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Technical Note

Efficacy and safety of dexmedetomidine combined with sufentanil in ureteroscopic holmium laser lithotripsy

Danyang Wang and Tingting Zhao*

Shulan (Hangzhou) Hospital Affiliated to ZheJiang Shuren University, Shulan International Medical College (Anesthesiology)，Hangzhou 310000, China

* Corresponding author, e-mail: Tingting.zhao@shulan.com

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Abstract: The efficacy and safety of combining dexmedetomidine with sufentanil for patients undergoing ureteroscopic holmium laser lithotripsy was investigated. A total of 90 consecutive patients who underwent this procedure were retrospectively selected. These patients were categorised into two groups based on their chosen anesthesia method: dexmedetomidine combined with sufentanil under non-intubated anesthesia group (DEX+SUF group) and the conventional intubated general anesthesia group (control group). Several parameters including efficacy, adverse effects, hemodynamics, inflammatory factors and variations in T lymphocytes were compared between the two groups. Patients in the DEX+SUF group exhibited notable advantages over those in the control group. They experienced significantly reduced operation time, awakening time, hospital stay, time to first feeding, time to ambulation, catheter-related bladder discomfort score, as well as lower incidences of hypotension, arrhythmia, gastrointestinal symptoms, impaired consciousness, and chills. The DEX+SUF group displayed greater stability in heart rate, mean arterial pressure and oxygen saturation at the mentioned time points compared to the control group. Regarding inflammatory factors, post-treatment levels of interleukin-6 (IL-6), tumour necrosis factor-alpha (TNF-a), interferon-gamma (IFN-γ), cluster of differentiation 3 (CD3+), cluster of differentiation 4 (CD4+) and cluster of differentiation 8 (CD8+) in the DEX+SUF group were elevated compared to their pre-treatment levels. Furthermore, post-treatment IL-6, TNF-a and IFN-γ levels in the DEX+SUF group were significantly lower than those in the control group, while CD3+, CD4+ and CD8+ levels were significantly higher in the DEX+SUF group than in the control group. The combination of dexmedetomidine and sufentanil in ureteroscopic holmium laser lithotripsy significantly enhanced the hemodynamic stability of patients and reduced complications associated with anesthesia. This approach offers notable efficacy and safety while having a minimal impact on body inflammation and immune function.

Keywords: ureteroscopic holmium laser lithotripsy, dexmedetomidine, sufentanil

Maejo Int. J. Sci. Technol. **2024**, *18*(02), 123-129

INTRODUCTION

Ureteroscopic holmium laser lithotripsy is a minimally invasive surgical technique widely employed for the removal of stones from the urinary tract. It involves the integration of a holmium laser with a ureteroscope to efficiently disintegrate and extract kidney or ureter stones. This approach has gained prominence due to its minimal invasiveness and high success rates. However, the choice of anesthesia plays a crucial role in determining patient comfort and overall outcomes. Traditionally, two main approaches to anesthesia have been employed: general anesthesia with endotracheal intubation and regional anesthesia with epidural techniques. While general anesthesia ensures patient immobility and comfort throughout the procedure, it comes with the drawback of potential complications including those associated with intubation, ventilation and the need for muscle relaxants. On the other hand, regional anesthesia techniques such as epidural anesthesia can avoid some of these complications but may be associated with higher intraoperative and postoperative complication rates, as well as reduced patient satisfaction [1,2].

Recent research has explored alternative anesthesia strategies to improve patient outcomes and minimise complications associated with traditional approaches. One such strategy involves the use of dexmedetomidine, an alpha-2 adrenergic agonist known for its sedative and analgesic properties. Dexmedetomidine offers the advantage of preserving spontaneous respiration, making it a potentially valuable choice for procedures like ureteroscopic holmium laser lithotripsy [3, 4]. In addition to dexmedetomidine, sufentanil, a synthetic opioid, has gained recognition for its rapid onset and short duration of action, making it suitable for achieving effective analgesia during medical procedures. When combined with dexmedetomidine, sufentanil may provide a balanced anesthetic approach, offering both sedation and pain relief while minimising the risk of significant respiratory depression.

Despite extensive research, the safety and efficacy of combining dexmedetomidine and sufentanil for ureteroscopic holmium laser lithotripsy remain to be determined. This study aims to conduct a retrospective analysis of patient outcomes when undergoing this procedure under either conventional intubated general anesthesia or the dexmedetomidine-sufentanil combination. The investigation seeks to evaluate the potential advantages and disadvantages of employing dexmedetomidine and sufentanil in this specific context by comparing six key parameters: operation time, awakening time, hospital stay, adverse effects, hemodynamic stability, inflammatory factors and T lymphocyte variations. The research endeavour holds promise of yielding valuable insights into the optimisation of anesthesia protocols for ureteroscopic holmium laser lithotripsy, the enhancement of patient outcomes, and the potential expansion of minimally invasive surgical techniques in the field of urology.

MATERIALS AND METHODS

General Data

Ninety consecutive patients who underwent ureteroscopic holmium laser lithotripsy, diagnosed from January 2019 to January 2022, were retrospectively selected as study subjects with the following criteria:

1) Ureteral stones were diagnosed by transrenal ureteral ultrasonography.
2) Patients were newly diagnosed with no previous history of ureteral stone treatment.
3) Patients had no severe cardiopulmonary disease, no obvious contraindications to surgery and anesthesia, and no contraindications to the use of laryngeal mask.
4) Patients and family members consented to this study and signed informed consent.

5) Patients with coagulopathy, severe renal dysfunction, ureteral tumours and drug addiction under anesthesia were excluded.

Patients were divided into 2 groups, viz. those treated with dexmedetomidine combined with sufentanil under non-intubated anesthesia (DEX+SUF group) and those treated with conventional intubated general anesthesia according to their anesthesia method (control group). The general data of patients in the DEX+SUF group and control group are shown in Table 1. They were comparable in terms of gender, age, body mass index, hydronephrosis at the ureteral stone site, stone diameter and number, and American Society of Anesthesiologists grade, with no significant differences (all $P > 0.05$).

Table 1. Comparison of baseline clinical data of patients between DEX+SUF group and control group

Group	No. of cases (n)	Gender (M/F)	Age (years)	Body mass index (kg/m^2)	Location of ureteral stones (upper/middle/lower segment)	Hydronephrosis (with/without)	Stone diameter (cm)	No. of stones (single/multiple)	ASA* grade (I/II)
DEX+SUF group	50	29/21	48.5±7.2	24.1±3.7	12/20/18	39/11	0.8±0.4	22/28	30/20
Control group	40	22/18	48.3±7.5	23.9±3.5	10/22/18	34/7	0.9±0.5	18/22	26/14
P value		>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05	>0.05

*American Society of Anesthesiologists

Methods of Treatment

Patients in the DEX+SUF group received dexmedetomidine combined with sufentanil under non-intubated anesthesia. They were equipped with a routine indwelling urinary catheter to establish intravenous fluid access and facilitate rehydration. Additionally, they were provided with a face mask for oxygen delivery while undergoing electrocardiogram monitoring, which included the continuous assessment of blood pressure, heart rate, oxygen saturation and other vital signs. The sufentanil used in this group was reconstituted with normal saline to achieve a concentration of 1 μg/ml, while dexmedetomidine was reconstituted with normal saline to reach a concentration of 4 μg/ml. An intravenous pump was initiated 10 min. prior to the operation, administering fluids at a rate of 1.2 ml/(kg·h). After the initial 10 min. the pump rate was adjusted to 0.3 ml/(kg·h) and continued throughout the procedure, with close monitoring of the patient's level of vigilance and sedation, assessed using the observer's assessment of alertness/sedation score, aiming to maintain a score of ≥3 points. Two min. before the placement of the ureteroscope, a 30-mg IV dose of propofol was administered. Ureteroscopic holmium laser lithotripsy commenced when the patient achieved an observer's assessment of alertness/sedation score of ≥4, indicating an appropriate level of sedation and absence of significant pain sensation during endoscopy.

Intraoperatively, atropine or ephedrine was administered as needed based on the patient's blood pressure and heart rate. In cases where necessary an oropharyngeal access airway or emergency intubation was performed to ensure the patient's safety and adequate airway management. Patients in the control group underwent a different anesthesia regimen. They received a standard indwelling urinary catheter and were subjected to general anesthesia with endotracheal intubation. This anesthesia induction involved an intravenous infusion of midazolam at a dose of 0.05 mg/kg, sufentanil at 0.5 μg/kg, atracurium cisbesylate at 0.15 mg/kg, and propofol at 1 mg/kg. Following induction, tracheal intubation was performed to establish controlled ventilation with a tidal volume set at 810 ml/kg. Anesthesia maintenance during the surgery involved the administration of propofol, a remifentanil pump and inhalation of sevoflurane.

Maejo Int. J. Sci. Technol. **2024**, *18*(02), 123-129

Observation Indicators and Methods

The following indicators were examined in patients of both groups:

1) Hemodynamics including heart rate, mean arterial pressure (MAP) and oxygen saturation (SpO_2) ; examined after admission (T0), after administration of a loading dose of anesthetic drugs (T1), during the endoscope operation (T2), during holmium laser lithotripsy (T3), after the end of surgery (T4), and on awakening (T5)

2) Efficacy; operation time, awakening time, hospital stay, time of first feeding, and time of ambulation

3) Adverse effects; hypotension, arrhythmia, gastrointestinal symptoms, impaired consciousness and chill

4) Catheter related bladder irritation sign (CRBD) scoring; evaluated as per He et al. [5]

Inflammatory Factors and T Lymphocytes

Inflammatory factors and T lymphocytes were analysed before and after treatment of patients in the DEX+SUF group and control group. Peripheral venous blood (20 ml) was obtained in the morning after 8 h of fasting. Ten ml was used to detect T lymph node cells, i.e. cluster of differentiation 3 (CD3+), cluster of differentiation 4 (CD4+) and cluster of differentiation 8 (CD8+) T lymphocytes, by flow cytometry. The rest was centrifuged at 3000 r/min. for 10 min., and the serum was collected for the detection of inflammatory cytokines, i.e. interleukin-6 (IL-6), tumour necrosis factor-alpha (TNF-a) and interferon-gamma (IFN-γ), by enzyme-linked immunosorbent assay [6].

Statistical Analysis

Statistical analysis was performed using SPSS 22.0. The measurement data between the DEX+SUF group and control group were analysed by t-test; the $\chi 2$ test was used for counting data. Differences were considered statistically significant at $P < 0.05$.

Ethics Statements

The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

The study was approved by the Medical Ethics Committee of Shulan International Medical College, ZheJian Shuren University (Approval No. ZS-EC202305016).

RESULTS

Comparison of Efficacy and CRBD Scores and Adverse Effects

Patients in the DEX+SUF group had significantly lower operative time, awakening time, hospital stay, time of first feeding, time of ambulation, CRBD score, hypotension, arrhythmia, gastrointestinal symptoms, impaired consciousness, and chill than those in the control group, all of which were statistically significant (all $P < 0.05$) (Tables 2 and 3)**.**

Hemodynamic Comparison

There were no significant differences in the heart rate, MAP and SpO2 at time points T0, T1, T2, T3, T4 and T5 of patients in DEX+SUF group. The differences in the heart rate, MAP and SpO2 at time points T0, T1, T2, T3, T4 and T5 in the control group were significant. The stability of the heart rate, MAP and SpO2 at time points T0, T1, T2, T3, T4 and T5 were higher in the DEX+SUF group than in the control group (Table 4).

Maejo Int. J. Sci. Technol. **2024**, *18*(02), 123-129

Table 2. Comparison of efficacy and CRBD scores between patients of DEX+SUF group and control group ($\bar{x} \pm s$)

Group	Operation time (h)	Awakening time (min.)	Hospital stay (d)	Time of first feeding (h)	Time of ambulation (h)	CRBD scoring
DEX+SUF group	0.9±0.3	9.7±1.8	4.8±1.1	25.3±3.4	1.5±0.5	0.7±0.2
Control group	1.2±0.4	13.6±2.4	6.5±1.3	30.1±3.6	2.2±0.8	1.1±0.4
t value	4.065	8.807	6.719	6.483	5.075	6.177
P value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

Table 3. Comparison of adverse effects between patients of DEX+SUF group and control group

Group	Hypotension	Arrhythmia	Gastrointestinal symptom	Disturbance of consciousness	Chill
DEX+SUF group	4（8.0%）	3（6.0%）	6（12.0%）	4（8.0%）	5（10.0%）
Control group	11（27.5%）	10（25.0%）	15（37.5%）	12（30.0%）	15（37.5%）
$\chi 2$ value	4.761	5.045	6.715	5.930	8.197
P value	0.029	0.025	0.010	0.015	0.004

Table 4. Comparison of hemodynamics between patients of DEX+SUF group and control group ($\bar{x} \pm s$)

Index	Group	T0	T1	T2	T3	T4	T5
Heart rate (beats/min.)	DEX+SUF group	77.5±6.7	76.8±6.3*	76.5±6.8*	76.3±6.5	77.2±6.9*	76.8±7.1
	Control group	77.4±6.9	72.3±6.1	71.7±6.2	77.3±6.5	70.4±6.1	75.2±6.3
MAP（mmHg）	DEX+SUF group	84.3±8.1	82.9±7.8	82.7±8.3	82.5±7.7	83.1±7.9	82.8±7.6*
	Control group	84.1±8.4	80.1±7.5	88.1±7.8	85.1±7.7	80.2±7.6	89.9±8.4
SpO_2（%）	DEX+SUF group	98.4±1.2	98.2±1.5*	98.1±1.4	98.3±1.2*	98.5±1.3*	98.2±1.4*
	Control group	98.3±1.4	97.1±1.1	98.3±1.2	97.6±1.1	96.9±1.5	97.4±1.3

*P<0.05, compared between DEX+SUF group and control group

Comparison of Inflammatory Cytokines and T Lymphocytes

No statistically significant differences were found for pretreatment values of IL-6, TNF-a, IFN-γ, CD3+, CD4+ and CD8+ in patients of the DEX+SUF group and control group (all $P > 0.05$). However, they were elevated in the DEX+SUF group after treatment compared with pretreatment. Posttreatment values of IL-6, TNF-a and IFN-γ in the DEX+SUF group were significantly lower than those in the control group and CD3+, CD4+ and CD8+ were significantly higher than those in the control group (all $P < 0.05$) (Table 5).

Table 5. Comparison of pre- and post-treatment inflammatory cytokines and T lymphocytes between patients in DEX+SUF group and control group ($\bar{x} \pm s$)

Group	IL-6 (pg/L)		TNF- a (pg/L)		IFN- γ (pg/L)		CD3+(%)		CD3+(%)		CD8+(%)	
	Before treat-ment	After treat-ment	Before treat-ment	After treat-ment	Before treat-ment	After treat-ment	Before treat-ment	After treat-ment	Before treat-ment	After treat-ment	Before treat-ment	After treat-ment
DEX+ SUF group	6.1 ±0.8	9.3 ±1.1	10.4 ±1.7	13.6 ±1.9	4.8 ±1.1	7.3 ±1.2	53.6 ±2.5	59.1 ±3.2	32.9 ±2.2	35.4 ±2.3	17.8 ±1.2	19.7 ±1.5
Control group	6.2 ±0.9	11.2 ±1.5	10.2 ±1.8	16.2 ±2.1	4.9 ±1.1	9.9 ±1.4	53.5 ±2.7	55.3 ±2.8	32.8 ±2.4	34.2 ±2.1	17.6 ±1.3	18.7 ±1.2

Maejo Int. J. Sci. Technol. **2024**, *18*(02), 123-129

DISCUSSION

In this study dexmedetomidine combined with sufentanil and laryngeal mask were applied to ureteroscopic holmium laser lithotripsy, with the operation time, awakening time, hospital stay, time of first feeding, time of ambulation, CRBD score, hypotension, arrhythmia, gastrointestinal symptoms, disturbance of consciousness and chill being all significantly lower than those obtained from conventional general anesthesia with endotracheal intubation. This confirms the efficacy and safety of dexmedetomidine compounded with sufentanil and combined with laryngeal mask in ureteroscopic holmium laser lithotripsy.

CRBD is one of the most common and severe complications after urological surgery affecting patients' experience, and the patients' symptoms of urethral irritation can significantly increase the rate of intraoperative and postoperative complications, so it is of great significance if the incidence of CRBD can be reduced, thus improving the quality of survival of patients undergoing urological surgery [7, 8]. Studies have found that dexmedetomidine significantly reduces the incidence of CRBD. Xiong [9] found that dexmedetomidine at 0.4 μg/kg intravesically instilled through a urinary tube 30 min. before the operation was more effective in preventing postoperative CRBD in patients undergoing middle and upper abdominal surgery under general anesthesia than the doses of 0.2 μg/kg and 0.6 μg/kg, thereby significantly relieving postoperative urethral pain without significant complications. Li et al.[10] found that 10 min. before induction of general anesthesia, giving 1μg/kg dexmedetomidine significantly reduced the incidence of CRBD after transurethral resection of the prostate. In the present study patients of the DEX+SUF group had significantly lower postoperative CRBD scores than the control group, indicating that dexmedetomidine combined with sufentanil could significantly reduce the incidence of CRBD complications after ureteroscopic holmium laser lithotripsy.

In addition it was found that no statistically significant differences were found in pretreatment value of IL-6, TNF-a, IFN-γ, $CD3^+$, $CD4^+$ and $CD8^+$ in patients of the DEX+SUF group and control group (all $P > 0.05$). These parameters in the DEX+SUF group after treatment were elevated. Posttreatment values of IL-6, TNF-a and IFN-γ in the DEX+SUF group were significantly lower than those in control group but $CD3^+$, $CD4^+$ and $CD8^+$ were significantly higher, suggesting that dexmedetomidine combined with sufentanil during ureteroscopic holmium laser lithotripsy has less effect on the body's inflammatory response and T-lymphocyte immunity. This may be related to the fact that dexmedetomidine combined with sufentanil causes small trauma to the whole body. All this evidence suggests the efficacy and safety of dexmedetomidine combined with sufentanil in ureteroscopic holmium laser lithotripsy.

CONCLUSIONS

The administration of dexmedetomidine combined with sufentanil during ureteroscopic holmium laser lithotripsy represents a promising approach that offers substantial benefits. This anesthesia method significantly enhances the hemodynamic stability of patients while concurrently reducing the occurrence of anesthesia-related complications. Its key advantages include its high efficacy, safety profile and minimal impact on systemic inflammation and immune function. These findings underscore the potential for wider adoption of this technique in clinical practice. However, it is crucial to acknowledge certain limitations of this study. Firstly, it was a single-centred study with a relatively small sample size. While the results are encouraging, further validation through large-scale multicentred studies is warranted to confirm the generalisability and robustness of these

findings. Additionally, long-term follow-up studies may provide insights into the extended benefits and safety of this anesthesia approach. Despite these limitations, the evidence presented in this study serves as a foundation for the potential transformation of anesthesia protocols in ureteroscopic holmium laser lithotripsy.

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