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Effect of Preoperative Intravenous Oxycodone After Transurethral Resection of Prostate Under General Anesthesia

Jinguo Wang[1], Yaowen Fu[1], Haichun Ma[2], Na Wang[2]

[1]*Department of Urology, First Hospital of Jilin University, Changchun, Jilin, China*

[2]*Department of Anaesthesiology, First Hospital of Jilin University, Changchun, Jilin, China*

The objective of this study was to investigate the effect of intravenous oxycodone administered before transurethral resection of prostate (TURP) on postoperative pain and tramadol consumption. Preemptive analgesia can decrease postoperative pain and analgesic consumption. Sixty patients undergoing elective TURP were divided into 2 groups: group O (n = 30) received intravenous oxycodone (0.1 mg/kg) 10 minutes before surgery over 2 minutes and group C (n = 30) received normal saline as a placebo. A standardized general anesthesia method was performed with a laryngeal mask airway device. Data with respect to pain intensity, incidence of lower urinary tract discomfort, time to the first tramadol requirement, tramadol consumption, overall patient satisfaction, and adverse effects were collected. Preoperative oxycodone contributed to better analgesia at 1, 2, 6, and 12 hours after shifting the patients to the recovery room, a longer time interval to the first tramadol request, fewer patients requiring tramadol analgesia, and reduced tramadol consumption. Adverse effects were comparable between the 2 groups. Preoperative intravenous oxycodone (0.1 mg/kg) 10 minutes before TURP improves postoperative analgesia, prolongs time to the first tramadol request, and reduces tramadol consumption without an influence on lower urinary tract discomfort and adverse effects.

Key words: Transurethral resection of prostate – Pain management – Preemptive analgesia – Opioids

Corresponding author: Na Wang, MD, PhD, Department of Anaesthesiology, First Hospital of Jilin University, No. 71 Xinmin Street, Changchun City, Jilin Province 130021, China.
Tel.: +86 135 788 99 126; Fax: +86 0431 85612908; E-mail: lilyly12345@163.com

Transurethral resection of prostate (TURP) is a kind of minimally invasive surgery, associated with less tissue trauma, but most patients still have postoperative pain. Pain after TURP is involved with tissue injury at the surgical site, pelvic organ nociception, irritation from irrigation, and lower urinary tract discomfort. Preemptive analgesia is a pretreatment of administering a powerful analgesic drug before the onset of the surgical stimulation; therefore, pain hypersensitization can be attenuated, resulting in reduced postoperative pain.[1] Oxycodone, a kind of opioids with fewer adverse effects than morphine, can be used for that purpose.[2] As reported in previous studies, controlled release oxycodone can decrease perioperative stress, postoperative pain intensity, and analgesic consumption for laparoscopic cholecystectomy and liposuction.[3,4] No literature was found associated with the effect of preoperative oxycodone after TURP under general anesthesia. In this prospective and placebo-controlled clinical trial, the hypothesis was tested that preoperative intravenous oxycodone would reduce postoperative pain and decrease postoperative analgesic consumption.

Methodology

After approval of the Institutional Ethics Committee (No. 2013-209), written informed consents were obtained from 60 American Society of Anesthesiologists (ASA) I/II patients scheduled for TURP. Patients with histories of substance abuse, mental disturbance, and neurologic disease, with liver or renal dysfunctions, and who have allergic reactions to study drugs were excluded from the trial.

Assuming that preoperative intravenous oxycodone would prolong time to the first tramadol request by 30 minutes, power analysis with a 2-sided α of 5% and β of 10% showed that 23 patients were required in each group. Thirty patients were enrolled in each group for possible dropouts.

With a random number sequence, patients were divided into 2 groups (group O, $n = 30$; group C, $n = 30$). One of the researchers prepared the study drug solution. The anesthetist and the patients were unware of the grouping situation.

Electrocardiogram, blood pressure (BP), bispectral index, and oxygen saturation (SpO_2) were performed on patients taken to the operation room without premedication. A 16-gauge intravenous canula was sited. Before anesthetic induction, the patients received 5 ml/kg normal saline over 30 minutes. The intravenous infusion was minimally maintained during the surgery to avoid fluid overload resulting from absorption of irrigation fluid.

Anesthesia induction was performed with 0.3 mg/kg etomidate, 3 μg/kg fentanyl, and 0.15 mg/kg cisatracurium. Three minutes later, intubation was performed using a laryngeal mask airway (LMA) device. Anesthesia was maintained with continuous infusions of propofol and remifentanil at the rates of 6 to 8 and 8 μg/kg per hour, respectively, and intermittent administration of cisatracurium as needed. Oxycodone (oxycodone, Hamol Ltd, Nottingham, United Kingdom) was diluted with saline to obtain a concentration of 1 mg/ml. Unlabeled study medication in 0.1 ml/kg containing either 1 mg/ml oxycodone in saline or simple saline was administered intravenously 10 minutes before surgical procedures over 2 minutes. Ten minutes before the approximated completion of surgery, patients received intravenous 100 μg/kg ondansetron and 1 μg/kg fentanyl in both groups. All of the participants were extubated in the operating room and shifted to the recovery room.

BP and heart rate were recorded every 5 minutes. Pain intensity, sedation status, and postoperative side effects were followed by both observing and questioning the patients. The data were recorded at 0, 1, 2, 6, 12, and 24 hours at rest after shifting the patients to the recovery room. Postoperative analgesia consisting of 1.5 mg/kg intravenous tramadol was given when the patients complained of pain and the visual analog scale (VAS) score was more than 3. Time to the first tramadol request, tramadol total dose given, and the number of patients who required tramadol analgesia were recorded. The study ended at 24 hours after shifting the patients to the recovery room.

An independent anesthesia registrar who was unaware of the grouping situation recorded pain intensity evaluated by VAS (0, no pain; 1, 2, 3, mild pain; 4, 5, 6, moderate pain; 7, 8, 9, severe pain; 10, worst imaginable pain) and sedation score using the Ramsay sedation scale (RSS: 1, anxious and agitated; 2, cooperative and tranquil; 3, drowsy but responds to command; 4, asleep but responds to tactile stimulation; 5, asleep and no response). The overall satisfaction degree for postoperative analgesic effects was also measured at the end of the study. The overall satisfaction degree was graded as follows: poor, moderate, good, and excellent. The incidence of postoperative lower urinary tract discomfort and adverse effects (such as nausea, vomiting, pruritis,

Table 1 Demographic data and surgical characteristics

Items	Group O	Group C	*P*
Age (years)	62.1 ± 9.4	65.2 ± 8.3	0.181
Weight (kg)	75.2 ± 8.3	73.5 ± 9.2	0.455
Height (cm)	172.2 ± 7.4	170.8 ± 9.6	0.529
ASA I/II (n)	10/20	12/18	0.789
Duration of operation (min)	57.3 ± 10.3	55.8 ± 11.9	0.603
Prostate volume (g)	69.1 ± 13.1	64.6 ± 10.3	0.144

Values are presented as mean ± SD and number of patients.

Table 2 Postoperative tramadol use

Items	Group O	Group C	*P*
Time to the first tramadol request (min)[a]	242.3 ± 121.7	166.4 ± 92.5	0.015
Tramadol consumption (mg)[a]	95.6 ± 41.9	129.3 ± 48.9	0.015
Number of patients requiring tramadol analgesia: n (%)[a]	20 (67%)	29 (97%)	0.005

Values are presented as mean ± SD and number of patients (%).
[a]$P < 0.05$ compared with the counterpart of group C.

and dizziness) within 24 hours was evaluated with a yes or no survey.

The data were analyzed using SPSS 17.0 (SPSS Inc, Chicago, Illinois). Independent sample *t*-test was used to analyze data with normal distribution between the 2 groups. Intergroup differences in VAS score were compared using the Mann-Whitney test. Categorical variables were analyzed using either the χ^2 or Fisher's exact test. A value of $P < 0.05$ was considered a statistically significant difference.

Results

The demographic data and surgical characteristics of the 2 groups were comparable (Table 1). VAS scores were lower in group O at 1, 2, 6, and 12 hours postoperatively (Fig. 1). Table 2 summarizes the postoperative tramadol requirement. In group C, time to the first tramadol request was much shorter, and the patients who required tramadol analgesia and the total tramadol consumption were more in group C. The overall satisfaction degree is shown in Table 3, and the patients in group O were more satisfied than in group C. There were no significant differences between the 2 groups for lower urinary tract discomfort or any of the adverse events (Table 4). RSS scores were not more than 3 in both groups at all time points during the study. All the SpO_2 and respiration rate data were within the normal range during the study period (93%∼100% for SpO_2 and 12∼16 breaths/min for respiration rate) in both groups.

Discussion

Intrathecal anesthesia is preferred for transurethral procedures due to advantages such as reduced postoperative pain, early patient mobilization, and shortened hospital stay.[5] However, now, more and more patients undergo TURP under general anesthesia, because they fear the procedure of intrathecal puncture and being awake during the surgery. In addition, intrathecal puncture for the elderly is somehow difficult because of spinal canal stenosis, ligament calcification, kyphosis, or scoliosis.

Most patients requiring TURP are elderly and are always associated with cardiopulmonary conditions, increased pain threshold, and decreased pain tolerance.[6] Therefore, it is important to choose proper anesthetics and anesthetic methods to

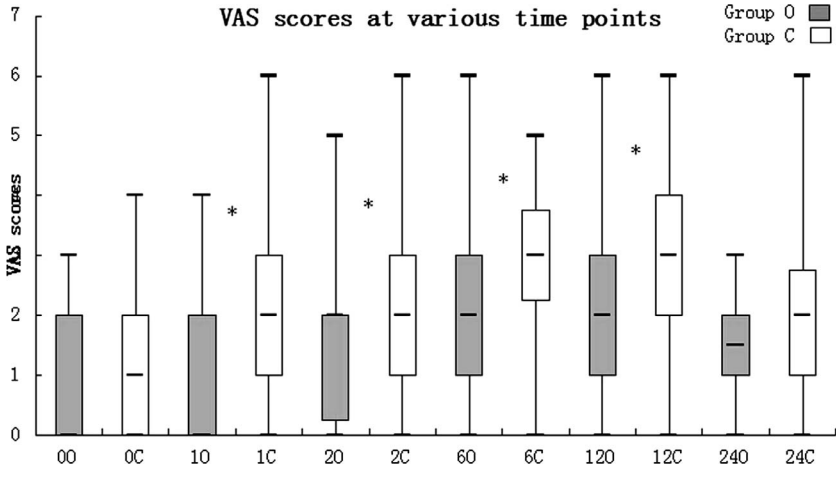

Fig. 1 VAS scores at various time points.

Table 3 Patient satisfaction

Groups	Poor	Moderate	Good	Excellent
Group O	1 (3)	4 (13)	7 (23)	18 (60)
Group C	3 (10)	8 (27)	12 (40)	7 (23)

$P = 0.036$, there is a significant difference between the 2 groups. Values are presented as number of patients (%).

minimize an undesirable cardiovascular reaction. For this purpose, an LMA device was chosen for airway management in this study. Etomidate is an excellent option with minimal hemodynamic responses to be used in combination with other anesthetics.[7] Etomidate and LMA will provide better hemodynamic stability.

In the present study, it was found that preemptive intravenous oxycodone could prolong time to the first analgesic request, reduce postoperative pain, and decrease analgesic consumption.

Tissue damage from surgical procedures could lead to peripheral and central sensitization, which could cause pain feeling expanded and prolonged. The preemptive analgesia strategy is an efficient method used for pain management by administering powerful analgesics to patients before surgical procedures to inhibit central sensitization. Preemptive analgesia can not only decrease the severity and duration of pain, but also delay the pain. Opioids are frequently used for preemptive analgesia.[1]

Oxycodone, a potent agonist interacting with the μ and κ opioid receptors, mainly works on the central nervous system, with fewer side effects than morphine.[8,9] One hour after intravenous administration of oxycodone, the concentration in cerebrospinal fluid is 3 times as high as that in plasma, so perhaps the preemptive analgesia effect of oxycodone is from its central analgesic effect.[8,9] Fanelli *et al* reported oral oxycodone 1 hour before laparoscopic cholecystectomy had a preemptive effect.[3]

The result of this study, however, did not align with the research of Konstantatos *et al*.[10] They reported that preprocedural controlled-release oxycodone did not provide any analgesic benefit to patients undergoing uterine artery embolization. It could be ascribed to too late administration of oral oxycodone, which was given just before surgery. An adequate time interval between drug administration and the start of the surgery was essential for the preemptive effect of oxycodone to be exhibited. The peak time of intravenous oxycodone is 5 minutes, so 10 minutes before the surgical procedure was selected as the administration time of preemptive analgesia in our study.

Table 4 Incidence of lower urinary tract discomfort and postoperative adverse effects

Groups	Lower urinary tract discomfort	Nausea	Vomiting	Pruritis	Dizziness
Group O	10 (33.3%)	3 (10.0%)	0 (0.0%)	1 (3.3%)	3 (10.0%)
Group C	16 (53.3%)	6 (20.0%)	0 (0.0%)	0 (0.0%)	1 (3.3%)
P	0.192	0.471	1.000	1.000	0.612

Values are presented as number of patients (%).

Preemptive intravenous oxycodone had no obvious effect on the incidence of lower urinary tract discomfort in this study. The reason was unknown. There was no significant difference on VAS score between the 2 groups at 0 hours, and it might result from the analgesic effect of intravenous 1 μg/kg fentanyl in both groups 10 minutes before the approximated end of surgery. The incidence of adverse effects was comparable between the 2 groups in this study. The result was consistent with the report that oxycodone had less side effect than morphine.[8,9]

The limitations of this study are its small scale and only associated with male patients undergoing TURP. Therefore, this protocol is not suitable for all patients undergoing all kinds of surgeries.

It was indicated in this study that a single dose of intravenous oxycodone (0.1 mg/kg) 10 minutes prior to TURP improves postoperative analgesia, prolongs time to the first analgesic request, and reduces tramadol consumption without any influence on lower urinary tract discomfort or any of side effects.

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