

# Effect of preoperative intravenous oxycodone administration on sufentanil consumption after retroperitoneal laparoscopic nephrectomy

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## Abstract

**Background:** The aim of this study was to evaluate the efficacy of preoperative intravenous oxycodone administration on postoperative sufentanil consumption in patients undergoing retroperitoneal laparoscopic nephrectomy.

**Methods:** Fifty patients scheduled for retroperitoneal laparoscopic nephrectomy were enrolled and randomly assigned to two groups — patients in Group O (n = 25) received intravenously 0.1 mg kg<sup>-1</sup> oxycodone; while the patients in Group C (n = 25) received 0.1 mL kg<sup>-1</sup> normal saline for 2 min, 10 min before the operation. All of the participants received intravenous sufentanil patient-controlled analgesia (PCA) after extubation, using a PCA device. The sufentanil consumption, rescue analgesia, Ramsay sedation scale (RSS) and visual analogue scale (VAS) scores at rest and during cough, the overall satisfaction and undesired events were all assessed.

**Results:** Cumulative sufentanil consumption delivered by PCA was significantly lower in Group O at all time points. VAS scores at rest and during coughing at 1, 2, 4, 8 and 12 hours after extubation of the patient were significantly lower in Group O than in Group C. There were no significant differences between the two groups according to the number of patients administered tramadol, RSS and the incidence of side effects. The degree of patients' satisfaction was higher in Group O.

**Conclusion:** Preoperative intravenous oxycodone can reduce postoperative cumulative sufentanil consumption and postoperative pain intensity without an increase in side effects.

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**Key words:** opioids, oxycodone, sufentanil; postoperative pain, prophylaxis; postoperative pain, treatment, patient-controlled analgesia; laparoscopic nephrectomy

Although laparoscopic surgery is performed using smaller skin incisions compared with those in open surgery, postoperative pain is still common [1]. Inappropriate management of postoperative pain extends the duration of hospital stay and may lead to undesirable adverse effects such as respiratory depression and thromboembolic complications [2]. As pre-emptive analgesia is defined as administering analgesics before the start of the painful stimulation, it may inhibit the development of hypersensitization and then result in less post-stimulus pain [3]. It has been shown that pre-emptive analgesia provides a reduction in intra- and post-operative stress, postoperative pain and produces an improvement in patients' satisfaction [1, 3].

Opioids are frequently used for that purpose. Oxycodone, which is an opioid with fewer side effects than morphine, is superior in the treatment of visceral pain [4].

We designed a prospective randomized study in order to investigate the efficacy of preoperative intravenous oxycodone on postoperative pain intensity, postoperative sufentanil consumption, the patient's overall satisfaction and the side effects in patients undergoing retroperitoneal laparoscopic nephrectomy.

## METHODS

Following the approval of the institutional ethics committee and written informed consent of the patients, 50 ASA

I or II individuals scheduled for retroperitoneal laparoscopic nephrectomy were admitted to the study. Patients with histories of substance abuse and mental illness, having allergic reactions to study drugs, with liver and/or renal dysfunctions were excluded from the study.

This study was conducted in a randomized, double-blind, controlled fashion. One investigator who was not involved in the management of the patients prepared the study drug before anaesthesia. Both the anaesthetists and the patients were blinded to the type of the patient groups. With a random number sequence generated by a computer and sealed envelopes, the patients were allocated into two groups (Group O,  $n = 25$ ; Group C,  $n = 25$ ). One day before the operation, all patients were visited and given instructions on the usage of the patient-controlled analgesia (PCA) device and pain assessment with the visual analogue scale (VAS, values from 0 to 10; 0 — no pain and 10 — the most severe pain).

All the patients were instructed to fast for eight hours prior to surgery. Routine monitorization (electrocardiography, noninvasive blood pressure, pulse oximetry, and end-tidal carbon dioxide pressure) was applied to the patients taken to the operation room without premedication. A 16 gauge intravenous canula was sited. Lactated Ringer's solution was given at the rate of  $8 \text{ mL kg}^{-1} \text{ h}^{-1}$ . Anaesthetic induction was performed with  $0.05 \text{ mg kg}^{-1}$  midazolam,  $0.3 \text{ mg kg}^{-1}$  etomidate,  $3 \text{ } \mu\text{g kg}^{-1}$  fentanyl and  $0.15 \text{ mg kg}^{-1}$  cisatracurium. Anaesthesia was maintained with continuous infusions of propofol and remifentanyl at the rates of  $6$  to  $8 \text{ mg kg}^{-1} \text{ h}^{-1}$  and  $0.012 \text{ mg kg}^{-1} \text{ h}^{-1}$  respectively, and cisatracurium was administered intermittently as needed. During the operation, the bispectral index (BIS) was kept between 45 and 60. Oxycodone was diluted with saline to obtain a concentration of  $1 \text{ mg mL}^{-1}$ . Unlabelled study medications of  $0.1 \text{ mL kg}^{-1}$  containing either  $1 \text{ mg mL}^{-1}$  oxycodone or normal saline was administered intravenously 10 min before the start of surgery over 2 min. All patients in both groups received intravenous  $4 \text{ mg}$  ondansetron and intravenous  $3 \text{ } \mu\text{g}$  sufentanil, 30 min before the approximated end of surgery. All patients were extubated in the operating room and then shifted to a post-anaesthesia care unit. All participants received intravenous sufentanil PCA after extubation from a PCA device (Aipeng ZZB-I Pump, nantong apon medical appliance CO LTD, Rudong, China). PCA was set on the demand mode without a loading dose or background infusion. The dose of sufentanil was set at  $1 \text{ } \mu\text{g}$  with a time-lock interval of 10 min.

An independent researcher who was unaware of the grouping status recorded postoperative cumulative sufentanil consumption, VAS and RSS scores. the sedation score was evaluated with 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; and 5- asleep and no response). RSS and VAS scores at rest and during coughing were assessed at 1, 2, 4, 8, 12, 24 and 48 h after extubation of the patient. The rescue analgesia (intravenous administration of  $1.5 \text{ mg kg}^{-1}$  tramadol) was given if the VAS score was more than three. The number of patients to whom tramadol was administered during the postoperative 48 h was noted. In addition, the overall satisfaction degree for postoperative analgesia was also measured at the end of the study. The overall satisfaction degree was divided as follows: poor, moderate, good, excellent. Side effects were observed and recorded for a total period of 48 h, including nausea, vomiting, hypotension, bradycardia, allergic reactions, drowsiness, paresthesia and respiratory depression. The incidence of adverse effects was evaluated with "yes" or "no".

The total amount of postoperative sufentanil consumption was the primary endpoint of this clinical trial. After a pilot study (7 patients in each group), a variance of  $30 \text{ } \mu\text{g}$  was detected in the total amount of postoperative sufentanil. Twenty-two patients per group were needed for detecting the difference with a power of 90% and a significance level of 5%. Finally, 50 patients were included in this study for possible dropouts.

Statistical analysis was performed using SPSS 17.0 (SPSS Inc, Chicago, USA). The data with normal distribution was evaluated using independent sample Student's *t*-test. Inter-group VAS and RSS scores were compared using the Mann Whitney *U*-test. Categorical data were analyzed between the two groups with either the chi-square or Fisher's exact test. A *P* value of  $< 0.05$  was considered statistically significant.

## RESULTS

None of the patients was excluded from this study and there was no need of a blood transfusion or conversion to open surgery. There were no significant differences between the two groups based on demographic data and surgical characteristics, ( $P > 0.05$ ) (Table 1).

Cumulative sufentanil consumption by PCA was lower in Group O than in Group C at all the time points (Fig. 1). VAS scores depicted in Figures 2 and 3 revealed that the intensity of pain was lesser at rest and during coughing at 1, 2, 4, 8 and 12 h in Group O than in Group C. There was no difference in RSS scores at each time point between the two groups (Fig. 4).

The satisfaction rate about the postoperative pain management was higher in Group O (Table 2). The incidence of tramadol analgesia and side effects were not significantly different between the two groups (Table 3).

**Table 1.** Demographic data and surgical characteristics

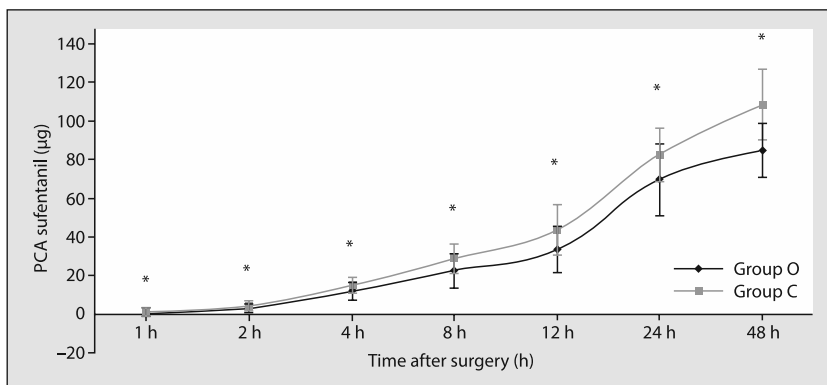
	Group O (n = 25)	Group C (n = 25)	P-value
Left/right nephrectomy (n)	10/15	12/13	0.775
Male/Female (n)	11/14	10/15	0.774
Age (year)	48.7 ± 11.6	51.9 ± 9.9	0.299
Body mass (kg)	58.3 ± 5.3	61.2 ± 6.7	0.096
Duration of surgery (min)	103.2 ± 27.4	109.4 ± 30.2	0.450
Duration of anaesthesia (min)	145.6 ± 43.4	157.5 ± 57.3	0.411
Intraoperative blood loss (mL)	157.8 ± 50.8	139.7 ± 48.9	0.205
Intraoperative fluid administration (mL)	1034.2 ± 258.8	1126.4 ± 313.7	0.262
Intraoperative urinary output (mL)	356.7 ± 81.6	377.1 ± 69.1	0.344

Data are presented as mean ± standard deviation or number of patients. Abbreviations: n, number of patients; Group O, the oxycodone group; Group C, the control group

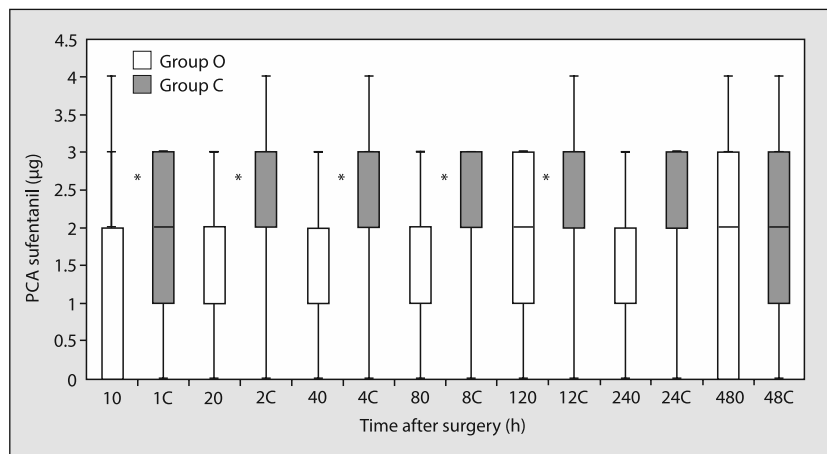
**DISCUSSION**

In this study, laparoscopic nephrectomy is performed through retroperitoneal way which is commonly used in China. As during the process of this kind of operation the external oblique, internal oblique and transverse muscles, which are involved in body support, are partially damaged, patients undergoing retroperitoneal laparoscopic nephrectomy may feel more pain than patients undergoing transperitoneal laparoscopic nephrectomy. About 30% patients undergoing transperitoneal laparoscopic nephrectomy experience shoulder tip pain postoperatively [1]. No shoulder tip pain was detected in this study. Although shoulder tip pain results from diaphragmatic irritation caused by CO<sub>2</sub> for pneumoperitoneum, CO<sub>2</sub> has no access to the peritoneal cavity in retroperitoneal laparoscopic nephrectomy. Therefore, it is essential to assess postoperative pain and analgesic requirements in these patients.

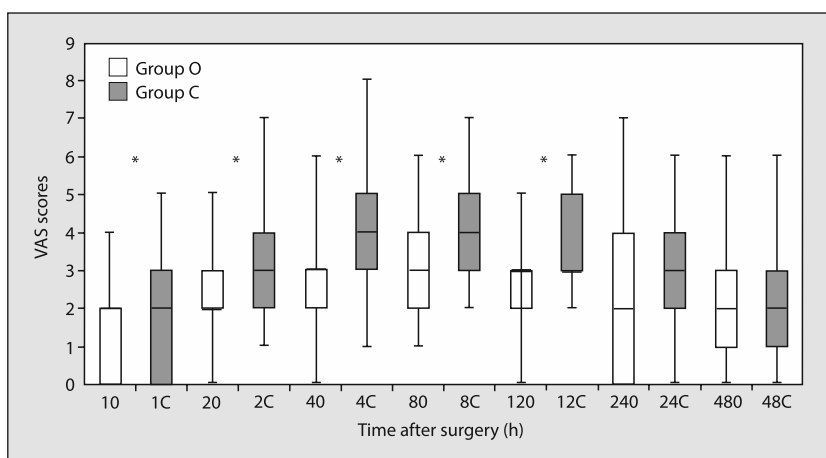
Pre-emptive analgesia may prohibit hypersensitivity and then decrease acute pain. Interventions which can pre-



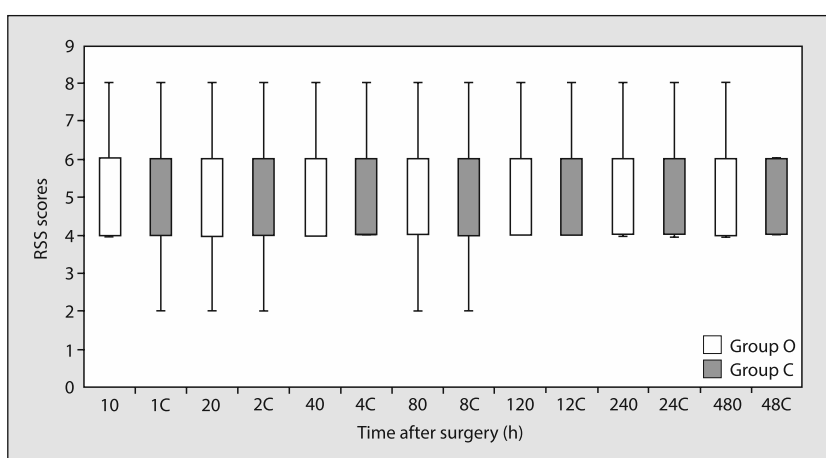
**Figure 1.** Cumulative sufentanil consumption at various time points



**Figure 2.** Box plots of postoperative VAS scores at rest at various time points



**Figure 3.** Box plots of postoperative VAS scores during coughing at various time points



**Figure 4.** Box plots of postoperative RSS scores at various time points

**Table 2.** Patients' satisfaction. Data are presented as number of patients (%)

	Poor	Moderate	Good	Excellent
Group O (n = 25)	5 (20)	11 (44)	6 (24)	3 (12)
Group C (n = 25)	1 (4)	5 (20)	10 (40)	9 (36)

*P* = 0.030, there was significant difference between the two groups. Group O — the oxycodone group; Group C — the control group

**Table 3** Tramadol analgesia and side effects. Data are presented as number of patients (%)

	Tramadol Analgesia	Nausea	Vomiting	Dizziness	Itching
Group O (n = 25)	2 (8)	5 (20)	0 (0)	5 (20)	0 (0)
Group C (n = 25)	1 (4)	4 (16)	1 (4)	3 (12)	1 (4)
<i>P</i>	1.000	1.000	1.000	0.709	1.000

Group O — the oxycodone group; Group C — the control group

vent the development of central sensitization may have the greatest benefit [5]. Oxycodone is a good choice for this purpose. One hour after intravenous administration, oxycodone concentration in plasma is three times as high as that in cerebrospinal fluid. This indicates that oxycodone has a strong analgesic effect on the central nervous system [6]. However, the mechanism of the analgesic action of oxycodone is still unknown.

The result of this clinical trial corresponds with the previous studies that preoperative controlled-release oxycodone could decrease postoperative pain without an increase of side effects [7, 8] Our results, however, are at variance with the results of Konstantatos *et al.* They demonstrated that the addition of preprocedural oral oxycodone to morphine PCA did not offer any analgesic advantage to patients undergoing uterine

artery embolization [9]. This could be ascribed to too late administration of oral oxycodone which was administered just before the procedure. It was proposed that an adequate time interval between drug administration and surgical procedure was necessary for the pre-emptive effect of oxycodone to be exhibited. As the onset time of intravenous oxycodone is 2–3 min and the peak time is 5 min, 10 min before skin incision was chosen as the time of pre-emptive analgesia in our study.

Opioids have several side effects such as postoperative nausea and vomiting, drowsiness, respiratory depression, gastrointestinal adverse effects and bladder dysfunction. The result was consistent with the report that oxycodone had less of a side effect profile than morphine [7, 8].

The limitation of the present study is that the patients were not followed up for the incidence of chronic pain. Future research should be performed in order to evaluate whether preoperative oxycodone could reduce chronic pain. Preoperative oxycodone decreases postoperative pain and sufentanil requirement in patients undergoing laparoscopic nephrectomy through the retroperitoneal way without an increase in side effects.

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2. Conflict of interest: none.

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