

Original Research Article

Effect of Sanjin Paishi Decoction combined with lithotripsy on clinical symptoms and renal function of patients with nephrolithiasis

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Abstract

Purpose: To determine the effect of Sanjin Paishi decoction (SJPSD) combined with lithotripsy on the improvement of clinical symptoms and renal function in nephrolithiasis patients.

Methods: A total of 100 patients with nephrolithiasis, who were treated in the outpatient department of the Affiliated Hospital of Jinggangshan University, Ji'an, Jiangxi, China from January 2019 to October 2021, were retrospectively analyzed and enrolled in the study. They were divided into control group (CG, n = 40) treated with holmium laser lithotripsy through flexible ureteroscope, and a study group (OG, n = 60) treated with SJPSD after holmium laser lithotripsy through flexible ureteroscope. Treatment effect and improvement in renal function indices (serum creatinine (Scr), cystatin C (CysC) and urinary N-acetyl-β-D glucosaminidase (NAG)), were compared. Postoperative clinical efficacy, time of disappearance of hematuria, postoperative extubation time, of hospital stay, Traditional Chinese medicine (TCM) symptom score, and the incidence of complications were evaluated.

Results: After treatment, OG showed significantly downregulated Scr, CysC, and NAG compared with CG, but the total clinical effectiveness was significantly higher than that of CG ($p < 0.05$). Kidney stone clearance rate of OG was higher than that of CG at 4 weeks post-operation ($p < 0.05$). The time of disappearance of postoperative hematuria, postoperative extubation time, and hospitalization time of OG was shorter than those of CG, while TCM symptom scores were lower than those in CG ($p < 0.05$).

Conclusion: The combination of SJPSD and holmium laser lithotripsy in the management of patients with renal calculi results in improvement in clinical efficacy, reduction in TCM symptom scores, and speed-up postoperative recovery, without increase in the incidence of complications. Prospective studies and long-term follow-up are anticipated in the future. Furthermore, established animal or in vitro models are required to determine the specific mechanism of action.

Keywords: Sanjin Paishi decoction, Holmium laser lithotripsy, Kidney stones, Renal function

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INTRODUCTION

Kidney stone is a common disease, with the highest incidence in the Department of Urological Surgery [1]. Survey has shown that the number

of new cases of urinary calculi in China is 100,000 every year, of which about a quarter of the patients require hospitalization [2]. Another study reported that the incidence of urinary calculi in southern China was higher than that in

northern China [3]. With the changes in the social and living environment, the incidence of urinary calculi in China has been on the increase, and now ranks among the top three worldwide [3]. Most patients with kidney stones have subtle symptoms, but a small number of patients have ureteral obstruction caused by the movement of the stones in the renal pelvis or ureter, resulting in severe pain [4]. The typical symptoms, mainly hematuria and renal colic can easily cause urinary tract obstruction and infection, and in severe cases may lead to renal damage. Therefore, an effective treatment plan is key to improving the condition of patients.

In recent decades, treatment options have developed rapidly. Options such as extracorporeal shock wave lithotripsy, ureteroscopy with holmium laser lithotripsy, percutaneous nephrolithotomy, ureteroscopic lithotripsy and other technologies have emerged one after the other. Most of the patients in China choose conservative treatments. When conservative treatment is ineffective, patients often require surgical treatment. Holmium laser lithotripsy through flexible ureteroscope is characterized by low trauma and quick recovery, and it has been widely performed in clinical practice [4]. However, some patients have problems of low stone clearance rate, long recovery time, high complication rate and high risk of stone recurrence after surgery [5]. Traditional Chinese medicine has a unique curative effect on urinary calculi, and has the advantages of low cost and low injury, and has been preferred by majority of calculi patients for a long time [6]. *Sanjin Tonglin Paishi* Decoction is prepared based on the clinical experience of experts at Yunnan Provincial Hospital of Traditional Chinese medicine (TCM) [7]. It is still unclear whether *Sanjin Tonglin Paishi* Decoction combined with holmium laser lithotripsy increases the clinical efficacy of patients after treatment, and whether it has any effect on renal function.

In this study, the effect of *Sanjin Paishi* decoction in combination with lithotripsy on the clinical symptoms and renal function in patients with renal calculi was observed, aiming to provide a reference treatment plan for kidney stones.

METHODS

Clinical data

The clinical data of 100 patients with kidney stones who were treated in the outpatient department of the Affiliated Hospital of Jinggangshan University, Ji'an, Jiangxi, China

from January 2019 to October 2021 were retrospectively analyzed. The patients were divided into study group and a control group according to different treatment options. The patients in the control group (n = 40) were treated with holmium laser lithotripsy through flexible ureteroscope, and the study group (n = 60) was treated with *Sanjin Paishi* Decoction. This study was approved by the hospital's Medical Ethics Committee (JGS-031) and carried out in line with the Helsinki Declaration [8]. All patients were informed about the study and signed the informed consent.

Inclusion criteria

Patients with the following features were included in the study: All patients with clinical indications in line with renal calculi, and were diagnosed via imaging examination. Patients that conformed to the diagnostic criteria of damp-heat accumulation syndrome in the "Criteria for Diagnosis and Efficacy of Chinese Traditional Medicine Diseases" [9]. The diameter of the stones ranged from 1 - 5 cm, in line with the indications of holmium laser lithotripsy with flexible ureteroscope. Patients with complete clinical data.

Exclusion criteria

The following patients were excluded: Patients with combined tumors; those who had previously undergone holmium laser lithotripsy; women who are pregnant or breastfeeding; those with cardiovascular and cerebrovascular disease, patients suffering from mental illness, serious urinary tract infection, congenital ureteral stenosis or malformation.

Treatment options

The patients in the control group were treated with holmium laser lithotripsy through flexible ureteroscope. Under general anesthesia, the patients were taken in the bladder lithotomy position, a F8/9.8 rigid ureteroscope was placed to explore the ureteropelvic junction, and the zebra guide wire was indwelled to exit the rigid ureteroscope. The ureteral dilation sheath was placed with a guide wire, and a flexible ureteroscope was placed along the dilating sheath. After detecting the calculi, a holmium laser fiber was inserted to perform lithotripsy. The lithotripsy power was 0.6 - 0.8 J to ensure that the stone fragments were less than 3 mm. After completion, the flexible ureteroscope was withdrawn, and the F6 double-J tube was indwelled to clean up the stones. After the cleaning was completed, the tube was extubated.

The patient was treated with antibiotics postoperatively.

Patients were instructed to drink water daily to increase urine output, thereby facilitating stone removal. Patients in the study group were treated with *SanJin PaiShi* Decoction, with the following formula: 30 g each of *Lysimachia nummularia* L., *Lygodium japonicum* (Thunb.) Sw., *Corneum Gigeriae Galli* Endothelium and *Astragali Radix*, 10 g each of *Alisma plantago-aquatica*, *Pyrrosia lingua* (Thunb.) Farwell, *Imperatae rhizoma*, *Dianthus superbus*, *Akebia quinata* and *Plantago asiatica*, and 6 g of *Glycyrrhiza uralensis*. The above herbs were boiled in water to get a final decoction of 300 mL. It was started on the 1st day after the operation, at 150 mL each time, 2 times/day for 2 weeks.

Parameters evaluated

Primary outcomes

According to the "Traditional Chinese Medicine Diagnosis and Efficacy Criteria" [9], patients' low back pain, backache, and urinary urgency after treatment were evaluated based on frequency, and each item was scored from 0 to 6 points. The changes of renal function indices (Scr, CysC, and NAG) were compared between the two groups before and after treatment. The clinical efficacy of the two groups of patients after treatment was compared. Total effective rate (Er) was calculated according to Eq 1.

$$Er = (TE/TP)100 \dots\dots\dots (1)$$

Where TE = total number of effective cases, and TP = total number of patients

Secondary outcomes

The differences in clinical data between the two groups were compared. The time to disappearance of hematuria, postoperative extubation time, hospitalization time, and postoperative complications in the two groups were compared. The patients were followed up for 1 year after operation, and recurrence rates in the two groups were compared.

Clinical efficacy

Cure

Stones are discharged, and the main clinical symptoms disappear completely. Abdominal plain film or ultrasound shows that the shadow of the stones disappeared.

Improvement

Stones move significantly, and a small amount was excluded, and the clinical symptoms improved.

Ineffective

No obvious movement or discharge of stones, no improvement or even worsening of clinical symptoms.

Statistical analysis

Statistical Package for the Social Sciences (SPSS) software (version 26.0) was used for statistical analysis of the data. Measurement data are expressed as mean \pm standard deviation (SD). The measurement data of the two groups were compared using students' *t*-test. Independent sample *t*-test was used for comparison between groups, and the paired *t*-test was used for comparison within the group. Enumeration data are expressed as n (%) and examined using χ^2 test. $P < 0.05$ was considered as statistically significant.

RESULTS

Clinical data

There was no significant difference in the age, gender, history of hypertension, diabetes, smoking and alcoholism between two groups (Table 1, $p > 0.05$).

Kidney function

The changes of Scr, CysC, and NAG in the two groups were compared before and after treatment, and there were no significant differences in the levels of Scr, CysC, and NAG between two groups before treatment ($p > 0.05$). After treatment however, the Scr, CysC and NAG levels in the two groups were significantly lower than those before treatment (Figure 1), ($p < 0.05$). Moreover, the serum levels of Scr, CysC, and NAG in the study group were significantly lower than those in the control group after treatment ($p < 0.05$) (Figure 1).

TCM symptom scores

The TCM symptom scores of the two groups after treatment was compared. There was no significant difference in the scores on low back pain, backache and urinary urgency between two groups before treatment ($p > 0.05$).

Table 1: Clinical data of the two groups

Parameter	Items	Study group (n = 60)	Control group (n = 40)	P-value
Gender	Male	42	25	0.434
	Female	18	15	
Age	>50	37	20	0.436
	≤50	27	20	
History of hypertension	Yes	30	17	0.462
	No	30	23	
Diabetes	Yes	25	13	0.355
	No	35	27	
Smoking history	Yes	45	25	0.181
	No	15	15	
History of alcoholism	Yes	8	5	0.590
	No	52	45	

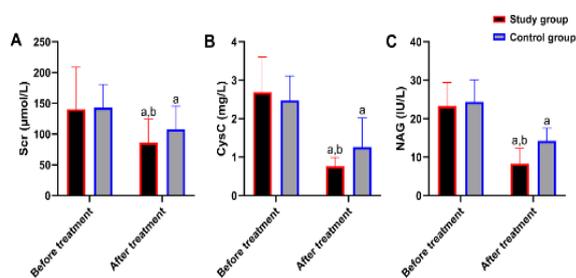


Figure 1: Changes in renal function indices. (A) Changes of serum Scr levels (B) Changes of serum CysC levels and (C) Changes in serum NAG levels in two groups before and after treatment: ^a*P* < 0.05 compared with before treatment, ^b*p* < 0.05 compared with the control group

After treatment, the scores on low back pain, backache, and urinary urgency in the two groups were significantly lower than those before treatment (Figure 2, *p* < 0.05). After treatment, the scores of low back pain, backache, and urinary urgency in the study group were significantly lower than those in the control group (Figure 2; *p* < 0.05).

Clinical efficacy/effectiveness

The changes in clinical efficacy between the two groups after treatment revealed that there are 40

Table 2: Clinical efficacy/effectiveness of treatment

Group	Cure	Improvement	Ineffective	Total effectiveness (%)
Study group (n = 60)	24	30	6	90.0
Control group (n = 40)	10	20	10	75.0
Z/χ ²		-2.083		4.018
P-value		0.037		0.045

cases of cure, 30 cases of improvement, and 6 cases where treatment was ineffective in the study group. There were 10 cases of cure, 20 cases of improvement, and 10 cases of ineffectiveness in the control group. Clinical efficacy after treatment was significantly higher than that of the control group (*p* < 0.05). The total effectiveness of treatment was also higher than that of the control group (Table 2; *p* < 0.05).

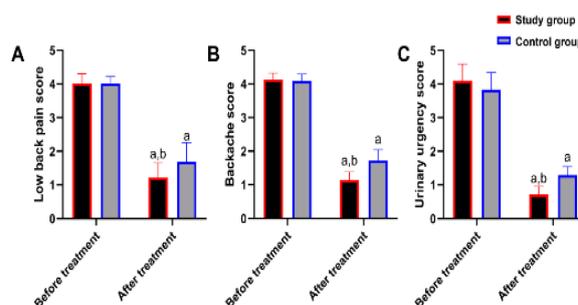


Figure 2: Comparison of TCM symptom scores: (A): Changes in low back pain scores, (B): Changes in lumbar acid scores, and (C): Changes in urinary urgency scores before and after treatment in the two groups. ^a*P* < 0.05 score was compared with group before treatment, and ^b*p* < 0.05 score was compared with the control group

Table 3: Comparison of the time to disappearance of hematuria, postoperative extubation time, and hospitalization time (mean \pm SD)

Group	Time to disappearance of hematuria	Postoperative extubation time	Duration of hospital stay (day)
Study (n = 60)	6.46 \pm 2.71	4.19 \pm 1.74	8.03 \pm 2.28
Control (n = 40)	8.70 \pm 3.14	7.16 \pm 2.12	10.23 \pm 2.72
T	3.788	7.883	4.369
P-value	0.003	< 0.001	< 0.001

Disappearance of hematuria, postoperative extubation, and hospitalization time

The time of disappearance of hematuria and postoperative extubation time in the study group were significantly shorter than those in the control group ($p < 0.05$). The hospitalization time of the study group was significantly shorter than that of the control group (Table 3, $p < 0.05$).

Incidence of complications

At the end of the study, the incidence of complications after treatment showed that the study group had 1 case of fever, 1 case of urinary tract irritation, and 1 case of low back and abdominal pain, while the control group had 2 cases of fever, 2 cases of urinary tract irritation, and 3 cases of low back and abdominal pain. There was no significant difference in the incidence of complications between two groups (Table 4; $p > 0.05$).

Table 4: Incidence of postoperative complications

Group	Fever	Urinary tract irritation	Low back pain
Study (n=60)	1 (1.67%)	1 (1.67%)	1 (1.67%)
Control (n=40)	2 (5.00%)	2 (5.00%)	3 (7.50%)
χ^2	0.916	0.916	2.127
P-value	0.338	0.338	0.145

DISCUSSION

Urinary calculi is one of the frequently-occurring diseases in the department of urology, among which kidney calculi are the most common type [10]. Recent studies have found that the incidence of kidney stones is increasing yearly, affecting primarily men. Patients are often accompanied by symptoms such as hematuria, dysuria, urgency and dysuria. In severe cases, kidney fibrosis is induced and the patient's life is endangered. [11]. Therefore, an effective treatment plan is key to improving the patient's condition.

Currently, most patients with renal calculi are often given conservative treatment, the efficacy

of which is not satisfactory [12]. Surgical treatment is the most effective option for the clinical treatment of kidney stones. Holmium laser lithotripsy with flexible ureteroscope is the most commonly used method, which can crush the stones and excrete them through repeated procedures, achieving good prognosis and less trauma [13].

The crushed stones cannot be excluded from the body for a period of time, which increases the risk of ureteral obstruction and infection [14]. Meanwhile, a small number of patients require multiple sessions, which increases the burden on renal functions and leads to postoperative complications [9]. Urinary calculi belongs to the categories of "sand streak" and "blood stranguria" in the stranguria syndrome of internal medicine in Traditional Chinese Medicine [15]. Traditional Chinese medicine believes that the etiology of kidney stones is complicated and related to the patient's dietary habits, downward diffusion of damp-heat, emotional disorders, chronic illnesses and congenital deficiencies [16]. In this study, the clinical effects of holmium laser lithotripsy was retrospectively observed using a flexible ureteroscope and combined with Sanjin Paishi decoction on patients with kidney stones. The changes in renal function indexes between the two groups was first compared. Scr is used as indices for the clinical evaluation of renal function, and its changes can directly reflect the renal damage [17]. As a cysteine protease inhibitor, CysC showed a good evaluation value for glomerular filtration capacity with high specificity, and can be significantly increased in the early stage of renal injury [18]. NAG is a common cellular enzyme and is widely distributed in the proximal convoluted tubules of the kidneys. An increase in this value indicates renal parenchymal damage. So it is a sensitive indicator of early tubular damage [19].

This study found that after treatment, the levels of Scr, CysC, NAG and the TCM symptom scores were also lower in the study group than those in the control group. The combined treatment reduced the burden of renal function and accelerate the recovery of renal function.

The present study showed that the times to disappearance of hematuria, postoperative extubation time and hospital stay in the study group were shorter than those in the control group. The clinical efficacy and total effective rate of the study group after treatment were significantly higher than those of the control group. This shows that the Sanjin Paishi Decoction combined with surgery can promote the postoperative recovery, shorten the postoperative extubation and hospitalization time, and improved the therapeutic effect. It has been speculated that the main reason for this is that the *Lygodium japonicum* (Thunb.) Sw in *Sanjin Paishi* Decoction helps to clear the stranguria. The *Pyrrosia lingua* (Thunb.) Farwell has the effect of clearing the lungs and expelling heat, and *Lysimachiae Herba* has an inhibitory effect on the formation of alcohol-induced stones. *Gallus gallus domesticus* Brisson helps to expel stones; *Achyranthes* can diuresis and relieve stranguria, remove blood stasis and disperse menstruation; *Plantaginis semen* clears heat and removes dampness, and licorice has the effect of relieving acute pain and relieving pain. Therefore, the postoperative curative effect is significantly improved. At the end of the study, there was no significant difference in the incidence of complications between two groups. This shows that the combined treatment did not increase the incidence of postoperative complications.

The combination of Sanjin Paishi decoction after holmium laser lithotripsy through flexible ureteroscopy significantly improved the clinical efficacy of patients.

Limitations of this study

First, this study is a retrospective study, which has limitations in the sample size used, and hence the analysis of the results may be biased. Second, this study did not involve short-term or long-term follow-up of patients, and it is still unclear whether combined therapy would reduce the recurrence rate after surgery.

CONCLUSION

Sanjin Paishi decoction in combination with holmium laser lithotripsy improves clinical efficacy, reduces TCM symptom scores, and accelerates postoperative recovery, without increasing the risk of complications in patients with renal calculi. The specific mechanism of *Sanjin Paishi* Decoction for the treatment of kidney stones is still unclear. Therefore, prospective studies and long-term follow-up are anticipated in future. Furthermore, animal or *in*

vitro models are required to analyze the specific mechanism of action involved.

DECLARATIONS

Acknowledgements

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Funding

None provided.

Ethical approval

This study was approved by the hospital's Medical Ethics Committee of Affiliated Hospital of Jinggangshan University, Ji'an, Jiangxi (approval no (JGS-031)..

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

The authors declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by them.

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