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Original Article

Protocolized sedation with dexmedetomidine in percutaneous nephrolithotomy: a randomized, controlled clinical trial

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Abstract: This study investigated the efficacy and safety of protocolized sedation with dexmedetomidine (Dex) in percutaneous nephrolithotomy (PCNL). Sixty patients with American Society of Anesthesiologists status I or II scheduled for PCNL under epidural anesthesia were randomly allocated to three groups. The patients in group D1 (n=20) received 0.5 μg/kg Dex, those in group D2 (n=20) received 0.75 μg/kg Dex, and those in the control group (n=20) received normal saline. The mean arterial pressure (MAP), heart rate, arterial oxygen saturation (SpO_2), body temperature, and observer's assessment of alertness/sedation (OAA/S) scale score were recorded intraoperatively, and perioperative adverse reactions were also assessed. The MAP and SpO_2 did not significantly differ among the three groups (P>0.05). The heart rate was significantly lower in groups D1 and D2 than in the control group. Groups D1 and D2 had significantly lower body temperatures, OAA/S scale scores, and intraoperative shivering rates than the control group (P<0.05). Sedation with Dex has good efficacy in PCNL under epidural anesthesia. Dex can effectively prevent perioperative shivering and elicits low respiratory inhibition. Additionally, 0.5 μg/kg Dex may be superior to 0.75 μg/kg Dex in reducing the incidence and severity of bradycardia.

Keywords: Nephrolithotomy, percutaneous, dexmedetomidine, clinical protocols, conscious sedation

Introduction

Percutaneous nephrolithotomy (PCNL) is a minimally invasive procedure used for the treatment of kidney stones [1]. During this procedure, the patient needs to change from the supine to the lithotomy position, and then to the prone position. Intrathecal anesthesia is preferred for PCNL because the patients can remain conscious and voluntarily change their position. However, patients under intrathecal anesthesia often experience intraoperative nervousness and anxiety, which may result in undesirable outcomes.

Protocolized sedation is intended to decrease intraoperative discomfort, inhibit sympathetic overactivity, and produce anterograde amnesia [2-6]. The aim of protocolized sedation in patients undergoing PCNL is to maintain an observer's assessment of alertness/sedation (OAA/S) scale score of 2-4 and to allow for easy awakening of the patient for position changing. Dexmedetomidine (Dex) is a highly selective α2 adrenergic receptor agonist that elicits sedation and analgesia, stabilizes the hemodynamics, and has an anti-shivering and diuretic effect, while inducing little respiratory depression [7]. Due to the importance of airway management in surgeries performed in the prone position and the potent respiratory depression effect of most sedatives, Dex has become a promising candidate for protocolized sedation in PCNL.

The present study aimed to compare the vital signs and complications among patients undergoing PCNL with protocolized sedation with different doses of Dex or normal saline.

Material and methods

Patients

Sixty patients were treated with PCNL for kidney stones under continuous epidural anesthe-

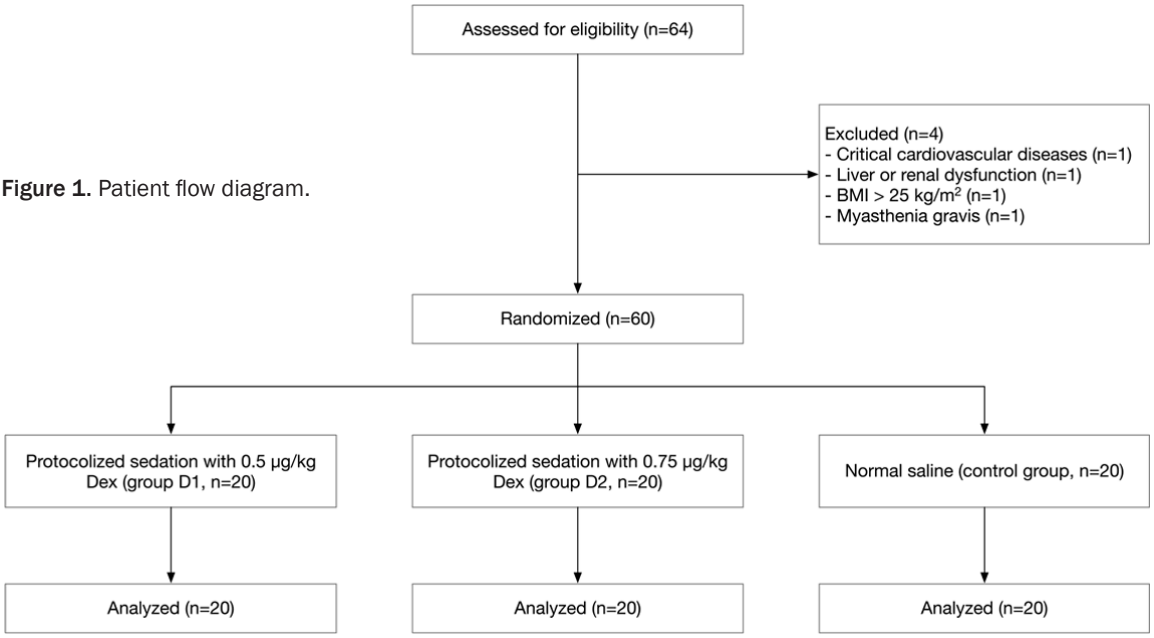

Figure 1. Patient flow diagram.

sia at The First Affiliated Hospital of Wenzhou Medical University between July and September 2014. They were randomly allocated to three groups. The patients in group D1 (n=20) received 0.5 μg/kg Dex, those in group D2 (n=20) received 0.75 μg/kg Dex, and those in the control group (n=20) received normal saline (**Figure 1**). The study was approved by the Institutional Review Board, and informed consent was obtained from each patient.

The inclusion criteria were as follows: (1) American Society of Anesthesiologists status I or II, and (2) Age of 18-65 years. Patients with the following conditions were excluded: critical cardiovascular diseases, liver or renal dysfunction, body mass index (BMI) >25 kg/m^2, allergy to Dex, myasthenia gravis, acute alcohol toxicity, brain damage, or respiratory insufficiency.

Anesthetic protocol

All PCNL procedures were performed under continuous epidural anesthesia administered by the same anesthetist. The patients underwent a 12-hour food fast and a 6-hour liquid fast prior to the surgery. Oxygen was administered via a nasal catheter at a flow rate of 3 L/min. Loading doses of Dex were administered to the patients in group D1 (0.5 μg/kg) and group D2 (0.75 μg/kg) over a period of 15 minutes. Dex was then administered at 0.5 μg/kg/h until the end of the surgery. The patients in the control group were administered normal saline instead of Dex. Epidural anesthesia (1% lidocaine + 0.375% ropivacaine [7-10 mL]) was administered to all patients at the T12-L1 or L1-L2 level. The level of anesthesia was controlled below T6. Atropine was administered if the heart rate was <50 bpm. Ephedrine was administered if the systolic blood pressure (SBP) was <90 mmHg or in the event of a >20% reduction in the SBP. The operating room temperature was 23°C. After the epidural anesthesia, 500 mL of a colloid fluid was infused, followed by a crystalloid fluid at 42°C.

Patient assessment

The mean arterial pressure (MAP), heart rate, arterial oxygen saturation (SpO_2), body temperature, and OAA/S scale score [8] were recorded at the following time points: before surgery (T0), after the loading dose of Dex or normal saline (T1), 20 minutes after epidural anesthesia administration (T2), before changing to the prone position (T3), immediately after changing to the prone position (T4), 10 minutes after changing to the prone position (T5), 20 minutes after changing to the prone position (T6), immediately after surgery (T7), and 2 hours after surgery (T8). Shivering was examined during surgery, 2 hours after surgery, and 24 hours after surgery. Intraoperative adverse reactions were assessed using the Iowa Satisfaction with Anesthesia Scale [9].

Table 1. Patients' general information

	D1 group (n=20)	D2 group (n=20)	Control group (n=20)
Gender (male/female)	8/12	10/10	7/13
Age, years	49.90±9.04	51.70±11.89	53.65±8.02
BMI	21.68±2.03	22.57±2.27	22.57±2.06
Anesthetics volume, mL	14.70±3.34	13.45±2.72	14.70±2.68
Operation time, min	67.00±26.97	70.00±24.71	65.50±28.92
Irrigation time, min	38.25±15.33	49.00±22.40	45.25±24.30
Irrigation fluid volume, mL	17700.00±11466.66	18200.00±11091.01	13475.00±9818.72
Infusion fluid volume, mL	660.00±211.26	790.00±214.97	755.00±369.17

Statistical analysis

Continuous data are presented as mean ± standard deviation and compared using a one-way ANOVA or Student's t-test. Categorical data are presented as frequencies and compared using a Chi-square test. All statistical analyses were performed using SPSS 17.0 (SPSS, Chicago, USA). $P<0.05$ was considered statistically significant.

Results

There was no significant difference in the sex, age, BMI, anesthetic volume, operative time, irrigation time, irrigation fluid volume, or fluid volume among the three groups (**Table 1**).

The MAP at T0 did not significantly differ among the three groups ($P>0.05$). In all three groups, the MAP was significantly decreased at time points T1-T8 compared to that at T0 ($P<0.05$). However, there were no significant differences in the MAP among the three groups at all time points, except at T1 (**Table 2**).

The heart rate at T0 did not significantly differ among the three groups ($P>0.05$). In groups D1 and D2, the heart rate was significantly lower at time points T1-T8 than at T0 ($P<0.05$). A heart rate reduction was not observed in the control group. The heart rate in groups D1 and D2 was significantly lower than that in the control group at time points T1-T8 ($P<0.05$). There were no significant differences in the heart rate among groups D1 and D2, except at T6 (**Table 3**).

The SpO_2 at T0 did not significantly differ among the three groups ($P>0.05$), and it did not change significantly in any group at time points T1-T8 compared to that at T0 ($P>0.05$). The SpO_2 at T2 and T4 in group D2 was significantly lower than that in the control group ($P<0.05$). There were no significant differences in the SpO_2 among groups D1 and D2, except at T2 ($P<0.05$) (**Table 4**).

The three groups exhibited no significant difference in body temperature at T0 ($P>0.05$). Groups D1 and D2 had significantly lower body temperature at T7 and T8 than the control group ($P<0.05$) (**Table 5**).

Groups D1 and D2 had significantly lower OAA/S scale scores at time points T1-T3 and T5-T6 than the control group ($P<0.05$) (**Table 6**).

Seventeen patients in the control group experienced intraoperative shivering, compared to one patient in group D1 and four patients in group D2. The postoperative shivering rate did not significantly differ among the three groups (**Table 7**).

The number of patients who reported feeling "cold", "hot", or "itchy" was significantly higher in the control group than in groups D1 and D2. A significantly higher number of patients in group D1 than in the control group stated that they would like to use the same anesthesia mode again (**Table 8**).

Discussion

Dex can be used as a sedative and analgesic, and induces little respiratory inhibition. Patients under Dex sedation can be easily awoken and can return to sleep promptly if needed [10]. Dex at 10-fold the regular dose has no significant effect on the patients' blood oxygen saturation [11]. A clinical trial involving 326 patients found that Dex was associated with a significantly lower incidence of severe respiratory depression (breathing rate <8 breaths per min or SpO_2 <90%) than that of midazolam and fentanyl [12]. The findings are consistent with those of previous studies. The patients in groups D1 and D2 had OAA/S scale scores of 2-4 and

Table 2. Intraoperative mean arterial pressure (mmHg)

	T0	T1	T2	T3	T4	T5	T6	T7	T8
Control group (n=20)	107.35±14.92	104.90±9.50	95.80±13.15	98.10±11.97	93.70±13.34	92.30±14.57	92.35±13.32	95.90±12.65	95.50±10.35
D1 group (n=20)	100.65±13.01	94.40±12.67*	90.65±11.18	83.95±30.12	93.95±9.62	92.90±10.18	91.05±9.42	92.20±14.64	89.00±11.30
D2 group (n=20)	109.05±15.44	97.75±13.57	88.45±13.92	87.70±15.44	87.70±15.44	89.35±16.20	90.55±12.56	91.95±13.64	89.35±16.07

*P<0.05, vs the control group.

Table 3. Intraoperative heart rate (bpm)

	T0	T1	T2	T3	T4	T5	T6	T7	T8
Control group (n=20)	80.75±15.19	80.45±9.92	75.50±11.45	77.05±9.28	80.50±15.37	75.05±11.97	75.05±10.26	77.75±12.30	82.55±19.25
D1 group (n=20)	76.95±14.27	64.85±10.30*	63.75±7.81*	66.00±11.21*	66.75±10.64*	61.20±6.80*	59.40±8.13*,#	61.45±5.75*	61.55±6.27*
D2 group (n=20)	84.90±12.16	71.90±13.78*	66.40±13.09*	68.85±10.72	71.50±15.08*	67.00±13.01	66.55±11.80*	67.50±12.90*	69.40±10.77*

*P<0.05, vs the control group; #P<0.05, vs the D2 group.

Table 4. Intraoperative SpO_2 (%)

	T0	T1	T2	T3	T4	T5	T6	T7	T8
Control group (n=20)	97.35±2.03	97.80±1.74	98.05±1.64	97.70±2.00	98.05±1.70	98.15±1.31	98.05±1.64	98.20±1.44	98.00±4.32
D1 group (n=20)	97.70±1.17	97.00±1.56	97.65±1.42#	97.55±1.19	97.65±1.27	97.70±1.72	97.50±1.76	99.05±0.89	98.45±0.89
D2 group (n=20)	97.45±1.61	96.55±1.50	96.25±1.50*	96.85±1.90	96.70±1.81*	97.35±1.63	97.60±1.79	98.45±1.54	98.35±1.23

*P<0.05, vs the control group; #P<0.05, vs the D2 group.

Table 5. Intraoperative body temperature (°C)

	T0	T1	T2	T3	T4	T5	T6	T7	T8
Control group (n=20)	37.08±0.28	37.04±0.28	36.83±0.31	36.78±0.37	36.75±0.39	36.64±0.40	36.49±0.45	36.32±0.69	37.31±1.13
D1 group (n=20)	36.99±0.39	36.87±0.37	36.70±0.36	36.69±0.39	36.66±0.40	36.78±0.38	36.27±0.49	35.88±0.50*	36.09±0.45*
D2 group (n=20)	36.98±0.42	36.92±0.45	36.79±0.44	36.79±0.47	36.77±0.46	36.59±0.46	36.28±0.52	35.95±0.51*	36.38±0.44*

*P<0.05, vs the control group.

Table 6. Intraoperative OAA/S scale scores

	T0	T1	T2	T3	T4	T5	T6	T7	T8
Control group (n=20)	5.00±0.00	5.00±0.00	5.00±0.00	5.00±0.00	5.00±0.00	5.00±0.00	5.00±0.00	5.00±0.00	5.00±0.00
D1 group (n=20)	5.00±0.00	4.10±0.85*	3.90±0.64*,#	4.10±0.79*	4.95±0.22	3.85±0.93*	3.65±1.04*	4.95±0.22	5.00±0.00
D2 group (n=20)	5.00±0.00	3.95±0.69*	2.95±1.19*	3.55±1.15*	4.75±1.12	3.40±1.10*	3.10±1.21*	4.75±0.64	5.00±0.00

*P<0.05, vs the control group; #P<0.05, vs the D2 group.

Table 7. Intraoperative and postoperative shivering

	Intraoperative shivering	Postoperative 2-h shivering	Postoperative 24-h shivering
Control group (n=20)	17	4	0
D1 group (n=20)	1*	3	1
D2 group (n=20)	4*	2	0

*$P<0.05$, vs the control group.

Table 8. Intraoperative adverse reactions [n, (%)]

	Sinus bradycardia	Hypotension	Nausea/vomiting	Feeling cold-hot-itchy	Uncomfortable position	Willing to use the same anesthesia mode
Control group (n=20)	1 (5)	5 (25)	4 (20)	14 (70)	4 (20)	14 (70)
D1 group (n=20)	2 (10)	2 (10)	1 (5)	1* (5)	1 (5)	20* (100)
D2 group (n=20)	4 (20)	5 (25)	2 (10)	5* (25)	6 (30)	17 (85)

*$P<0.05$, vs the control group.

experienced satisfactory sedation. None of our patients exhibited signs of respiratory depression. Despite the small SpO_2 reduction at T2 and T4 in the sedated patients, the SpO_2 values were >96%.

Epidural anesthesia can suppress the sympathetic nervous system, leading to peripheral vasodilation. The patients in all three groups exhibited decreased blood pressure. Dex has also been demonstrated to elicit effects of sympathetic inhibition and vasodilation [13]. Conversely, our sedated patients did not exhibit significantly lower blood pressure than those in the control group. It can be speculated that this may be associated with the rapid blood volume expansion in our patients; 500 mL of colloid fluid were rapidly administered before the anesthesia, which likely compensated for the blood pressure drop caused by vasodilation.

Dex can bind to the α2 adrenergic receptors in the central and peripheral nervous systems, which causes an anti-sympathetic effect and decreases the heart rate [14]. Sinus bradycardia is a common adverse reaction to Dex, and its incidence can be as high as 25% [15]. The heart rate in the sedated patients in the study was lower than that in the control group patients. Bradycardia occurred in two patients in group D1, and in four patients in group D2. One patient in the D2 group had severe bradycardia with a heart rate that was temporarily <30 bpm. Prompt administration of atropine raised the heart rate in this patient.

Shivering is a common complication of epidural anesthesia with an incidence as high as 26-74% [16-19]. This can be worsened by continuous irrigation with large volumes of cold fluid during PCNL. Despite being a protective mechanism, shivering is uncomfortable for the patients and may disrupt surgical manipulation and vital sign monitoring. Dex may lower the temperature threshold for shivering in the peripheral vessels and the central nervous system, and thus prevent shivering [20]. Another study demonstrated that Dex accelerates the inflow of potassium ions and hyperpolarizes neurons, leading to decreased nerve conduction velocity and decreased sensitivity to cold [21]. This study found that 17 patients (85%) in the control group experienced shivering, which was a significantly higher number than that among the sedated patients. The body temperature was also significantly lower in the sedated patients than in those of the control group, suggesting that Dex lowered the temperature threshold for shivering.

In conclusion, sedation with 0.5 or 0.75 μg/kg Dex has good efficacy in patients undergoing PCNL under epidural anesthesia. Dex can effectively prevent perioperative shivering and induces little respiratory inhibition. Additionally, 0.5 μg/kg Dex may be superior to 0.75 μg/kg Dex in reducing the incidence and severity of bradycardia.

Disclosure of conflict of interest

None.

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