

Dexmedetomidine intravesical instillation reduces postoperative catheter-related bladder discomfort in male patients under general anesthesia: a randomized controlled study

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Research article

Keywords: dexmedetomidine; intravesical instillation; catheter-related bladder discomfort; general anesthesia

Posted Date: July 14th, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-39598/v1>

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Version of Record: A version of this preprint was published on October 22nd, 2020. See the published version at <https://doi.org/10.1186/s12871-020-01189-2>.

Abstract

Background The catheter-related bladder discomfort (CRBD) of male patients is a common clinical problem, albeit lacking effective solutions. The present study aimed to investigate whether dexmedetomidine intravesical instillation alleviates the postoperative urinary discomfort in male patients with catheter under general anesthesia.

Methods This single-blinded, prospective, randomized study included a total of 167 male patients American Society of Anesthesiologists (ASA) physical status I-II scheduled for surgery under general anesthesia were allocated to two groups: 84 in the dexmedetomidine (Dex) group and 83 in the control group. Dex group patients received intravesical instillation of the drug 0.5 µg/kg and normal saline 20 mL, while the control group received intravesical instillation of 20 mL normal saline. The catheter was clamped for 30 min after intravesical instillation for all patients. Bladder stimulation scales and urethra pain numerical rating scale (NRS) scores were measured at admittance to post-anesthesia care unit (PACU) (T0), intravesical instillation (T1), 30 min (T2), 60 min (T3), 2 h (T4) after intravesical instillation, discharged from PACU (T5), and 6 h (T6) and 24 h (T7) after the operation. Patient satisfaction at discharge from PACU and 24 h post-operation were compared between the two groups.

Results Bladder stimulation scales and urethra pain NRS scores after 30 min of dexmedetomidine intravesical instillation to 24 h post-operation were significantly lower than the control group ($p < 0.001$), and patient satisfaction was higher at discharge from PACU and 24 h post-operation ($p < 0.001$). No differences were detected in Steward score out of PACU ($p = 0.213$) and from the time of the end of operation to fully awake ($p = 0.417$).

Conclusion Dex intravesical instillation reduces postoperative urinary discomfort and urethra pain and improves satisfaction in male patients under general anesthesia.

Clinical Trial Registration: Chinese Clinical Trial Registry (No. ChiCTR1800016429), date of registration 1st June 2018

Background

Catheter-related bladder discomfort (CRBD) after the operation is a common adverse reaction; however, many surgery patients need an indwelling catheter during or after the operation. The incidence of CRBD is 47–90%[1, 2], and catheter maladjustment is common, especially in male patients[3, 4]. Reportedly, 27–55% of the patients experience moderate or severe catheter-related bladder discomfort symptoms in the post-anesthesia care unit (PACU)[3, 5]. CRBD leads to restlessness, delirium, decreased satisfaction, and a rise in postoperative complications, such as incision rupture, bleeding, hemodynamic instability, the severity of coronary heart disease.[1] Thus, how to relieve postoperative CRBD, reduce the incidence of related complications, improve patient satisfaction, and shorten the time of anesthesia recovery observation has become needs to be resolved urgently in clinical practice[6–9].

Dexmedetomidine (Dex) is a type of high selective adrenergic α -2 receptor agonist, which has the effects of sedation, analgesia, and anti-anxiety. Several studies have confirmed that Dex can reduce the incidence of postoperative agitation and delirium[10–14]. Moreover, Dex might reduce bladder contractility via α -2 receptor agonism, M3 muscarinic receptor antagonism[15–17], and the incidence and severity of catheter-related bladder discomfort after general anesthesia[16, 18–21]. These studies were based on the intravenous administration of Dex, which increases the risk of arrhythmia.[22]

A large number of studies[23–25] showed that intravesical instillation is an effective way of drug administration, which exerts an obvious effect on the treatment of bladder-related diseases. Concurrently, the intravesical instillation of drugs can reduce the systemic response. However, whether Dex can be used by intravesical instillation to reduce CRBD and improve the tolerance to indwelling catheter has not yet been reported. Thus, the present study aimed to investigate whether Dex intravesical instillation can alleviate the postoperative urinary discomfort in male patients with general anesthesia.

Methods

Study design

This single-center, blinded, prospective, randomized study was approved by the Institutional Review Board and Hospital Research Ethics Committee of the Second Affiliated Hospital of Anhui Medical University [No. PJ-YX2018-004 (F2)]. The protocol of the study was registered in the Chinese Clinical Trial Registry (No. ChiCTR1800016429) and executed in accordance with the CONSORT checklist. Each patient provided written informed consent before participation in the study. Patients can withdraw from the study at any time according to their wishes. All patients were enrolled between June 2018 and April 2019. The inclusion criteria were as follows: male patients aged 18–70 years and American Society of Anesthesiologists (ASA) physical status II undergoing elective surgery, scheduled general anesthesia, and intraoperative catheter insertion. The exclusion criteria were as follows: urology patients, end-stage renal disease, pathological obesity, central nervous system dysfunction, chronic pain, cerebral infarction, mental disorder of consciousness, change in surgical and anesthesia plans, without CRBD when admitted to PACU.

Sample Size

PASS 11.0 software was used to compare the mean of two independent samples. According to the pre-experiment CRBD score, the mean value of the control group was 2.25, and the standard deviation was 0.66. The mean value of the Dex group was 1.9 and the standard deviation was 0.67. Set α as 0.05, power as 0.1, using bilateral test, the sample size of each group is 75. Increase the sample size 20% to prevent the sample drop-out, so we chose 90 patients in each group.

Patient Randomization

Male patients with CRBD into PACU were randomly divided into two groups with an allocation ratio of 1:1 according to the computerized randomization table in a blinded manner. Random numbers to each patient while the nurses collected postoperative data from the patients.

Anesthesia Application

The surgery and anesthesia program of the patient was similar to that of the other patients. Electrocardiography (ECG), peripheral oxygen saturation (SpO₂), non-invasive blood pressure (NBP), and respiratory rate (RR) were monitored routinely after the patients were admitted to the operating room. The vein channel was established with a 22-gauge indwelling needle. Oxygen was inhaled by mask (oxygen flow rate was 4–5 L/min). Midazolam 0.025 mg/kg, sufentanil 2–4 µg/kg, etomidate 1–2 mg/kg, and rocuronium 0.9 mg/kg were injected intravenously for anesthesia induction. After intubation, a 16F ureteral catheter was used for catheterization, followed by anesthesia maintenance propofol 2–4 mg/kg/h, remifentanil 10–20 µg/kg/h, and continued addition of cisatracurium to maintain muscle relaxation. At the end of the operation, the muscle relaxation and consciousness of the patient were restored, the tracheal tube was removed and sent to PACU for observation.

Interventions

In the Dex group, 0.5 µg/kg Dex was solubilized in 20 mL normal saline infused from the ureteral catheter to bladder for Dex intravesical instillation. In the control group, 20 mL of normal saline was infused from the ureteral catheter to the bladder. After instillation, the ureteral catheter was clipped for 30 min and then unclipped.

Assessments

The primary outcome endpoint was CRBD grade, and the second outcome endpoint was urethra pain NRS score and patient's satisfaction. The duration of anesthesia, the time length of operation, the time from the end of the operation to full consciousness, and patient characteristics were recorded. Mean arterial pressure (MAP), heart rate (HR), RR, SpO₂, CRBD grade, and urethra pain NRS score were recorded when the patient was sent to PACU (T0), the time of intravesical instillation with Dex or normal saline (T1), 30 min after intravesical instillation (T2), 1 h after intravesical instillation (T3), 2 h after intravesical instillation (T4), the time point of leaving PACU (T5), 6 h after operation (T6), and 24 h after operation (T7). The NRS score of urethra pain and the complications after intravesical instillation were also recorded. The patient satisfaction score were recorded when leaving PACU and 24 h after the operation. The NRS score was used for the assessment of urethra pain in both groups. CRBD grade: grade 0, patients have no discomfort at all; grade 1, patients have slight discomfort, only when asked to show discomfort; grade 2, patients have moderate discomfort, frequency of urination, the urgency of urination, feeling of lower abdominal distension, which is not easy to bear; grade; 3, the patient had severe

discomfort, intolerable distension, urethral pain, frequent urination with strong restlessness, and needed to be removed. Ramsay score: 1 point, the patient is restless and fidgety; 2 points, the patient is quiet and cooperative; 3 points, the patient is sleepy and can follow the instructions; 4 points, the patient is in a sleep state and can wake up; 5 points, the respiratory response of the patient is slow; 6 points, the patient is deep asleep and has no response to stimulation. Patient satisfaction score is consisting of integers from 1 point to 5 points: 1 point means dissatisfied and 5 points mean very satisfied. The urethra pain NRS scores consists of integers from 0–10 points; 0 point means no urethra pain, and 10 points indicate intense urethra pain. Subsequently, the patients selected an integer to describe the intensity of their urethra pain while using a ureteral catheter.

Statistical analysis

SPSS software (version 22.0, Chicago, USA) and were used for statistical analysis. The age, weight, blood, and other measurement data of patients were presented as mean \pm standard deviation. The ASA classification data were expressed as counts. Student's *t*-test or the Mann-Whitney U test was used for continuous variables, such as age and weight. The χ^2 or Fisher's exact tests were assessed for categorical variables, such as ASA grade and patient satisfaction score. ANOVA was used for the comparison of MAP, HR, SpO₂, and other data at different time points. *p*-value < 0.05 was accepted as statistically significant.

Results

Study demographics

A total of 279 male patients were screened in this study, of which, 109 did not meet the inclusion criteria; among them, 102 did not present CRBD, 5 refused to participate in the study, and 2 were excluded for other reasons. A total of 180 male patients with CRBD were randomly and equally divided into both groups when into PACU. Six cases in the Dex group and 7 cases in the control group did not complete the experiment. None of the patients were lost follow-up. Finally, 84 patients in the Dex group and 83 patients in the control group were included in the analysis (Fig. 1). A total of 279 patients were enrolled in PACU, including 180 patients with CRBD, and 96 patients were excluded from this study due to the absence of CRBD. The incidence of CRBD was 64.5%.

No significant difference was detected between the two groups in age, weight, ASA grade, duration of operation, duration of anesthesia, Steward's score when leaving PACU, the time length of operation end to fully awake, catheter removal time (Table 1) and type of operation. There was no significant difference was observed in HR, RR, MAP, and SpO₂ in the two groups from T0 to T7 (Table 2), as well as no complications, occurred in either of the groups.

Table 1
Descriptive variables of the group control and group Dex.

	Group Control(n = 83)	Group Dex(n = 84)	p-value
Age (year)	51.2 ± 13.2	54.7 ± 12.5	0.076
Weight (kg)	68.1 ± 10.5	68.3 ± 11.1	0.919
ASA grade (I/II)	7 / 76	9 / 75	0.617
Time length of operation (min)	146.6 ± 70.8	160.2 ± 62.7	0.193
Time length of anesthesia (min)	175.2 ± 72.2	190.2 ± 67.6	0.122
Steward score out of PACU	5.98 ± 0.15	5.95 ± 0.21	0.213
Time length of operation end to fully awake (min)	13.6 ± 6.5	14.9 ± 7.3	0.417
Ureteral catheter removal time (6–12 h / 12–24 h / more than 24 h after operation)	12 / 46 / 25	9 / 38 / 37	0.173
Operation type (general surgery / thoracic surgery / orthopedics / otolaryngology / stomatology / plastic surgery)	33/14/31/5/0/0	31/20/23/7/1/2	0.343
Values are presented as mean (standard deviation) or counts.			
Dex: dexmedetomidine, ASA: American society of anesthesiologists.			

Table 2
Patients vital signs of group Dex (n = 84) and group Control (n = 83) at different time points.

	group	T0	T1	T2	T3	T4	T5	T6	T7
HR	Group Control	76.6 ± 15.4	75.9 ± 15.0	77.4 ± 14.7	79.0 ± 14.0	80.1 ± 14.3	80.9 ± 14.2	80.2 ± 12.4	79.7 ± 12.5
	Group Dex	75.6 ± 15.2	75.4 ± 15.1	75.8 ± 14.5	77.8 ± 13.9	79.1 ± 14.3	79.1 ± 14.1	78.7 ± 11.0	79.7 ± 12.5
RR	Group Control	18.8 ± 1.1	18.8 ± 1.1	18.9 ± 1.3	19.2 ± 1.0	19.1 ± 1.0	19.1 ± 0.9	19.1 ± 0.9	18.9 ± 0.9
	Group Dex	18.8 ± 1.5	18.7 ± 1.2	18.5 ± 1.2	18.5 ± 1.4	18.7 ± 1.1	19.0 ± 1.0	18.7 ± 0.8	18.8 ± 0.8
MAP	Group Control	98.9 ± 16.1	97.9 ± 14.4	97.8 ± 14.5	97.3 ± 14.4	95.6 ± 14.4	94.3 ± 12.7	91.4 ± 11.5	89.6 ± 10.5
	Group Dex	98.4 ± 15.2	97.7 ± 15.5	95.4 ± 14.3	94.8 ± 14.2	94.1 ± 12.8	92.8 ± 12.3	91.5 ± 10.6	89.6 ± 8.6
SPO ₂	Group Control	98.7 ± 1.1	98.9 ± 1.2	98.6 ± 1.3	98.7 ± 1.2	98.7 ± 1.1	98.6 ± 1.2	98.3 ± 1.0	98.3 ± 0.7
	Group Dex	98.7 ± 1.8	98.9 ± 1.4	98.8 ± 1.4	98.8 ± 1.4	98.8 ± 1.1	98.8 ± 1.1	98.4 ± 0.9	98.3 ± 0.7
Values are presented as mean (standard deviation)									
MAP, mean arterial pressure; HR, heart rate; RR, respiratory rate; SpO ₂ , pulse oximetry; group Dex, dexmedetomidine group. Time course, the time point of the patient sent to PACU (T0), intravesical instillation (T1), 30 minutes after intravesical instillation (T2); 1 hour after intravesical instillation (T3), 2 hour after intravesical instillation (T4), leaving PACU (T5), 6 hours after the operation (T6), 24 hours after the operation (T7).									

Crbd And Urethra Pain Nrs Scores

Compared to the control group, the CRBD in the Dex group was significantly improved at T3, T4, T5, T6, and T7 ($p < 0.05$) (Fig. 2A), while the urethra pain NRS scores of patients was significantly decreased ($p < 0.05$) (Fig. 2B).

Patient's Satisfaction

Compared to the control group, the patient's satisfaction in the Dex group in PACU (Fig. 3A) and 24 h post-operation (Fig. 3B) increased significantly ($p < 0.001$).

Discussion

In the present study, we observed that 0.5 µg/kg Dexmedetomidine intravesical instillation can significantly reduce the symptoms of postoperative catheter-related bladder discomfort and the urethral pain caused by catheter in male patients who received general anesthesia, and consequently, their satisfaction was improved. The improvement of these symptoms can sustain from 0.5–24 h after Dex intravesical instillation.

CRBD is common in PACU, especially male patients[26]. Therefore, in this study, we included male patients as the study subject, and the incidence of CRBD was 64.5%, which was consistent with that reported previously[1, 2, 26]. The high incidence of CRBD in male patients might be related to the anatomical characteristics, such as the long urethra and large catheter[26]. Because several urological operations need to operate on the urethra, which markedly impacts this study, and the degree of impact is different, so this study was not included in the urological patients.

In this study, we observed that Dex intravesical instillation can significantly reduce the symptoms of postoperative CRBD according to the following underlying mechanism. Alpha 2-adrenoceptor, i.e., the α_{2A}-subtype, is expressed in the bladder, urethra, and prostate. The intra-arterial administration of an α₂ agonist reduced the micturition pressure, bladder capacity, and micturition volume[27, 28]. Dex is a high selective adrenergic α₂ receptor agonist which may reduce the micturition pressure, bladder capacity, and micturition volume. There are several muscarinic receptors in bladder epithelium and efferent nerves, including M₂ and M₃. The M₃ receptor is mainly responsible for bladder contraction[29]. The catheter can stimulate the afferent nerves of the bladder to release acetylcholine, which leads to the contraction of detrusor mediated by muscarinic receptors. Therefore, muscarinic antagonists alleviate CRBD in different degrees.[1] Some studies showed that Dex might reduce bladder contractility via α₂ receptor and M₃ muscarinic receptor antagonism.[16, 17] On the other hand, catheter stimulation can cause inflammation and increase prostaglandin secretion, which is one of the plausible reasons for CRBD.[30] Therefore, some anti-inflammatory drugs can also alleviate CRBD. Another study showed that Dex reduces the release of prostaglandins of inflammation, and hence, relieves CRBD[31]. In addition, Dex exerts a sedative effect and relieves CRBD[10].

In the current study, Dex plays a role in intravesical instillation. Several studies[23–25] showed that intravesical instillation is an effective way of administration of drugs, which had an obvious effect on the treatment of bladder-related diseases and reduce the systemic response. Dex is well absorbed through the mucous membrane. Iriola *et al.*[32] reported that peak plasma concentrations of Dex were 38 min after intranasal administration, and the pharmacological effects were similar to the intravenous administration but with a later onset time. In the current study, Dex was able to work through the bladder mucosa, with a significant effect at half an hour after administration.

In this study, Dex intravesical instillation alleviates the pain caused by catheter while in situ and on removal. The main causes of the pain during catheter in situ were as follows: the material and size of the catheter, the traction of the catheter drainage bag, the urethral discomfort, the stimulation of the bladder wall by the catheter, the obstruction of the catheter, catheter blockage, the hemorrhagic pseudopolyps, the

fear of the catheter, and the psychological rejection.[33] In the present study, all patients were observed and nursed closely, and the material and size of the catheter were identical, and no catheter drainage bag traction, catheter obstruction, hemorrhagic pseudopolyps were observed. Therefore, we speculated that the main reason for the difference in the urethral pain between the two groups was the tolerance of catheter stimulation of the bladder wall and the difference in the fear and psychological rejection of the catheter. Dex is a solution to bladder irritation and psychological maladjustment of patients, thereby reducing the catheter-induced urethral pain.

Patients' satisfaction at the time point out of PACU and 24 h after the operation was significantly improved after Dex intravesical instillation because there were reductions in CRBD and catheter-induced urethral pain and patient satisfaction is closely related to the postoperative outcomes[34]. The improvement in the patients' satisfaction might reduce their CRBD and urethral pain.

No complications were detected in the control and experimental groups. Since the sample size of this study is small, and the patients selected are ASA I-II, their basic conditions are well. Clinically, we will encounter CRBD to aggravate the condition of patients with coronary heart disease, and Dex might also lead to arrhythmia and other risks.

Nevertheless, the present study has some limitations. The number of cases is small as only 167 patients were included in this single-center study. In the future, large sample and multi-center clinical verification is essential. The patients included in this study were male patients with catheter placement under general anesthesia. The type of operation is not uniform, and the duration of operation is varied. Further subgroup study can be carried out after expanding the sample size in the future. All the patients included in this study were ASA I-II patients with elective surgery, and the basic condition of the patients was good. Also, critical patients have not been analyzed previously. Moreover, the effect of different doses of Dex on CRBD was not assessed in this study.

Conclusions

Dex 0.5 µg/kg intravesical instillation reduces postoperative urinary discomfort and urethra pain caused by catheter in male patients under general anesthesia and improves patient satisfaction after the operation.

Abbreviations

CRBD catheter-related bladder discomfort

ASA American Society of Anesthesiologists

Dex dexmedetomidine

NRS numerical rating scale

PACU post-anesthesia care unit

ECG electrocardiography

SpO₂ peripheral oxygen saturation

NBP non-invasive blood pressure

RR respiratory rate

MAP mean arterial pressure

HR heart rate

Declarations

Ethics approval and consent to participate:

This study was approved by the Institutional Review Board and Hospital Research Ethics Committee of the Second Affiliated Hospital of Anhui Medical University [No. PJ-YX2018-004 (F2)]. Each patient provided written informed consent before participation in the study.

Consent for publication:

Not applicable.

Availability of data and materials

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

Competing interests:

The authors declare that they have no competing interests.

Funding

This study was supported by the Department of Science and Technology of Anhui Province, Hefei, China (No. 201904a07020065).

Authors' contributions:

Study design: HC, BW, RL, YZ. Study conduct: HC, QL, JZ. Data analysis: HC, BW, RL, YZ. Writing paper: HC, BW, QL, JZ, RL, YZ. All authors read and approved the final manuscript.

Acknowledgements:

We thank our colleagues at the Department of Anesthesiology and Perioperative Medicine, The Second Affiliated Hospital of Anhui Medical University for their help with the samples. In addition, we thank the patients who participated in this study.

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Figures

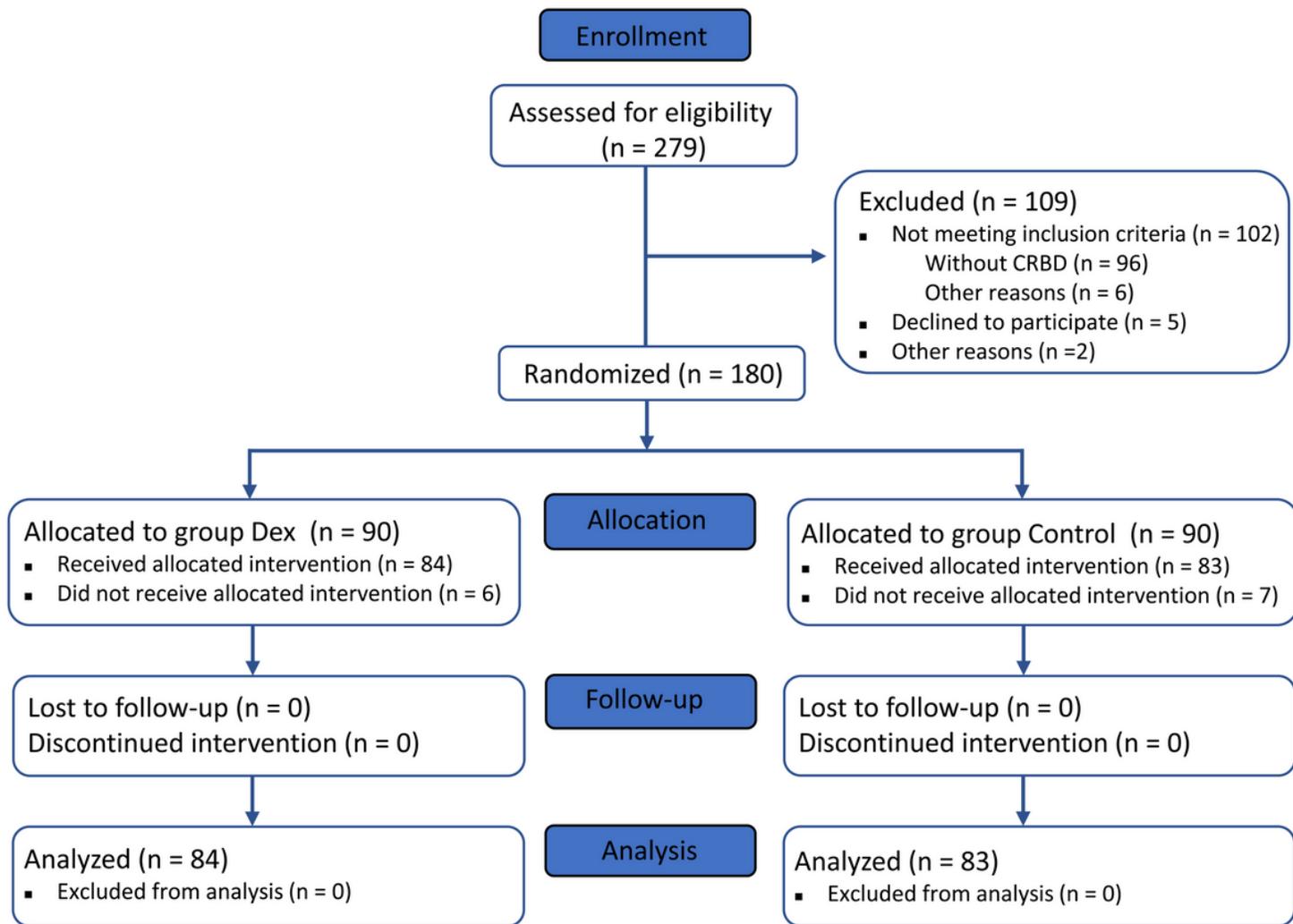


Figure 1

Schematic of the study with a CONSORT diagram. CRBD, catheter-related bladder discomfort; group Dex, dexmedetomidine group.

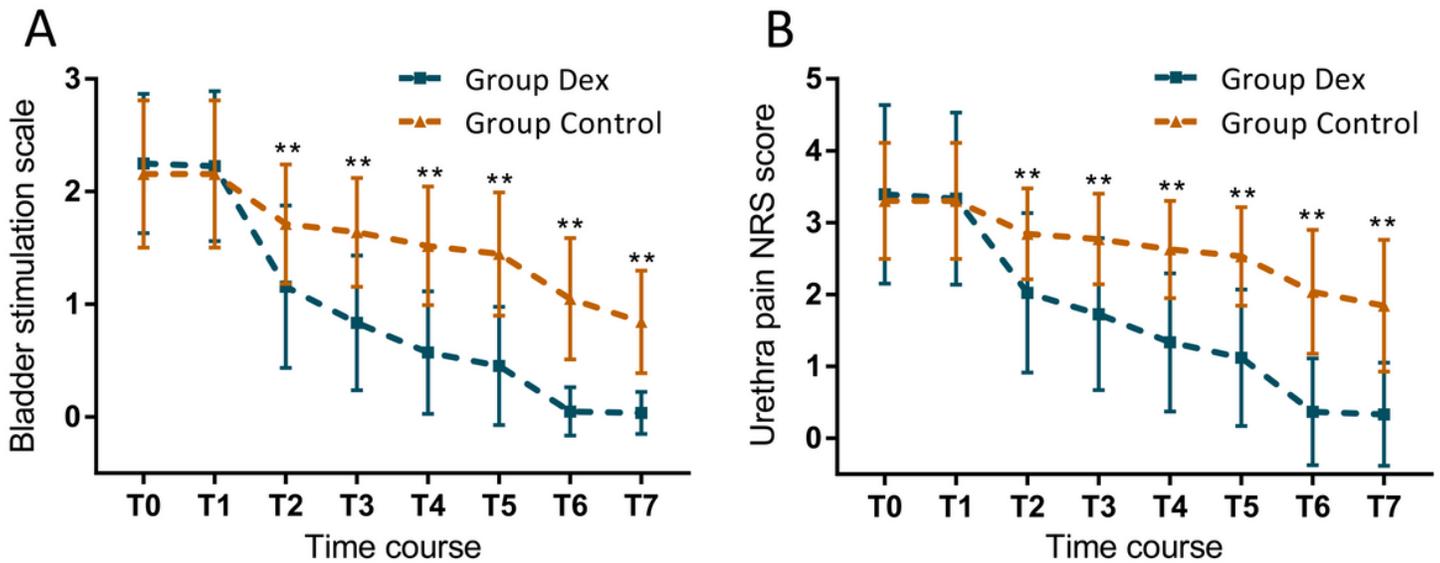


Figure 2

Bladder stimulation scale (Fig. 2A) and urethra pain NRS score (Fig. 2B) in Dex and control groups at various time points. CRBD, catheter-related bladder discomfort; group Dex, dexmedetomidine group. Time course, the time point at which the patient sent to PACU (T0), intravesical instillation (T1), 30 min after intravesical instillation (T2); 1 h after intravesical instillation (T3), 2 h after intravesical instillation (T4), leaving PACU (T5), 6 h after operation (T6), 24 h after operation (T7); ** $p < 0.05$.

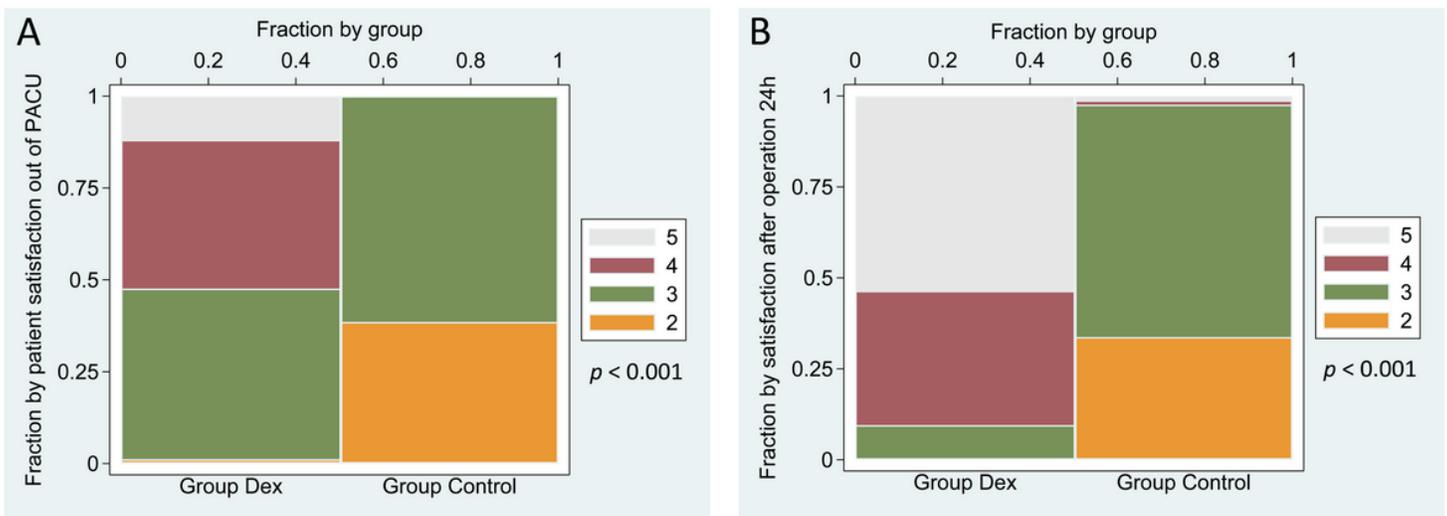


Figure 3

Spine plot of patient satisfaction score out of PACU (Fig. 3A) and 24 h after the operation (Fig. 3B) in Dex and control groups. Patient satisfaction score: 5 points, very satisfied; 4 points, satisfied; 3 points, relatively satisfied; 2 points, basically satisfied; 1 point, dissatisfied.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [CONSORT2010Checklist.doc](#)