control group (P<0.05), as shown in Table 2.

### Renal function indexes in two groups before and after treatment

Before treatment, there was no significant difference in the levels of Scr and BUN between the two groups (P>0.05). Compared with pre-treatment data, the levels of Scr and BUN in the two groups were decreased significantly after treatment (P<0.05), and the levels of Scr and BUN in observation group were significantly lower than those in control group (P<0.05), as shown in Table 3.

Table 2. Comparisons of clinical efficacy and APACHE II between two groups

						<i>U</i> 1		
			Clinical effic	acy [cases (%)]		APACHE II (score)		
Group	Case	Cure	Effective	Ineffective	The total effective	Before treatment	After treatment	
The		23 (46.00)			46 (92.00)	22.65±2.43	13.54±2.12a	
observation group	50		23 (46.00)	4 (8.00)				
The control group	50	20 (40.00)	17 (34.00)	13 (26.00)	37 (74.00)	22.76±2.65	17.66±2.43ª	
$t/X^2$					5.741	-0.216	-0.903	
P					0.017	0.829	< 0.001	

Note: Compared with pre-treatment data, <sup>a</sup>P<0.05

Table 3. Renal function indexes in two groups before and after treatment  $(\bar{x}\pm s)$ 

Crown	Coso	Scr (µı	mol/L)	BUN (mmol/L)		
Group	Case	Before treatment	After treatment	Before treatment	After treatment	
The observation group	50	156.34±24.54	102.76±16.67a	6.99±1.34	4.97±1.22a	
The control group	50	157.65±25.76	$126.45 \pm 18.54^a$	6.78±1.37	$5.67 \pm 1.26^a$	
t		-0.260	-6.719	0.775	-2.822	
P		0.795	< 0.001	0.440	0.006	

Note: Compared with pre-treatment data, <sup>a</sup>P<0.05

## Comparison of microcirculation indexes between the two groups before and after treatment

Before treatment, there was no significant difference in UAER, 24h-UTP and  $\beta$ 2-MG levels between the two groups (P>0.05). Compared with pre-treatment data, the levels of UAER, 24h-UTP and  $\beta$ 2-MG in the two groups were significantly reduced after treatment (P<0.05), and the levels of UAER, 24h-UTP and  $\beta$ 2-MG in observation group were significantly lower than those in control group (P<0.05), as shown in Table 4.

## Comparison of inflammatory factors between the two groups before and after treatment

Before treatment, there were no significant differences in IL-6, IL-8 and CRP levels between two groups (P>0.05). Compared with pre-treatment data, the levels of IL-6, IL-8 and CRP in the two groups were significantly decreased after treatment (P<0.05), and the levels of IL-6, IL-8 and CRP in observation group were significantly lower than those in control group (P<0.05), as shown in Table 5.

Table 4. Comparison of microcirculation indexes between the two groups before and after treatment ( $\bar{x}\pm s$ )

		UAER (µg/min)		24h-U	ΓP (g/24h)	β <sub>2</sub> -MG (mg/L)		
Group	Case	Before	After treatment	Before	After treatment	Before	After treatment	
		treatment		treatment		treatment		
The observation	50	120 56±20 54	82.54±16.35a	2.11±0.34	0.97±0.20a	14.65±2.56	3.56±0.34a	
group	30	120.30±20.34	02.34±10.33	2.11±0.54	0.57±0.20	14.03±2.30	3.30±0.34	
The control group	50	122.54±21.22	92.33±17.87a	2.13±0.30	$1.22 \pm 0.22^a$	13.96±2.34	$5.76 \pm 0.50^a$	
t		-0.474	-2.858	-0.312	-5.946	1.407	-25.728	
P		0.637	0.005	0.756	< 0.001	0.163	< 0.001	

Note: Compared with pre-treatment data, <sup>a</sup>P<0.05

Table 5. Comparison of inflammatory factors between the two groups before and after treatment ( $\bar{x}\pm s$ )

		UAER (µg/min)		24h-U7	ΓP (g/24h)	β <sub>2</sub> -MG (mg/L)		
Group	case	Before	After treatment	Before	After treatment	Before	After treatment	
		treatment		treatment		treatment		
The observation	50	120.56±20.54	82.54±16.35a	2.11±0.34	0.97±0.20 <sup>a</sup>	14.65±2.56	3.56±0.34 <sup>a</sup>	
group	30	120.30±20.34						
The control	50	122.54±21.22	92.33±17.87a	2.13±0.30	1.22±0.22a	13.96±2.34	5.76±0.50a	
group	30	122.34±21.22	92.33±17.87°	2.13±0.30	1.22±0.22	13.90±2.34	3.70±0.30°	
t		-0.474	-2.858	-0.312	-5.946	1.407	-25.728	
P		0.637	0.005	0.756	< 0.001	0.163	< 0.001	

Note: Compared with pre-treatment data, <sup>a</sup>P<0.05

#### Discussion

Acute kidney injury is mainly caused by ischemia-reperfusion, drug toxicity and sepsis, with renal tubular epithelial cell injury accompanied by endothelial injury and inflammatory cell aggregation as common pathological features. If it can not be treated in time, acute kidney injury may develop into chronic kidney disease or even end-stage kidney disease, which seriously affects patients' health and quality of life [8]. In traditional Chinese medicine, acute kidney injury can be classified into the categories of "Guan Ge", "confinement" "intoxication". On the one hand, the pathogenesis of acute kidney injury is the deficiency of qi in internal factors. On the other hand, "six evils", drug poison and insect poison serving as the external factors could invade the human body, causing heat to become heat toxin, damaging yin and qi, hindering the circulation of qi and blood, and transforming into blood stasis, damp turbidity, and dampness of Sanjiao, which will aggravate visceral deficiency to trigger acute kidney injury<sup>[9]</sup>. Therefore, the primary treatments of patients with acute kidney injury are tonifying kidney and spleen, activating blood circulation and removing blood stasis. In this study, the control group was treated with CBP, and the observation group was treated with Buyang Huashi Quzhuo prescription on the basis of the control group. The results manifested that the total effective rate in the observation group was significantly higher than that in control group, which indicated that Buyang Huashi Quzhuo prescription combined with CBP had a better effect in treating patients with acute kidney injury of spleen and kidney qi deficiency as well as the accumulation of turbidity-stasis syndrome.

Acute renal injury is caused by the decrease of systemic blood circulation, which gives rise to insufficient renal perfusion, microcirculation disturbance as well as aggravation of renal injury, and then further leads to renal dysfunction<sup>[10]</sup>. Scr is the product of muscle metabolism, BUN is the product of protein catabolism in human body, and their levels can reflect kidney function. UAER is an effective index to judge early kidney damage, that is, the more serious

the kidney damage is, the higher its level is. 24 h-UTP refers to the concentration of protein in all urine of the body for 24 h and its level can reflect the body's condition. B2-MG is a globulin synthesized by lymphocytes, polymorphonuclear leukocytes and other cells, and  $\beta$ 2-MG level is significantly increased under the condition of kidney damage. Moreover, the results of this study showed that the APACHE II score, and Scr, BUN, UAER, 24h-UTP as well as β2-MG levels of patients in the two groups were decreased significantly after treatment, and APACHE II score, and Scr, BUN, UAER, 24h-UTP as well as β2-MG levels in observation group were significantly lower than those in control group. It indicated that Buyang Huashi Quzhuo prescription combined with CBP could improve the renal function and microcirculation of patients with acute renal injury caused by spleen and kidney qi deficiency as well as the accumulation of turbidity-stasis syndrome. Solutes and water in the body were slowly and continuously cleared by convection, CBP was able to improve microcirculation perfusion, and maintain water electrolyte, extracellular osmotic pressure as well as acid-base balance, which result in restoration of normal kidney function[11]. Besides, the basic ingredients of Buyang Huashi Quzhuo prescription were astragalus, poria cocos, alisma, semen plantaginis, rhizoma acori graminei, herba epimedium, magnolia officinalis, radix curcumae, fructus lipuidambaris, ligusticum chuanxiong, rhizoma curculiginis, fried rhizoma dioscoreae, rhizoma sparganii and rhubarb. Astragalus, rhizoma dioscoreae and poria cocos have the functions of nourishing spleen as well as kidney and promoting diuresis. Alisma and semen plantaginis can promote excretion. Rhizoma acori graminei, radix curcumae and rhizoma Sparganii can reduce proteinuria. Herba epimedium and rhizoma curculiginis have the functions of promoting diuresis, removing toxin and warming and recuperating the kidney. Magnolia officinalis has analgesic and anti-inflammatory effects. Ligusticum chuanxiong is able to inhibit glomerular fibrosis. Fructus Lipuidambaris and rhubarb have diuretic and detumescence effects. In view of the

efficacy of the above mentioned traditional Chinese medicines, the combination of all medicines has the effects of resolving phlegm and turbidity, invigorating spleen and kidney, promoting blood circulation and removing blood stasis. In addition, astragalus contained selenium to protect the glomerular basement membrane machinery, reduce permeability of glomerular basement membrane, improve renal proteinuria, preserve glomerular tissue structure, decrease water and sodium retention, which could promote urinary excretion and recovery of renal function<sup>[12]</sup>. On the one hand, poria cocos can inhibit the reabsorption of sodium ions (Na+) and excretion of potassium ions (K+) in renal tubules, and increase the value of Na+/K+ in urine, so as to induce diuresis. On the other hand, poria cocos polysaccharides contains hemiacetal hydroxyl, which can undergo oxidation-reduction with active oxygen free radicals, combine with OH hydrogen atoms to form water, inhibit renal interstitial fibrosis, and help improve renal function[13].

There is inflammatory infiltration in the kidney of patients with acute kidney injury, resulting in the synthesis as well as release of various inflammatory factors and the aggravation of the kidney injury, which further worsens the disease progress. Moreover, IL-6 can bind to receptors on mesangial cells, leading to mesangial thickening and decreasing glomerular filtration rate. In addition, being an important pro-inflammatory factor, IL-8 can promote renal tubular atrophy as well as renal fibrosis and aggravate renal injury. CRP is an acute protein, and CRP level rises sharply when the body is infected or damaged. The results of this study manifested that the levels of IL-6, IL-8 and CRP in the two groups were significantly decreased after treatment, and the levels of IL-6, IL-8 and CRP in observation group were significantly lower than those in control group. This meant that Buyang Huashi Quzhuo prescription combined with CBP can alleviate the inflammatory response of patients with acute renal injury of qi deficiency of spleen and kidney and the accumulation of turbidity-stasis syndrome. Besides, CBP remove and adsorb inflammatory mediators through strong

convection and relatively large pore size of filtration membrane, which can regulate immune disorder and maintain internal homeostasis[14]. A related study has shown[15] that the extract of alisma can inhibit the mRNA expression of tumor necrosis factor-α, down-regulate the expression of nitric oxide synthase cyclooxygenase-2 downstream noncanonical nuclear factor-kappaB (NF-κB), and reduce local inflammatory reaction. Semen plantaginis has a diuretic effect, which can promote the excretion of urea, chloride and uric acid, down-regulate the expression of NLRP3 inflammatory corpuscle, apoptosis-associated speck-like protein and cysteine protease in kidney tissue, and reduce the level of inflammatory factors such as interleukin-12, thus alleviating the body's inflammatory response<sup>[16]</sup>.

In general, the clinical efficacy of Buyang Huashi Quzhuo prescription combined with CBP in the treatment of patients with acute renal injury of qi deficiency of spleen and kidney and the accumulation of turbidity-stasis syndrome is significant, and it can improve the renal function, microcirculation and reduce the inflammatory response of patients' body.

#### **Declaration of conflict-of-interest**

The authors declare no conflict-of-interest.

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