

Original Article

Effects of spinal anesthesia combined with dexmedetomidine on patients with infected urinary calculus

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Abstract: Objective: To investigate the effects of spinal anesthesia (SA) combined with dexmedetomidine (Dex) on patients with infected urinary calculus. Methods: A total of 105 patients with infected urinary calculus admitted to Affiliated Cixi Hospital, Wenzhou Medical University were enrolled, of which 55 patients were given both SA and Dex as a SD group, and the rest were given SA alone as a SA group. The procalcitonin (PCT), interleukin-1 (IL-1), and cystatin C (CysC) in the serum of the patients were determined, and the effect of SD combined with SA on those factors in the patients was analyzed. The following items of the two groups were compared: operation time, intraoperative blood loss, visual analogue scale (VAS) score, hospitalization time, and incidence of postoperative complications. In addition, the risk factors affecting the postoperative complications of the patients were analyzed. Results: The incidence of postoperative complications, operation time, intraoperative blood loss, VAS score, hospitalization time, mean arterial pressure (MAP), and heart rate (HR) of the SD group were significantly lower than those of the SA group, and the two groups were not significantly different in the arterial blood oxygen saturation (SPO₂). Moreover, after operation, the PCT, IL-1, and CysC levels of the SD group were significantly lower than those of the SA group, and multiple calculi, diabetes mellitus, PCT, IL-1, CysC, and SA alone were risk factors for postoperative complications in the patients with infected urinary calculus. Conclusion: SA combined with Dex is beneficial to suppress inflammatory response in patients and improve their hemodynamic parameters, and it is also helpful to shorten their operation time and hospitalization time, reduce their intraoperative blood loss and postoperative complications, and alleviate their pain.

Keywords: Spinal anesthesia, infected urinary calculus, complication

Introduction

Urinary calculi are a urinary disease affecting people of all age, whose incidence is on the rise [1]. The golden standard for its diagnosis is imaging method, such as the abdominal kidney-ureter-bladder plain film and intravenous urography, which is efficient and accurate for diagnosis [2]. According to statistics, the lifetime incidence of urinary calculi is 10%, and the patients with infected urinary calculus account for 15% of all urinary calculi patients [3, 4]. The progression of infected urinary calculus will make it harder to treat the disease for medical staff, and the symptoms of infected urinary calculus are insidious, which is prone to delay treatment and may impair the patient's renal function and even endanger his/her life

[5]. One study uncovered that infected urinary calculus was a risk factor for concurrent septicemia after operation [6], suggesting that patients with positive urinary calculi detection result faced a higher risk of postoperative septicemia [6]. Percutaneous nephrolithotomy is the first-line treatment for patients with urinary calculi, which is usually carried out under general anesthesia. Recently, there are studies reporting that spinal anesthesia (SA) can not only save medical expense for patients, but also reduce relevant complications [7]. However, patients under SA will suffer from hypothermia and shivering. Dexmedetomidine (Dex) has a sedative function, so it can prevent patients from shivering when used with SA together [8]. Based on the above, we decided to study and compare the effects of Dex com-

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combined with SA on patients with infected urinary calculus and those of SA alone on the patients, which is of great significance for the treatment of patients with infected urinary calculus.

SA is a safe and effective anesthesia method widely applied in clinical practice, which can not only be used for percutaneous nephrolithotomy, but also be used for the total hip replacement and cesarean section [9-11]. A study by Karabulut et al. [12] concluded that SA had similar effects to general anesthesia in patients with kidney calculi, and it alleviated more pain and cost less, indicating that SA was a more cost-effective anesthesia method. Dex is a pleiotropic α_2 adrenoceptor agonist, which not only has sedative, anxiolytic, and analgesic functions, but also causes minimal inhibitory effect on respiratory function [13]. One study revealed that Dex could inhibit the inflammatory reaction of calculi patients by lowering the concentration of inflammatory factors, thus lowering the risk of systemic inflammatory response syndrome after operation [14].

At present, there have been few studies on the effects of SA and Dex on patients with infected urinary calculus, so we studied the effects from the aspects of operation indicators, hemodynamics, serum cytokines, and postoperative complications, so as to provide clinical reference for the treatment of patients with infected urinary calculus.

Materials and methods

General materials

A total of 105 patients with infected urinary calculus admitted to Affiliated Cixi Hospital, Wenzhou Medical University from November 2016 to November 2019 were enrolled, of which 55 patients were treated with both SA and Dex before operation as a SD group, and the rest were treated with SA alone before operation as a SA group. The SD group consisted of 32 males and 23 females between 22 and 68 years old, with an average age of 45.57 ± 6.84 years, while the SA group consisted of 30 males and 20 females between 25 and 70 years old, with an average age of 46.20 ± 7.08 years. This study was approved by the Ethics Committee of Affiliated Cixi Hospital, Wenzhou Medical University, and the study subjects and their family members signed informed consent forms after understanding the study.

The inclusion criteria of the patients were as follows: Patients diagnosed with infected urinary calculus [15]; Patients who did not take drugs with possible influence on indicators of this study in the past 3 months; Patients receiving treatment for infected urinary calculus for the first time; Patients at I or II grade of anesthesia according to the American Society of Anesthesiologists (ASA) [16]; Patients who did not undergo surgery within the last six months.

The exclusion criteria of them were as follows: Patients comorbid with malignant tumor, severe dysfunction of heart, liver or lung; Patients with mental disease or unable to communicate normally; Patients who had a history of allergy to this medication or contraindications to SA.

The inclusion criteria were applicable to the two groups.

Anesthesia methods

Patients in the SA group were anesthetized with SA alone as follows: SA puncture was carried out to the third and fourth thoracic vertebral spaces of each patient, and a 25 gauge needle was punctured into the subarachnoid space to anesthetize the patient with 3 mL of 0.5% bupivacaine hydrochloride (T2524, Shanghai Harvest Pharmaceutical Co., Ltd., China).

In contrast, patients in the SD group were anesthetized with both SA and Dex as follows: Each patient was additionally anesthetized with 4 $\mu\text{g/mL}$ Dex (H20090248, Shanghai Jingke Chemical Technology Co., Ltd., China) through intravenous drip based on anesthesia measures to the SA group.

Outcome measures

The following items of the two groups were compared: Operation time, intraoperative blood loss, visual analog scale (VAS) score [17], hospitalization time, incidence of postoperative complications, mean arterial pressure (MAP) at different times points (T_0 : 10 min before operation; T_1 : at medication; T_2 : after 10 min of operation; T_3 : at the end of operation), heart rate (HR), arterial blood oxygen saturation (SPO_2), and procalcitonin (PCT), interleukin-1 (IL-1), and cystatin C (CysC) in the serum after operation. The PCT, IL-1, and CysC levels of

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Table 1. Baseline data of the two groups [n (%), mean \pm SD]

Factor	n	The SD group (n=55)	The SA group (n=50)	χ^2/t	P-value
Sex				0.036	0.850
Male	62	32 (58.18)	30 (60.00)		
Female	43	23 (41.82)	20 (40.00)		
Age (Y)				3.341	0.068
<45	49	21 (38.18)	28 (56.00)		
\geq 45	56	34 (61.82)	22 (44.00)		
Average age (Y)	105	45.57 \pm 6.84	46.20 \pm 7.08	0.464	0.644
Calculus type				2.318	0.509
Kidney calculi	38	23 (41.82)	15 (30.00)		
Urethral calculi	5	2 (3.64)	3 (6.00)		
Ureteral calculi	56	28 (50.91)	28 (56.00)		
Bladder calculi	6	2 (3.63)	4 (8.00)		
Multiple calculi				0.625	0.429
No	76	38 (69.09)	38 (76.00)		
Yes	29	17 (30.91)	12 (24.00)		
Pathogen				3.787	0.151
Gram-positive bacteria	33	13 (23.64)	20 (40.00)		
Gram-negative bacteria	65	37 (67.27)	28 (56.00)		
Fungi	7	5 (9.09)	2 (4.00)		
Hydronephrosis				0.064	0.800
No	37	20 (36.36)	17 (34.00)		
Yes	68	35 (63.64)	33 (66.00)		
Acute renal failure				0.664	0.415
No	87	44 (80.00)	43 (86.00)		
Yes	18	11 (20.00)	7 (14.00)		
Diabetes mellitus				1.468	0.226
No	83	46 (83.64)	37 (74.00)		
Yes	22	9 (16.36)	13 (26.00)		
Drinking history				1.376	0.241
No	71	40 (72.73)	31 (62.00)		
Yes	34	15 (27.27)	19 (38.00)		
Smoking history				0.347	0.556
No	77	39 (70.91)	38 (76.00)		
Yes	28	16 (29.09)	12 (24.00)		
Place of residence				0.252	0.615
Rural area	25	12 (21.82)	13 (26.00)		
Urban area	80	43 (78.18)	37 (74.00)		

Statistical analysis

In this study, enumeration data were expressed by the number of cases/percentage (n/%). Inter-group comparison in terms of enumeration data was carried out using the chi-square test. Data with theoretical frequency in chi-square test less than 5 were analyzed using the continuity correction chi square test. Measurement data were expressed by the mean \pm standard error of mean (mean \pm SEM), and inter-group comparison in terms of measurement data was carried out using the independent-samples T test. Indexes at different time points were analyzed by the repeated measurement variance, and expressed by F, and comparison within groups was carried out using the paired t test. The data were visualized into figures using GraphPad Prism 6 (GraphPad Software, San Diego, the United States), and logistics multivariate regression analysis was carried out using SPSS22.0 (Beijing EASYBIO Technology Co., Ltd., China) to analyze the risk factors for complications in patients with infected urinary calculus. $P < 0.05$ indicated a significant significance.

Results

Baseline data

There was no significant difference between the two groups in sex, age, average age, calculus type, multiple calculi, pathogen, hydronephrosis, acute renal failure, drinking history, smoking history, and place of residence (all $P > 0.05$). See **Table 1**.

the patients were determined using corresponding human PCT enzyme-linked immunosorbent assay (ELISA) kit, human IL-1 ELISA kit, and human CysC ELISA kit (XF-HUMAN-1451, XF-H10502, and XF-HUMAN-0575, Shanghai Xinfan Biological Technology Co., Ltd., China) in strict accordance with kit instructions, respectively [18].

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Table 2. Complications of the two groups [n (%)]

Item	The SD group (n=55)	The SA group (n=50)	χ^2 value	P-value
Systemic inflammatory response syndrome	5 (9.09)	10 (20.00)	-	-
Septicemia	3 (5.45)	4 (8.00)	-	-
Hematuria	1 (1.82)	2 (4.00)	-	-
Pyelonephritis	2 (3.64)	4 (8.00)	-	-
Total	12 (21.82)	20 (40.00)	4.086	0.043

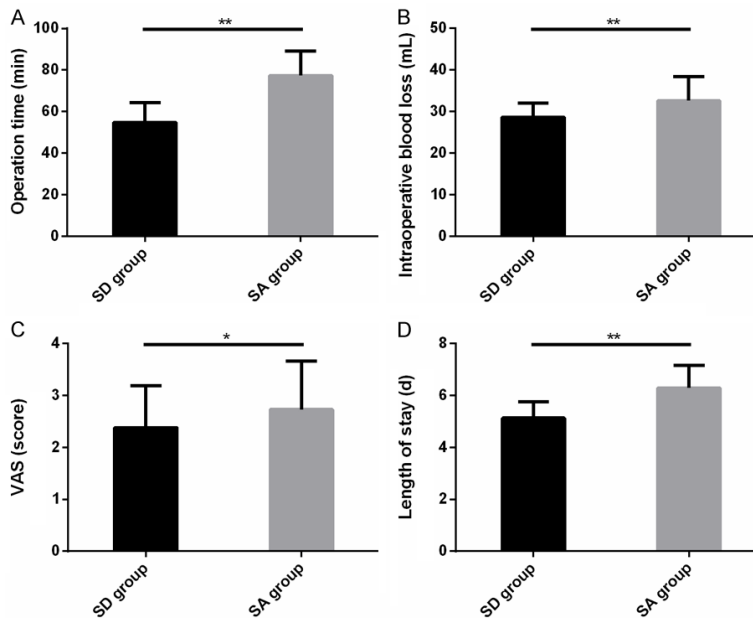


Figure 1. Clinical indicators of the two groups. A. The operation time of the SD group was significantly shorter than that of the SA group. B. The intraoperative blood loss of the SD group was significantly less than that of the SA group. C. The VAS score of the SD group was significantly lower than that of the SA group. D. The hospitalization time of the SD group was significantly shorter than that of the SA group. Note: ** indicates $P < 0.01$.

Complications of the two groups

The incidence of complications (systemic inflammatory response syndrome, septicemia, hematuria, pyelonephritis, etc.) in the SD group was significantly lower than that in the SA group (21.82% vs. 40.00%) ($P < 0.05$). See **Table 2**.

Clinical indicators of the two groups

The operation time, intraoperative blood loss, VAS score and hospitalization time of the SD group were dramatically lower than those of the SA group ($P < 0.05$). See **Figure 1**.

MAP, HR, and SPO_2 of the two groups at different time points

At T_0 , the two groups were not dramatically different in MAP, HR, and SPO_2 (all $P > 0.05$),

and at T_1 , T_2 , and T_3 , the trend of the MAP and HR of the two groups was consistent. The MAP of the two groups decreased significantly at T_1 and T_2 , respectively, followed by a slight increase at T_3 , and MAP and HR of the SD group were significantly lower than those of the SA group (both $P < 0.05$). In addition, the difference of SPO_2 between the two groups was not significant ($P > 0.05$). See **Figure 2**.

The levels of serum PCT, IL-1, and CysC of the two groups after operation

After operation, the PCT, IL-1, and CysC levels of the SD group were greatly lower than those of the SA group (all $P < 0.05$). See **Figure 3**.

Risk factors affecting postoperative complications of patients with infected urinary calculus

In order to compare the differences of clinical parameters and related indexes between patients with postoperative complications and those without postoperative complications, we assigned the 26 patients with postoperative complications into a complication group, and 79 patients without postoperative complications into a non-complication group. There was no significant difference between the complication group and the non-complication group in terms of sex, age, average age, calculus type, pathogen, hydronephrosis, acute renal failure, drinking history, smoking history, and place of residence (all $P > 0.05$), while there were significant differences between them in multiple calculi, diabetes mellitus, PCT, IL-1, CysC, and anesthesia method (all $P < 0.05$). Multivariate

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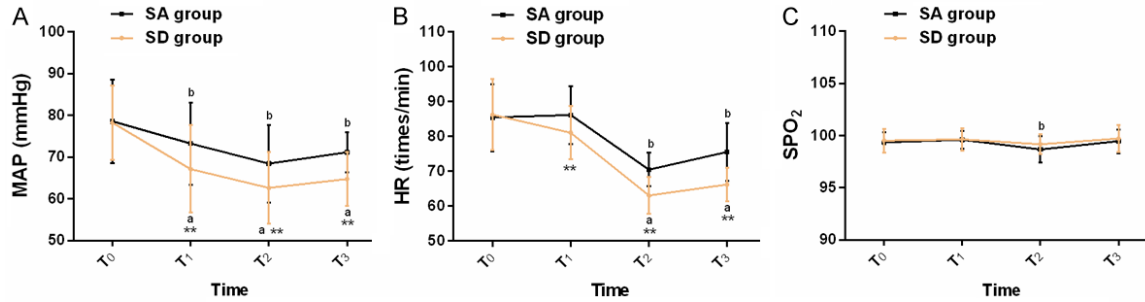


Figure 2. MAP, HR, and SPO₂ of the two groups at different time points. A. The MAP of the SD group was significantly lower than that of the SA group. B. The HR of the SD group was significantly lower than that of the SA group. C. There were no significant differences between the two groups in SPO₂. Note: * indicates that in comparison with the SA group, $P < 0.05$; ^a indicates that in terms of comparison between the indexes of the SD group at different time points and those at T₀, $P < 0.05$, and ^b indicates that in terms of comparison between the indexes of the SA group at different time points and those at T₀, $P < 0.05$.

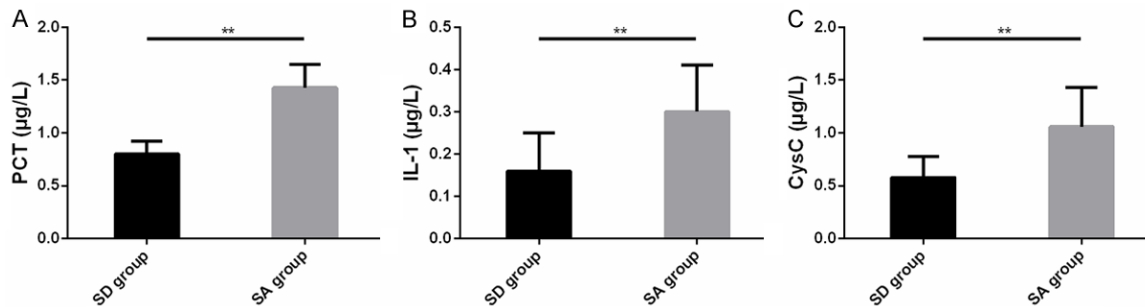


Figure 3. The levels of serum PCT, IL-1, and CysC of the two groups after operation. A. The serum PCT level of the SD group was dramatically lower than that of the SA group after operation. B. The serum IL-1 level of the SD group was dramatically lower than that of the SA group after operation. C. The serum CysC level of the SD group was dramatically lower than that of the SA group after operation. Note: ** indicates $P < 0.01$.

logistic regression analysis was carried out to analyze factors with differences, finding that multiple calculi ($P = 0.021$), diabetes mellitus ($P = 0.004$), PCT ($P = 0.007$), IL-1 ($P = 0.001$), CysC ($P = 0.014$), and anesthesia method ($P = 0.005$) were independent risk factors affecting complications in patients with infected urinary calculus. Infected urinary calculus patients with multiple calculi, diabetes mellitus, high PCT, IL-1, and CysC levels and treated with SA alone faced a higher risk of treatment failure. See **Tables 3-5**.

Discussion

Urinary calculi are mainly divided into kidney calculi, urethral calculi, ureteral calculi, and bladder calculi, and its formation mechanism is related to bacteria and cell processes induced by oxidative stress [19, 20]. According to statistical data, 1 in 11 American suffers from urinary calculi, and the annual medical

expenses for urinary calculi exceed 10 billion US dollars [21]. Accounting for 15% of all urinary calculi, infectious calculi are difficult to treat and show a relatively high recurrence [22]. SA has become a good choice for the treatment of urinary calculi, but there are few studies on its effects on patients with infected urinary calculus [23]. Therefore, it is of great value to study the effects of SA on patients with infected urinary calculus in lowering the incidence of infected urinary calculus and easing medical burden of patients.

There are a growing number of studies on the role of SA in the treatment of urinary calculi. For example, a study by Baran et al. [24] revealed that SA exerted excellent anesthesia effect as general anesthesia on percutaneous nephrolithotomy in patients with kidney calculi, and it contributed to a higher calculi-free rate and cost less operation time, which suggested that SA could be the best replacement of general

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Table 3. Univariate analysis of factors affecting complications in patients with infected urinary calculus [n (%), mean \pm SD]

Factor	n	The non-complication group (n=79)	The complication group (n=26)	χ^2/t	P-value
Sex				0.026	0.871
Male	62	47 (59.49)	15 (57.69)		
Female	43	32 (40.51)	11 (42.31)		
Age (Y)				0.154	0.695
<45	49	36 (45.57)	13 (50.00)		
\geq 45	56	43 (54.43)	13 (50.00)		
Average age (Y)	105	45.29 \pm 6.57	46.46 \pm 7.21	0.769	0.444
Calculus type				1.142	0.767
Kidney calculi	38	30 (37.97)	8 (30.77)		
Urethral calculi	5	3 (3.80)	2 (7.69)		
Ureteral calculi	56	42 (53.16)	14 (53.85)		
Bladder calculi	6	4 (5.07)	2 (7.69)		
Multiple calculi				15.056	<0.001
No	76	66 (83.54)	10 (38.46)		
Yes	29	13 (16.46)	16 (61.54)		
Pathogen				0.961	0.619
Gram-positive bacteria	33	23 (29.11)	10 (38.46)		
Gram-negative bacteria	65	51 (64.56)	14 (53.85)		
Fungi	7	5 (6.33)	2 (7.69)		
Hydronephrosis				0.757	0.384
No	37	26 (32.91)	11 (42.31)		
Yes	68	53 (67.09)	15 (57.69)		
Acute renal failure				0.106	0.745
No	87	66 (83.54)	21 (80.77)		
Yes	18	13 (16.46)	5 (19.23)		
Diabetes mellitus				17.605	<0.001
No	83	70 (88.61)	13 (50.00)		
Yes	22	9 (11.39)	13 (50.00)		
Drinking history				0.079	0.779
No	71	54 (68.35)	17 (65.38)		
Yes	34	25 (31.65)	9 (34.62)		
Smoking history				2.458	0.117
No	77	61 (77.22)	16 (61.54)		
Yes	28	18 (22.78)	10 (38.46)		
Place of residence				0.923	0.337
Rural area	25	17 (21.52)	8 (30.77)		
Urban area	80	62 (78.48)	18 (69.23)		
PCT (μ g/L)	105	0.63 \pm 0.11	1.20 \pm 0.19	18.830	<0.001
IL-1 (μ g/L)	105	0.12 \pm 0.08	0.25 \pm 0.12	6.295	<0.001
CysC (μ g/L)	105	0.44 \pm 0.17	0.91 \pm 0.31	9.776	<0.001
Anesthesia methods				11.897	<0.001
SD	55	49 (62.03)	6 (23.08)		
SA	50	30 (37.97)	20 (76.92)		

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Table 4. Assignment in logistic multivariate regression analysis

Factor	Variable	Assignment
Multiple calculi	X1	None =0, Yes =1
Diabetes mellitus	X2	None =0, Yes =1
PCT (µg/L)	X3	Continuous variable
IL-1 (µg/L)	X4	Continuous variable
CysC (µg/L)	X5	Continuous variable
Anesthesia methods	X6	SD=0, SA=1

Table 5. Multivariate logistic regression analysis of factors affecting complications in patients with infected urinary calculus

Variables	B	S.E	Wals	P-value	OR	95% CI
Multiple calculi	1.141	0.468	5.296	0.021	3.074	1.142-7.680
Diabetes mellitus	0.319	0.012	9.068	0.004	1.415	1.119-1.784
PCT (µg/L)	0.501	0.186	7.689	0.007	1.647	1.158-2.137
IL-1 (µg/L)	0.183	0.054	10.287	0.001	1.208	1.083-1.363
CysC (µg/L)	1.985	0.681	5.308	0.014	2.752	1.236-6.342
Anesthesia methods	2.108	0.753	6.732	0.005	5.928	1.534-10.571

anesthesia. One other study by Cicek et al. [25] revealed that compared with general anesthesia, SA contributed to a lower complication rate, which may be related to the fact that SA requires less analgesic. In this study, the operation time, intraoperative blood loss, and VAS score of the SD group were lower, which implied that SA combined with Dex can contribute to higher safety, milder pain, and faster recovery for patients with infected urinary calculus. We analyzed the hemodynamic parameters such as MAP, HR, and SPO₂ of the two groups, finding that there were no significant differences between them in SPO₂, while the SD group showed significantly lower MAP and HR than the SD group at all times, which implied that SA combined with Dex may be able to improve the hemodynamics of patients with infected urinary calculus. One study by Naithani et al. [26] has pointed out that SA combined with Dex has certain inhibitory effects on MAP and HR of patients and the mechanism is related to the inhibition of sympathetic outflow by intrathecal local anesthetic. We analyzed the serum PCT, IL-1, and CysC levels in the two groups. PCT is an infection-related biological indicator, and IL-1 is a cytokine reflecting the inflammation degree. CysC is an important renal function indicator [27]. Our studies showed that after operation, the serum PCT, IL-1, and CysC levels in the SD group were dramatically lower than those of the SA group, which implied that SA

combined with Dex was beneficial to alleviate infection, inflammatory response, and renal function damage of patients.

One study has shown that systemic inflammatory response syndrome and septicemia are common complications of patients with urinary calculi [28]. In this study, we found that patients with infected urinary calculus mainly suffered from complications such as systemic inflammatory response syndrome, septicemia, hematuria, and pyelonephritis, and the incidence of complications in the SD group was significantly lower than that in the SA group, which implied that the anesthesia with both SA and Dex may help reduce the incidence of postoperative complications in patients. A study by Tan et al. [29] reported that Dex was related to lower incidence of postoperative complications after percutaneous nephrolithotomy, and it could strongly reduce the incidence of systemic inflammatory response syndrome in the patients, which was similar to the results of our study. Finally, we analyzed the risk factors for postoperative complications in patients with infected urinary calculus, finding that patients with multiple calculi, diabetes mellitus, high PCT, IL-1, and CysC levels and treated with SA alone faced a higher risk of postoperative complications. A study by Yang et al. [30] concluded that patients with a larger calculus and urinary tract infection before operation faced a higher risk of postoperative complications, and a study by Rashid et al. [31] reported that the duration of operation, intraoperative bleeding, and postoperative hemoglobin level were all risk factors for postoperative septicemia in patients with kidney calculi.

To sum up, SA combined with Dex is superior to SA alone in the treatment of patients with infected urinary calculus. However, there is still a room for improvement in this study. We can supplement a comparative study on treatment methods for patients with infected urinary cal-

culus to explore the best treatment strategies for infected urinary calculus. Furthermore, we can also expand the research population to children and adolescents to improve the universality of research results. We will gradually supplement the research from the above aspects in the future.

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Disclosure of conflict of interest

None.

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