Intravenous Lidocaine for the Prevention of Postoperative Catheter-Related Bladder Discomfort in Male Patients Undergoing Transurethral Resection of Bladder Tumors: A Randomized, Double-Blind, Controlled Trial

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BACKGROUND: Male patients undergoing transurethral resection of bladder tumors (TURBT) are prone to suffer from catheter-related bladder discomfort (CRBD). Lidocaine administration has been widely performed to reduce postoperative pain. Here, the effect of intravenous lidocaine administration on moderate-to-severe CRBD was evaluated in male patients undergoing TURBT. **METHODS:** Patients were randomly allocated to receive intravenous lidocaine (1.5 mg/kg bolus dose followed by a 2 mg/kg/h continuous infusion during the intraoperative period, which was continued for 1 hour postsurgery; group L) or placebo (normal saline; group C). The primary outcome was moderate-to-severe CRBD at 0 hour postsurgery (on admission to the postanesthetic care unit), analyzed using the χ^2 test. The secondary outcome was opioid requirement during the 24-hour postoperative period. None, mild, and moderate-to-severe CRBD at 1, 2, and 6 hours postsurgery, postoperative pain, patient satisfaction, side effects of lidocaine and rescue medications (tramadol and fentanyl), and surgical complications were also assessed.

RESULTS: A total of 132 patients were included in the study (66 patients in each group). The incidence of moderate-to-severe CRBD at 0 hour postsurgery was significantly lower in group L than in group C (25.8% vs 66.7%, P < .001, relative risk: 0.386, 95% confidence interval: 0.248–0.602). Opioid requirements during the 24-hour postoperative period were significantly lower in group L than in group C (10.0 mg [interquartile range (IQR), 5.0–15.0 mg] vs 13.8 mg [IQR, 10.0–20.0 mg], P = .005). At 1 and 2 hours postsurgery (but not at 6 hours), the incidence of moderate-to-severe CRBD was significantly lower in group L than in group C (1 hour: 10.6% vs 27.3%, P = .026; 2 hours: 0.0% vs 15.2%, P = .003). Patient satisfaction was significantly greater in group L than in group C (5.0 [IQR, 4.8–6.0] vs 4.0 [IQR, 4.0–5.0], P < .001). No lidocaine-related side effects were reported. Rescue medication-related side effects and surgical complications did not differ significantly between the 2 groups.

CONCLUSIONS: Intravenous lidocaine administration resulted in lower incidence of moderateto-severe CRBD, lower opioid requirement, and higher patient satisfaction in male patients undergoing TURBT without evidence of significant side effects. (Anesth Analg XXX;XXX:00–00)

KEY POINTS

- Question: Does intravenous lidocaine reduce postoperative catheter-related bladder discomfort (CRBD) in male patients undergoing transurethral resection of bladder tumors (TURBT)?
- **Findings:** Intravenous lidocaine administration during the intraoperative period and 1-hour postoperative period resulted in lower incidence of moderate-to-severe CRBD, lower opioid requirement, and higher patient satisfaction without evidence of significant side effects.
- Meaning: Intravenous lidocaine administration may be an effective approach to reduce the incidence of moderate-to-severe CRBD in male patients undergoing TURBT.

GLOSSARY

BIS = bispectral index; **CI** = confidence interval; **CONSORT** = Consolidated Standards of Reporting Trials; **CRBD** = catheter-related bladder discomfort; **GPES** = global perceived effects on a 7-point scale; **IQR** = interquartile range; **LM** = laryngeal mask; **NRS** = numeric rating scale; **NSAID** = nonsteroidal anti-inflammatory drugs; **PACU** = postanesthetic care unit; **RR** = relative risk; **TOF** = trainof-four; **TURBT** = transurethral resection of bladder tumors

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atheter-related bladder discomfort (CRBD) is defined as the urge to void or a burning sensation in the suprapubic area.¹ Mild CRBD is experienced by >80% of patients in the postanesthetic care unit (PACU) who have undergone intraoperative urinary catheterization, although it is tolerable in most patients.^{2,3} However, moderate-to-severe CRBD is experienced in 27%-55% of patients with urinary catheterization and can be distressing, requiring additional analgesic therapy.²⁻⁴ CRBD is strongly associated with the use of large diameter urinary catheters, male patients, and transurethral resection of bladder tumors (TURBT).^{5,6} CRBD can be a major cause of distress to patients in the PACU, thereby impacting on the quality of postoperative care.7.8 Therefore, appropriate management of CRBD is important to improve postoperative outcomes and patient satisfaction in male patients undergoing TURBT, who require a large diameter urinary catheter.

CRBD is induced by involuntary contractions of the urinary bladder smooth muscle as a result of urinary catheter-related muscarinic receptor activation or inflammatory stimulation.⁹ Therefore, a range of agents, such as anticholinergics, ketamine, tramadol, gabapentin, and paracetamol, have been evaluated for the prevention or treatment of CRBD.^{2,9-12} Despite the availability of a variety of agents for the management of CRBD, there is little evidence of effective treatment without side effects.¹³ Therefore, we have explored a different approach to the prevention of CRBD using lidocaine. Intravenous lidocaine is widely used during the perioperative period to reduce postoperative pain.¹⁴ It has multifactorial pharmacological effects, including analgesic, antimuscarinic, anti-inflammatory, and antihyperalgesic properties.¹⁵ Based on these considerations, we hypothesized that intravenous lidocaine administration could reduce the incidence of moderate-to-severe CRBD. Therefore, the effect of intravenous lidocaine administered before anesthetic induction until 1 hour postsurgery was evaluated in male patients undergoing TURBT, who require a large diameter urinary catheter.

METHODS

Study Design and Patients

This prospective, randomized, double-blind, placebo-controlled study was conducted at the Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea. All patients were enrolled between September 2018 and January 2019. The study protocol was approved by the institutional review board of the Asan Medical Center (2018-0840), and written informed consent was obtained from all participants. Before enrollment of any patients, the study protocol was registered with the Clinical Research Information Service (KCT 0003030) by the primary investigator (Y.-K.K.) on July 26, 2018.

Clinical Research Information Service: KCT 0003030. Registry URL: https://cris.nih.go.kr/cris/index.jsp.

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Address correspondence to Young-Kug Kim, MD, PhD, Department of Anesthesiology and Pain Medicine, Asan Medical Center, University of Ulsan College of Medicine, 88, Olympic-ro 43-gil, Songpa-gu, Seoul 05505, Republic of Korea. Address e-mail to kyk@amc.seoul.kr; and Gi-Ho Koh, MD, Department of Anesthesiology and Pain Medicine, Chosun University Hospital, 365, Pilmun-dearo, Dong-gu, Gwangju 61453, Republic of Korea. Address e-mail to gramsci1015@gmail.com. All male patients scheduled for elective TURBT under general anesthesia were assessed for eligibility. Patients were included if they were aged 20–79 years with an American Society of Anesthesiologists physical status \leq II. Patients were excluded if they had heart failure (ejection fraction <40%), coronary artery disease, liver cirrhosis, chronic kidney disease, or an allergy to lidocaine. Patients who had arrhythmias, such as sinus bradycardia, heart block, and atrial fibrillation, were also excluded.

Randomization, Concealment, and Blinding

Web-based randomization software (Random Allocation Software version 1.0; Isfahan University of Medical Sciences, Isfahan, Iran) was used to randomly allocate patients to the 2 study groups. Randomization was determined with block sizes of 4 and an allocation ratio of 1:1. Eligible participants were assigned to receive either intravenous lidocaine (group L) or intravenous normal saline as placebo (group C) according to a computer-generated randomization schedule. Randomization codes held in sequentially numbered opaque envelopes, concealed by the first investigator, were given to the second investigator who prepared 1% lidocaine or normal saline solutions. These medications were prepared in identical syringes and volumes and were identified with the patient name and hospital registration number. Before anesthetic induction, these medications were given to a third investigator who was blinded to the allocation groups; this investigator was responsible for anesthetic induction, management, and emergence. A fourth investigator, who was also blinded to the allocation groups, assessed the severity of CRBD in the PACU or general ward. Other than the first and second investigators, all other investigators and participants were unaware of the treatment assignments until data analyses were complete.

Study Protocol

Noninvasive blood pressure, pulse oximetry, 3-lead electrocardiogram, body temperature, capnography, train-of-four (TOF) system, and bispectral index (BIS) were applied to all patients. General anesthesia was induced using propofol (2 mg/kg) and rocuronium (0.6 mg/kg). Once the patient was unconsciousness, a laryngeal mask (LM) was inserted. Anesthesia was maintained with sevoflurane (2-3 vol%) in a mixture of N₂O 50% and oxygen 50%; the end-tidal concentration of sevoflurane was adjusted to maintain a target BIS value of 40–60 and appropriate vital signs. To reverse the neuromuscular blockade, neostigmine (0.04 mg/kg) and glycopyrrolate (8 µg/kg) were administered if a TOF count of 4 was present at the end of surgery. Urinary catheterization was conducted using a ≥ 20 Fr catheter, and the balloon was inflated with 10 mL of distilled water. A 2% lidocaine gel was used to lubricate the catheter, which was fixed in the suprapubic area with adhesive tape. Normal saline was infused continuously through the urinary catheter to irrigate the bladder. After confirming that the patient was fully conscious (BIS ≥90) and had recovered from neuromuscular blockade (TOF ratio \geq 90%), the LM was removed and the patients were moved to the PACU.

The lidocaine dosage regimen was determined based on previous studies with some modifications.^{16,17} In group L, an intravenous bolus of 1% lidocaine (10 mg/1 mL) 1.5 mg/

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kg was administered just before the induction of anesthesia, followed by an intravenous infusion of <u>2 mg/kg/h</u> during the intraoperative period, which was continued in the PACU for <u>1 hour after</u> surgery. In group *C*, patients received normal saline at the same bolus volume and continuous infusion rate as group L (before induction: intravenous bolus of normal saline 0.15 mL/kg; during the intraoperative period and the 1-hour postoperative period: intravenous infusion of normal saline 0.2 mL/kg/h).

In the PACU, fentanyl $(1 \, \mu g/kg)$ was administered to the patients if postoperative pain, assessed using a numeric rating scale (NRS), was \geq 4; tramadol (1 mg/kg) was administered when moderate or severe CRBD was identified.^{2,18} If the patient complained of both moderate or severe CRBD and postoperative pain (NRS \geq 4) simultaneously, either tramadol or fentanyl was administered according to the more significant complaint. The patient was then reassessed 10 minutes after drug administration. The same analgesic protocol was maintained after transfer to the general ward. However, 30 mg of ketorolac (up to the recommended maximum daily dose of 60 mg/d) was used instead of tramadol to treat moderate or severe CRBD on the day of surgery. If patients had contraindications to nonsteroidal anti-inflammatory drugs (NSAIDs) or the severity of CRBD was not reduced, patients received tramadol (1 mg/kg).

Outcomes

The primary outcome was moderate-to-severe CRBD at 0 hour postsurgery (on admission to the PACU). The secondary outcome was opioid requirement during the 24-hour postoperative period. Other outcomes included none, mild, and moderate-to-severe CRBD at 1, 2, and 6 hours postsurgery, postoperative pain, patient satisfaction, the side effects of lidocaine and rescue medications (tramadol and fentanyl), and surgical complications.

All patients were educated about the symptoms of CRBD (characterized as the urge to void or a burning sensation in the suprapubic area) during a preoperative visit. The severity of CRBD was recorded as follows: none (patients did not complain of CRBD when questioned); mild (reported by patients only when asked); moderate (reported by patients independently, ie, without being asked, and not accompanied by any behavioral response); or severe (reported by patients independently along with behavioral responses such as flailing limbs, strong vocal response, and attempts to pull out the catheter).^{2,5,11} This qualitative method of assessing CRBD has been used in previous studies, although there is currently insufficient evidence to support its use.

Doses of all opioids and NSAIDs administered to patients were converted to intravenous morphine equianalgesic doses according to published conversion factors (intravenous morphine 10 mg = fentanyl 100 µg = tramadol 100 mg = ketorolac 30 mg).^{19,20} Postoperative pain was also evaluated when assessing CRBD at 0, 1, 2, and 6 hours after surgery, using a single 11-point NRS, in which 0 = no pain and 10 = worst pain imaginable. In addition, postoperative pain was assessed in a subanalysis of patients with a postoperative NRS value \geq 1. Patient satisfaction was assessed at 6 hours postsurgery by global perceived effects on a 7-point scale (GPES) with some modifications (question: how would you rate your satisfaction with this medication

for the prevention of CRBD?, grade: 1 = very dissatisfied, 2 = somewhat dissatisfied, 3 = slightly dissatisfied, 4 = neither satisfied nor dissatisfied, 5 = slightly satisfied, 6 = somewhat satisfied, and 7 = very satisfied).^{21,22} To obtain valid NRS and GPES outcomes data, all patients were instructed on how to rate their pain using an NRS and their satisfaction using a GPES during a preoperative visit. Patient satisfaction was also assessed in a subanalysis according to the grade of patient satisfaction (grades 1, 2, and 3, dissatisfied patients group; grade 4, neither satisfied nor dissatisfied patients group; grades 5, 6, and 7, satisfied patients group). In addition, the side effects of lidocaine (including drowsiness, lightheadedness, metallic taste, visual disturbances, or perioral numbness)16 and of rescue medications (including somnolence, dizziness, nausea, vomiting, respiratory depression, or hypotension)^{23,24} were assessed during the 24-hour postoperative period. Surgical complications were also assessed until discharge.

Statistical Analyses

Data are expressed as mean ± standard deviation, median (interquartile range), number (proportion), or relative risk (RR) and 95% confidence interval (95% CI). We focused the primary outcome as the incidence of moderate-to-severe CRBD at 0 hour postsurgery. Therefore, our primary outcome was compared using the χ^2 test. Because the analyses at other time points of assessment of CRBD between the 2 groups were explorative analysis, they were also compared using the χ^2 test or Fisher exact test, as appropriate. Normal distribution of continuous data was assessed using the Kolmogorov-Smirnov test. Non-normally distributed continuous data such as opioid consumption and patient satisfaction were compared using the Mann-Whitney U test. P < .05 was considered significant. NRS scores of both groups and subgroups of patients with postoperative pain (NRS \geq 1) at each evaluation time after the operation were compared using a 2-way repeated measures analysis of variance with Huynh-Feldt correction. The Bonferroni method was used as post hoc analysis to adjust for pairwise comparisons. After using Bonferroni correction, P < .0125(0.05/4) was considered to be significant. Data were analyzed using MedCalc (version 11.3.3.0; MedCalc Software bvba, Mariakerke, Belgium) and the Statistical Package for the Social Sciences (SPSS, Version 21.0, IBM SPSS Statistics; IBM Corporation, Armonk, NY).

The sample size calculation was based on previous data from 20 patients in our institution. The incidence of moderate-to-severe CRBD at 0 hour postsurgery after TURBT in groups C and L was 60% and 35%, respectively. With a 2-sided significance level of 0.05 and power of 0.8, a minimum of 62 subjects per group were required. Considering a dropout rate of 5%, 66 subjects in each group were included. The analyses were performed on the intention-to-treat population; all patients who were enrolled and randomly allocated to treatment should be included in the analysis.

RESULTS

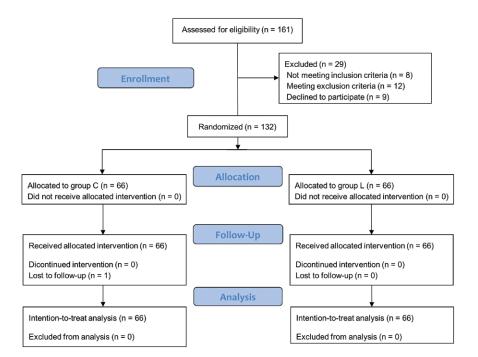
Study Population

A total of 161 patients were assessed for eligibility before surgery; 29 patients were excluded and 132 were randomized (Figure 1). After randomization, no patients

discontinued or were lost to follow-up in group L; 1 patient in group C was lost to follow-up because he was discharged on postoperative day 0. However, this patient was included in the intention-to-treat analysis. Therefore, all 132 patients were included in the final analysis. The clinical and surgical characteristics of study participants are shown in Table 1.

Outcomes

The incidence of moderate-to-severe CRBD at 0 hour postsurgery was significantly lower in group L than in group C (25.8% vs 66.7%, P < .001, RR: 0.386, 95% CI, 0.248– 0.602; Figure 2). Opioid requirements during the 24-hour



postoperative period were significantly lower in group L than in group C (10.0 mg [5.0–15.0 mg] vs 13.8 mg [10.0–20.0 mg], P = .005; Figure 3). The dosages of tramadol administered in groups C and L were 67.4 ± 54.4 and 33.3 ± 47.5 mg, respectively, and those of fentanyl were 10.6 ± 24.0 and $11.4 \pm 22.9 \mu$ g, respectively. Only 26 patients received fentanyl. At 1 and 2 hours postsurgery, the incidence of moderate-to-severe CRBD was significantly lower in group L than in group C (1 hour: 10.6% vs 27.3%, P = .026, RR: 0.389, 95% CI, 0.174-0.869; 2 hours: 0.0% vs 15.2%, P = .003, RR: 0.048, 95% CI, 0.003-0.796; Figure 2). The incidence of moderate-to-severe CRBD did not differ significantly between groups

Figure 1. CONSORT flow diagram of patients included in the study. Group C comprised patients who received intravenous normal saline as placebo. Group L comprised patients who received intravenous lidocaine. CONSORT indicates Consolidated Standards of Reporting Trials.

Table 1. Clinical and Surgical Characteristics									
	Group C (n = 66)	Group L (n = 66)	Standardized Differences						
Age (y)	66.5 (59.0-73.0)	65.0 (56.0-72.0)	0.222						
Body mass index (kg/m ²)	24.6 ± 3.3	24.6 ± 3.0	0.024						
ASA physical status									
1/11	17 (25.8)/49 (74.2)	28 (42.4)/38 (57.6)	0.357						
Duration of surgery (min)	60.0 (55.0-75.0)	65.0 (55.0-80.0)	0.086						
Urethral stricture	16 (24.2)	13 (20.0)	0.110						
T stage			0.179						
≤Ta	41 (62.1)	41 (62.1)							
Tis	6 (9.1)	6 (9.1)							
T1	14 (21.2)	11 (16.7)							
T2	5 (7.6)	8 (12.1)							
Tumor size (cm)			0.225						
<3	40 (60.6)	47 (71.2)							
≥3	26 (39.4)	19 (28.8)							
Tumor multiplicity									
Single/multiple	22 (33.3)/44 (66.7)	30 (45.5)/36 (54.5)	0.250						
Foley catheter diameter (Fr)			0.082						
≤18	1 (1.5)	1 (1.5)							
20 ≥22	<mark>53</mark> (80.3)	55 (83.3)							
<mark>≥2</mark> 2	<mark>12</mark> (18.2)	10 (15.2)							

Data are expressed as mean \pm standard deviation, median (interquartile range), or number (%). Group C, intravenous normal saline as placebo; group L, intravenous lidocaine. \leq Ta, no tumor or noninvasive papillary carcinoma; Tis, carcinoma in situ; T1, tumor invading lamina propria; T2, tumor invading muscularis propria. Abbreviation: ASA, American Society of Anesthesiologists.

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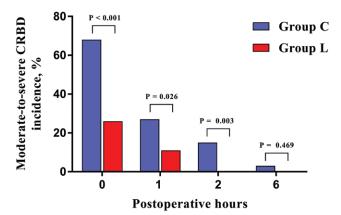


Figure 2. Comparison of the incidence of moderate-to-severe CRBD between the 2 groups at 0 (on admission to the postanesthetic care unit), 1, 2, and 6 h postsurgery. Group C comprised patients who received intravenous normal saline as placebo. Group L comprised patients who received intravenous lidocaine. Data were analyzed using the χ^2 test or Fisher exact test. CRBD indicates catheter-related bladder discomfort.

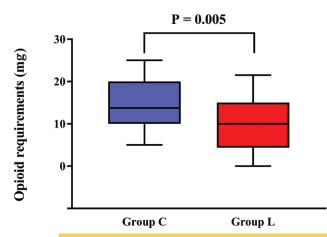


Figure 3. Comparison of opioid requirements within the 24 h postoperative period between the 2 groups. Group C comprised patients who received intravenous normal saline as placebo. Group L comprised patients who received intravenous lidocaine. The horizontal line inside the boxes shows the median values; the upper and lower edges of the box represent the third and first quartiles, respectively. Whiskers above and below the boxes represent 90% and 10%, respectively. Data were analyzed using the Mann-Whitney *U* test.

C and L at 6 hours postsurgery (3.1% vs 0.0%, P = .469). Although the incidence of mild CRBD was significantly higher in group L than in group C (72.7% vs 31.8%, P < .001) at 0 hour postsurgery, there were no significant differences in the incidence of mild CRBD between the 2 groups at 1 and 2 hours postsurgery (Table 2). At 6 hours postsurgery, the incidence of mild CRBD was significantly lower in group L than in group C (56.1% vs 80.0%, P = .006).

NRS values did not differ significantly between the 2 groups throughout the 6-hour postoperative period (main effect of time: P < .001, main effect of group: P = .285, time-by-group interaction: P = .605; Supplemental Digital Content, Table 1, http://links.lww.com/AA/C925). In the subanalysis of only those patients with postoperative pain (NRS \geq 1), we observed a significant main effect of time (P < .001), main effect of group (P = .004), but no significant

interaction between group and time (P = .260). A subanalysis of patients with postoperative pain showed that the NRS was significantly lower in group L than in group C at 0 and 6 hours postsurgery (0 hour: 2.0 [2.0–4.0] vs 4.0 [3.0–6.0], P = .008; 6 hours: 0.0 [0.0–1.0] vs 1.0 [0.0–2.0], P = .009; Supplemental Digital Content, Table 1, http://links.lww. com/AA/C925).

Patient satisfaction was significantly greater in group L than in group C (5.0 [4.8–6.0] vs 4.0 [4.0–5.0], P < .001; Figure 4). In addition, subanalysis according to the grade of patient satisfaction showed that significantly more patients were dissatisfied in group C than in group L (23.1% vs 3.0%) and significantly more patients were satisfied in group L than in group C (75.8% vs 47.7%, P = .001; Supplemental Digital Content, Table 2, http://links.lww.com/AA/C925). No lidocaine-related side effects were reported. However, there were 2 reports of side effects associated with the rescue medications (somnolence and nausea) in group C and 1 (hypotension) in group L (2 [3%] vs 1 [1.5%], P > .99). One surgical complication (postoperative surgical bleeding) was reported in group C, whereas there were no surgical complications in group L (1 [1.5%] vs 0 [0%], P > .99).

DISCUSSION

This study demonstrated 3 key findings. First, the incidence of moderate-to-severe CRBD was significantly reduced by intravenous lidocaine administration in male patients undergoing TURBT who required large diameter urinary catheters. Second, patient satisfaction was significantly increased by intravenous lidocaine administration for the prevention of CRBD. Third, there was no evidence of significant lidocaine-related side effects.

The urinary bladder receives cholinergic innervation from the pelvic nerves. Activation of muscarinic receptors caused by stimulation of the urinary catheter results in contraction of the smooth muscle around the urinary bladder and, as a consequence, the symptoms of CRBD.^{2,13} Therefore, a range of agents that can block muscarinic receptors, including ketamine, tolterodine, dexmedetomidine, and tramadol, have been investigated and shown to be effective in the prevention of CRBD.^{2,10,11} However, the use of these agents is associated with a range of side effects, such as dry mouth, facial flushing, blurred vision, and sedation.¹³ Another main mechanism underlying the development of CRBD is urinary bladder contraction triggered by elevated prostaglandin levels. The presence of a urinary catheter and subsequent mucosal layer damage could trigger local inflammation with the release of prostaglandin.²⁵

Lidocaine has significant antimuscarinic and antiinflammatory properties as a result of its interaction with sodium channels, other receptors such as muscarinic and *N*-methyl-D-aspartate receptors, and nociceptive transmission pathways.¹⁵ Previous studies have shown that lidocaine has a significant inhibitory effect on muscarinic receptors, and it is known to suppress immune cell-mediated inflammatory reactions.^{26,27} In addition, lidocaine has shown antihyperalgesic effects in healthy volunteers and patients undergoing laparoscopic nephrectomy.^{28,29} In the present study, intravenous lidocaine was seen to reduce the incidence of moderate-to-severe CRBD. It is possible that this effect is mediated by a reduction or block of urinary

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Table 2. Severity of Catheter-Related Bladder Discomfort											
		Postoperative Time (h)									
		0 1		1	2		6				
Group	Group C	Group L	Group C	Group L	Group C	Group L	Group C	Group L			
Severity of CRBD											
None	1 (1.5)	1 (1.5)	1 (1.5)	2 (3.0)	4 (6.1)	7 (10.6)	11 (16.9)	29 (43.9) ^a			
Mild	21 (31.8)	48 (72.7) ^a	47 (71.2)	57 (86.4)	52 (78.8)	59 (89.4)	52 (80.0)	37 (56.1) ^a			
Moderate	33 (50.0)	12 (18.2)ª	18 (27.3)	7 (10.6) ^a	10 (15.2)	0 (0.0) ^a	2 (3.1)	0 (0.0)			
Severe	11 (16.7)	5 (7.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)			

Data are expressed as number (%). Group C, intravenous normal saline as placebo; group L, intravenous lidocaine; 0 h postsurgery, on admission to the postanesthetic care unit. Data were compared using the χ^2 test or Fisher exact test.

Abbreviation: CRBD, catheter-related bladder discomfort.

 $^{a}P < .05$ versus group C.

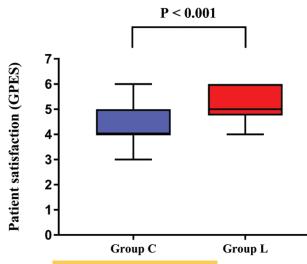


Figure 4. Comparison of patient satisfaction scores between the 2 groups at 6 h postsurgery. Group C comprised patients who received intravenous normal saline as placebo. Group L comprised patients who received intravenous lidocaine. The horizontal line inside the boxes shows the median values; the upper and lower edges of the box represent the third and first quartiles, respectively. Whiskers above and below the boxes represent 90% and 10%, respectively. Data were analyzed using the Mann-Whitney *U* test. GPES indicates global perceived effects on a 7-point scale.

catheter-related muscarinic, inflammatory, and hyperalgesic responses.

When using intravenous lidocaine in male patients undergoing TURBT who required large diameter urinary catheters, patient satisfaction was significantly increased. Because patient satisfaction is significantly associated with postoperative surgical outcomes, including hospital readmission and postoperative complications,³⁰ the increased patient satisfaction associated with lidocaine administration may be the most important advantage, along with a reduction in the incidence of moderate-to-severe CRBD. Therefore, we believe that patient satisfaction should be tracked as long as the urinary catheter is indwelling.

The use of intravenous lidocaine is associated with some concerns, including the risk of neurologic and cardiac side effects,^{31,32} which can occur when the plasma lidocaine concentration exceeds 5 µg/mL.³³ However, intravenous lidocaine administered at the standard dose (1–2 mg/kg as an initial bolus, followed by a continuous infusion of 0.5–3 mg/kg/h)³³ generally results in plasma concentrations that remain below 5 µg/mL.^{33,34} In the present study, no

lidocaine-related side effects were reported, and we, therefore, suggest that intravenous lidocaine administration is well tolerated in male patients undergoing TURBT. In addition, because the intravenous lidocaine dosing regimen varies between studies,^{33–35} further research is required to evaluate the effect of lidocaine administered at higher doses on postoperative CRBD.

Male gender and the use of large diameter urinary catheters are known risk factors for the development of CRBD.^{6,13} TURBT destroys the normal barrier mechanism of the urinary bladder wall, and continuous irrigation of the urinary bladder triggers urinary bladder spasms. Therefore, male patients undergoing TURBT, requiring large diameter urinary catheters, experience a higher degree of CRBD severity in comparison with those undergoing other types of urological and nonurological surgery.^{13,36,37} In the present study, the incidence of moderate-to-severe CRBD was seen to be 66.7% in the control group, which is higher than that reported in previous studies (16%–38%).^{5,18,36,38} This difference in incidence may be explained, at least in part, by the fact that only male patients were included in the present study.

There are some limitations to the current study. First, plasma lidocaine concentrations were not measured and therefore it could not be confirmed that concentrations were maintained within the therapeutic range. However, as no lidocaine-related side effects were reported, and many previous studies have demonstrated the safety of intravenous lidocaine use,^{16,35,39,40} we suggest that the lidocaine dose used in this study is appropriate for the management of CRBD. Second, it may be difficult to distinguish between severe CRBD with behavioral responses and postoperative delirium because the patients were not assessed using a standardized tool for postoperative delirium. In future studies, a verified tool may be required to accurately distinguish between severe CRBD and postoperative delirium. Third, because the analysis for CRBD at 1, 2, and 6 hours postsurgery was explorative, it should be interpreted with care.

In conclusion, intravenous lidocaine was seen to effectively reduce the incidence of moderate-to-severe CRBD in male patients undergoing TURBT and there was no evidence of significant side effects. These data suggest that intravenous lidocaine administration may be an effective option to decrease the incidence of moderate-to-severe CRBD in male patients undergoing TURBT who require a large diameter urinary catheter.

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DISCLOSURES

Name: Doo-Hwan Kim, MD.

Contribution: This author helped design and conduct the study, collect and analyze the data, and prepare and approve the final manuscript.

Name: Jun-Young Park, MD.

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