

Original Article

Sufentanil induced more effective analgesia than tramadol and dezocine for immediate postoperative pain management after thyroid surgery

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Abstract: Background: It is important for patients to receive effective postoperative analgesia that exerts few side effects. In this study, a double-blinded and randomized study was performed to investigate the effectiveness of sufentanil, tramadol, and dezocine for postoperative pain management after thyroid surgery. Methods: A total of 90 ASA I-II patients undergoing thyroid surgery were randomly separated into three equal groups, which were intravenously administered 0.2 $\mu\text{g}\cdot\text{kg}^{-1}$ sufentanil (S group), 2 $\text{mg}\cdot\text{kg}^{-1}$ tramadol (T group), or 0.1 $\text{mg}\cdot\text{kg}^{-1}$ dezocine (D group). Visual analog scale (VAS), overall pain performance scores (OPPS), Bruggemann comfort scale (BCS), Observer's assessment of alertness/sedation (OAA/S), and Ramsay sedation scale (RSS) were assessed after extubation. The time of palinesthesia, the time of extubation, and side effects were recorded. Results: The VAS scores were lower in the S group than in the D group at 5 min after extubation and were lower in the S group than in the T group at 30 min after extubation. The extubation time in the S group was longer than in the D group. The BCS, OPPS, OAA/S, and RSS scores were no difference between the three groups. The hemodynamic parameters remained no intergroup differences. No differences on consciousness recovery and other side effects were observed between the three groups. Conclusions: The administration of sufentanil induced more effective analgesia than tramadol and dezocine for postoperative pain management after thyroidectomy. Sufentanil transiently depressed respiratory and delayed the extubation compared with dezocine.

Keywords: Sufentanil, tramadol, dezocine, postoperative analgesia, thyroid surgery

Introduction

The aim of postoperative pain management is to reduce pain, advance the quality of resumption, and improve recovery to the normal activities of daily life [1]. Pain is still common complaint after thyroid surgery though it is not severe in this stage. Opioids are effective drugs for postoperative acute pain management that provide superior analgesia [2-4]. Sufentanil was shown to control cardiovascular changes induced by pain or anxiety during the early postoperative stage via efficacious analgesia after neurosurgery [5]. However, an overdose of sufentanil typically causes respiratory depression [6]. Tramadol may cause earlier awakening, more rapid recovery, and equivalent pain relief compared with morphine after abdominal hysterectomy [7]. Nonetheless, side effects of

nausea and vomiting were observed in patients who received tramadol [8]. Dezocine, an kind of opioid agonist/antagonist agent, required fewer doses to achieve patient satisfaction and was more efficacious than morphine for the rapid relief of acute pain [4]. Less sedation and gastrointestinal adverse effects were observed in patients receiving dezocine [9]. Due to their ceiling effect on respiratory depression and lower dependence liability, the opioid agonist/antagonist agents are the good choices for analgesia.

Sufentanil, tramadol, and dezocine are commonly used to provide effective pain relief after general anesthesia [5, 6, 10]. No previous studies compared the effects of sufentanil, tramadol, and dezocine used for postoperative analgesia after thyroid surgery. In this report, a

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Table 1. Overall pain performance scores

Scores	0	1	2	3
Facial grimace	No humor, serious, flat	Furrowed brow, pursed lips, holding breath	Wrinkled nose, raised upper lips, rapid breathing	Eyes closed, moaning, crying
Activity	Lying quietly, normal position, moving easily	Uneasy, restless, tense	Squirming, shifting back and forth	Arched, rigid or jerking
Verbal descriptor	No pain	Mild pain	Moderate pain	Severe pain
Emotion	Content, relaxed	Slightly uneasy	Fidgety and anxious	Difficult to console or comfort

Table 2. Demographic data and anesthetic consumption in the three groups

	Sufentanil	Tramadol	Dezocine	P value
Age (y)	50.3±8.1	47.5±9.2	47.9±7.9	0.32
Sex (F/M)	25/5	28/2	28/2	0.49
ASA status (I/II)	26/4	24/6	27/3	0.65
Body weight (kg)	67.1±9.2*	62.8±10.0	60.8±9.1	0.02
Operation time (min)	104.7±20.9	98.9±16.7	98.7±21.8	0.58
Propofol (mg)	730±221	688±196	666±170	0.61
Remifentanil (µg)	1,310±445	1,200±509	1,130±310	0.40

*Significant difference compared with the tramadol and the dezocine groups.

double-blinded and randomized study was performed to compare the analgesic effects, the recovery of cognitive function, and the side effects of these three drugs at the preferred dosage used for postoperative analgesia in patients undergoing thyroidectomy.

Materials and methods

This study was approved by the ethics committee of the Third Affiliated Hospital, Harbin Medical University, and was registered in the Chinese Clinical Trial Registry (Registration #: ChiCTR-TRC-13004194). Informed consent was obtained from the patients before the study. Ninety adult patients (18-70 years, ASA physical status I and II) scheduled for thyroid surgery were enrolled in this study. The exclusion criteria included known severe neurological, cardiovascular, hepatic, or renal dysfunction, pregnancy, a long history of using opioids, and contraindications for opioids (a history of hypersensitivity, bronchial asthma, or myasthenia gravis). Patients without exclusion criteria during the pre-anesthetic evaluation were randomly assigned to three groups (n = 30 each) using a randomization table, sufentanil (S) group, tramadol (T) group, and dezocine (D) group.

The method of anesthesia was standardized for three groups. The patients were induced

using 2 µg.kg⁻¹ fentanyl, 0.05 mg.kg⁻¹ midazolam, 1-2 mg.kg⁻¹ propofol, and 0.6 mg.kg⁻¹ rocuronium. A laryngeal mask was inserted after 2 min of rocuronium administration. The entire course of anesthesia was maintained using 4-8 mg.kg⁻¹.h⁻¹ propofol and remifentanil 5-12 µg.kg⁻¹.h⁻¹, which sustained the changing of BP and HR within 20% of the initial levels. The analgesics of three groups used in this study were prepared in a 20

ml syringe and were encoded to maintain the double-blinded nature of the study. When surgeons sutured the platysma muscle during the course of the operation, 0.2 µg.kg⁻¹ sufentanil (S group), 2 mg.kg⁻¹ tramadol (T group), or 0.1 mg.kg⁻¹ dezocine (D group) was administered intravenously for postoperative pain control depending on different groups. According to reports, 0.2 µg.kg⁻¹ sufentanil [11, 12], 2 mg.kg⁻¹ tramadol [13, 14], and 0.1 mg.kg⁻¹ dezocine [10, 15] were the optimal dosages of each drug for postoperative analgesia considering analgesia, side effects, and the overall satisfaction index. Anesthetic infusion was terminated when skin suturing was initiated.

The examiner for data collection was blinded to group assignment. BP and HR of the patients were recorded at baseline (T1), the time of postoperative analgesics administration (T2), the time of termination of anesthetic infusion (T3), extubation (T4), and 5 (T5), 30 (T6), and 60 (T7) min after extubation. The respiration rate (RR) was recorded at T1, T4, T5, T6, and T7. The time of palinesthesia (from the discontinuation of propofol and remifentanil infusion to the patients opening their eyes), the time of extubation (from the discontinuation of propofol and remifentanil infusion to TV > 300 ml and RR > 10 breaths.min⁻¹), and the time of submitting orders (from the discontinuation of propo-

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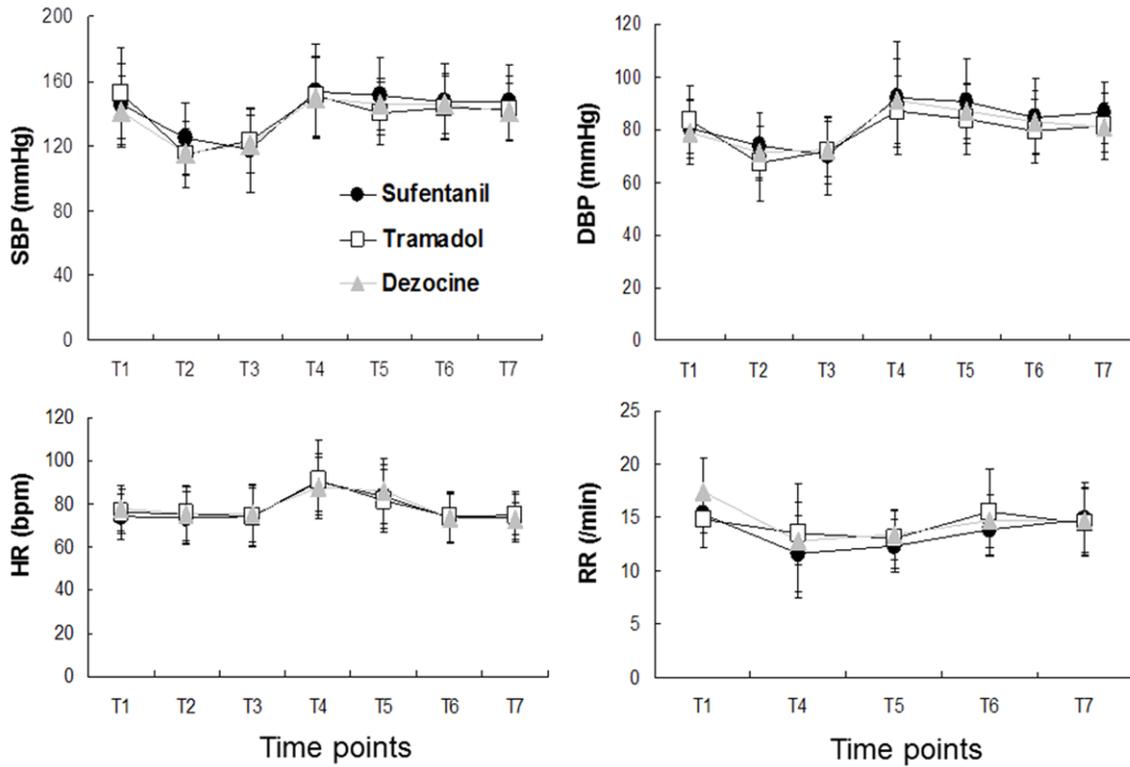


Figure 1. SBP, DBP, HR, and RR of the three groups at different time points. No intergroup differences were found at any time point. T1 = prior to anesthesia; T2 = administration of the study drugs; T3 = end of anesthesia; T4, T5, T6, and T7 = 0, 5, 30, and 60 min after extubation, respectively.

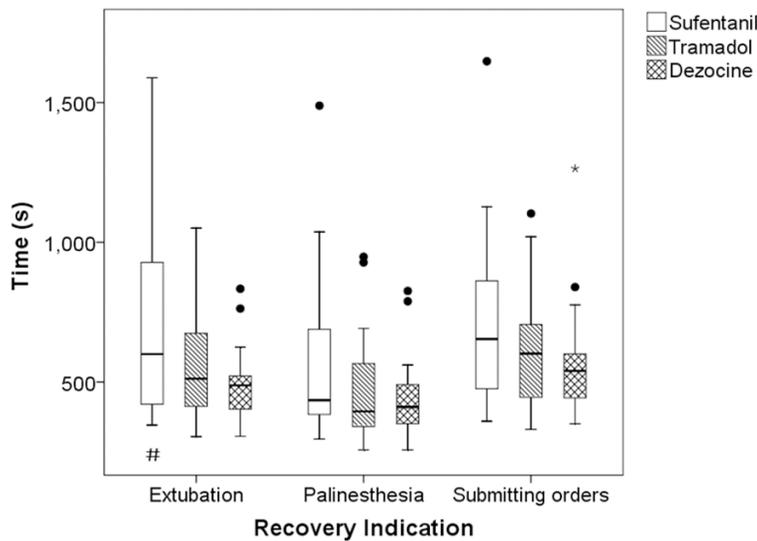


Figure 2. The time of extubation, palinesthesia, and submitting orders in the three groups. *Represents the highest value; *Represents an outlier; #Significant difference compared with the dezocine group.

the tongue and shaking hands by patients) were recorded.

The analgesic effects and the frequency of side effects during the first hour of the post-anesthesia period were evaluated. Visual analog scale (VAS, 0 = no pain, 10 = the most excruciating pain) [16] and overall pain performance scores (OPPS, showed in **Table 1**, 0 = no pain, 3 = severe pain) were assessed for pain management at T5, T6, and T7. Bruggemann comfort scale (BCS, 0 = persistent pain, 4 = no pain at coughing) [17] were evaluated at T4, T5, T6, and T7. Observer's assessment of alertness/sedation (OAA/S, 0 = does not respond to mild prodding and shaking, 5 = responds readily to name spoken in normal tones) [18] and Ramsay sedation scale (RSS, 1

fol and remifentanyl infusion to the successful performance of the commands of sticking out

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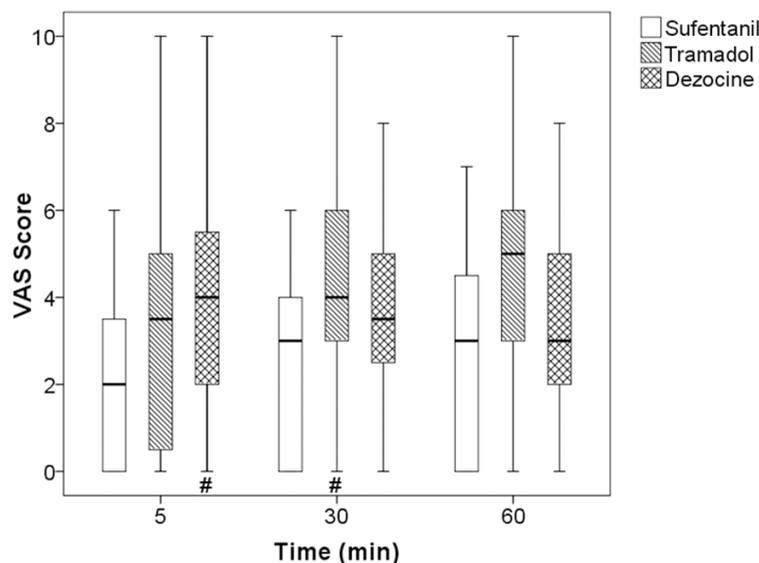


Figure 3. VAS scores at 5, 30, and 60 min after extubation in the three groups. #Significant difference compared with the sufentanil group.

= anxious and agitated or restless, 6 = no response) [19] were assessed for consciousness and sedation at T4, T5, T6, and T7. If the patient indicated a VAS score ≥ 4 , 1/3 of the initial dose of the analgesic was administered (IV) to obtain a VAS score < 4 . If the VAS score remained ≥ 4 ten minute later, the same dose was administered. The frequencies of additional study drugs were recorded. Side effects, including nausea, vomiting, headache, dizziness, respiratory depression (RR < 10 breaths. min^{-1}), and itching, were recorded at T5, T6, and T7. If vomiting occurred, 8 mg of ondansetron was administered.

Statistical analysis

Statistical analysis was performed using the SAS program. The data were presented as either the means \pm SD or numbers. The ASA physical status and sex were analyzed using Fisher's exact test. The general characteristics of the patients and the times of extubation, palinesthesia, submitting orders, and the frequencies of using each postoperative analgesic drug were analyzed using a Kruskal-Wallis *H* test. A Chi-square test was used to detect differences of side effects. The VAS, BCS, OPPS, OAA/S, and RSS scores and the hemodynamic and respiratory parameters were analyzed via ANOVA followed by the Bonferroni's test. *P* values < 0.05 were considered significantly different.

Results

There were no differences in age, ASA status, and sex between the three groups (Table 2). The doses of propofol and remifentanyl during general anesthesia were no difference between the three groups. The body weight of the patients in the S group was larger than that in groups T and D ($P < 0.05$). BP, HR, and RR were no intergroup differences throughout the observation period (Figure 1).

The extubation time was 705 ± 323 s, 571 ± 200 s, and 492 ± 124 s in groups S, T, and D, respectively (Figure 2). The extubation time in the S group was longer than in the group

D ($P < 0.05$). The times of palinesthesia and submitting orders were no difference between the three groups. The VAS scores of the S group were lower than the D group at T5 and were lower than the T group at T6 ($P < 0.05$, Figure 3). The VAS score were no differences at T7 between the three groups. RSS, OAA/S, OPPS, and BCS scores were no difference between the three groups at any time point (Figure 4). The frequency of additional analgesic administration in the S group was less than in the T group (Table 3). No significant differences in the side effects of the study analgesics were observed between the three groups (Table 4).

Discussion

It is generally recognized that postoperative pain is inefficiently treated by physicians and nurses. The major cause of this attitude by the medical staff is their fear of the side effects of the narcotic analgesics, especially of respiratory depression and addiction liability. The selection of postoperative analgesics should balance enhancing postoperative analgesia, reducing side effects, delaying the time of extubation, and prolonging the stay at PACU. From our results, the administration of sufentanil induced more effective analgesia than tramadol and dezocine for postoperative pain management after thyroidectomy. Sufentanil transiently depressed respiratory and delayed the extubation compared with dezocine. Sufentanil

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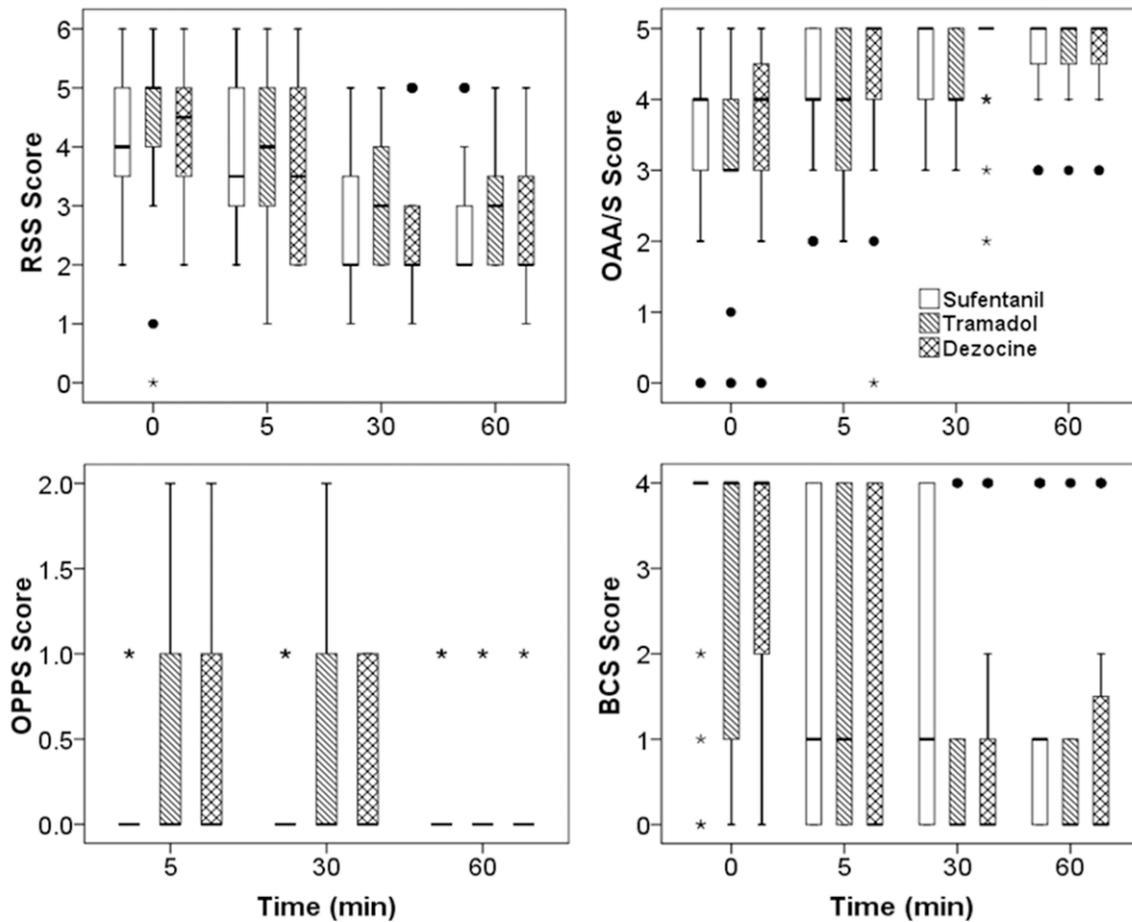


Figure 4. BCS, OPSS, OAA/S, and RSS scores at 0, 5, 30, and 60 min after extubation in the three groups. No inter-group differences were found at any time point. *Represents the highest value; *Represents an outlier.

Table 3. The frequency of additional analgesic administration in the three groups

	Sufentanil*	Tramadol	Dezocine
	n (%)	n (%)	n (%)
No additional doses	23 (76.7)	15 (50.0)	15 (50.0)
One additional dose	5 (16.7)	4 (13.3)	8 (26.7)
Two additional doses	2 (6.6)	11 (36.7)	7 (23.3)

*Significant difference compared with the tramadol group ($P = 0.043$).

did not prolong the time of palinesthesia and submitting orders compared with tramadol and dezocine. No differences on nausea, vomiting, headache, dizziness, and itching were observed between the three groups.

The optimal dosages of the analgesics used in this study, $0.2 \mu\text{g.kg}^{-1}$ sufentanil, 2mg.kg^{-1} tramadol, and 0.1mg.kg^{-1} dezocine, were chosen according to previous reports which were com-

monly administrated for postoperative pain management [10-15]. Increased cardiocirculatory stability and superior intraoperative and postoperative analgesia was achieved by treating patients with $0.2 \mu\text{g.kg}^{-1}$ sufentanil rather than remifentanyl or fentanyl [11, 12]. A treatment dose of 50mg tramadol has been shown to satisfy the requirements for moderate postoperative pain control, whereas a larger dose was needed for the control of severe pain [13]. The intraoperative administration of 2mg.kg^{-1} tramadol has been shown to exert the same postoperative analgesic effects as morphine while resulting in earlier recovery and less sedation [14]. In a different study, patients treated with 5mg or 15mg of dezocine exhibited similar analgesic effects, but less sedation was observed in the 5mg dezocine group compared with the 15mg dezocine group [10]. Considering the side effects and overall satis-

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Table 4. Side effects in the three groups

	Sufentanil	Tramadol	Dezocine	P value
	n (%)	n (%)	n (%)	
Nausea	2 (6.7)	6 (20.0)	2 (6.7)	0.17
Vomiting	0 (0)	2 (6.7)	2 (6.7)	0.35
Headache and dizziness	8 (26.7)	11 (36.3)	12 (40.2)	0.53
Respiratory depression	1 (3.3)	0 (0)	1 (3.3)	0.60
Total	11 (36.7)	19 (63.0)	17 (56.9)	0.10

faction index, 0.1 mg.kg⁻¹ dezocine has been shown to be the optimal dosage for postoperative analgesia in elderly patients [15].

In this study, the VAS scores in the sufentanil group were lower than in the dezocine group at 5 min after extubation and were lower than in the tramadol group at 30 min after extubation. Meanwhile, the frequency of additional administration of tramadol was more than that of sufentanil during the study period. Sufentanil treatment resulted in greater control of postoperative pain than tramadol or dezocine. Pain and intension induce an increase in sympatho-adrenergic activity leading to cardiac ischemia [20]. The control of postoperative pain is important, especially for patients who are at risk of cardiac diseases [21]. Sufentanil significantly decreased MAP and HR upon extubation and 5 minutes after extubation compared with tramadol in patients undergoing major abdominal surgery [6]. Sufentanil administration was shown to result in less agitation at the end of surgery and to induce greater hemodynamic stability than tramadol during neurosurgery [5]. In this study, BP and HR increased a little bit but not remarkable when extubation compared with baseline. BP and HR were no difference between the three groups. The possible reason may be that post thyroidectomy caused moderate pain leading to less sympatho-adrenergic agitation than the major operation caused severe pain.

The extubation time of the sufentanil group was longer than the dezocine group. It was reported an overdose causing respiratory depression may be more likely in patients receiving sufentanil than in those receiving tramadol [6]. These indicated that sufentanil exerted more influence on respiration than tramadol and dezocine. The times of palinesthesia and submitting orders, OAA/S, and RSS scores were no difference between the three groups in this study. It

indicated there was no difference on the influence of consciousness recovery between sufentanil, tramadol, and dezocine at the dosage of this study.

Nausea and vomiting were the most common postoperative side effects and may be critical factors in postoperative rehabilitation [22]. As reported by Ewalenko et al. [23], thyroidectomy is associated with a high rate of postoperative nausea and vomiting. In our study, no difference on nausea and vomiting were observed between the three groups. In agreement with Cafiero et al. [5, 6], no significant differences in the side effects were observed between sufentanil analgesia and tramadol analgesia after neurosurgery and abdominal surgery. In contrast, according to the study by Vercauteren et al. [8], more failures and more significant side effects, such as nausea and vomiting, were found in using of tramadol for patient-controlled extradural analgesia compared with sufentanil after cesarean section. The influence of sufentanil, tramadol, or dezocine analgesia on nausea and vomiting may depend on the dosages and the different kinds of surgery.

Regarding the limitations of our study, analgesic effects and side effects were evaluated during the first hour of the postoperative period. No data were acquired to evaluate the extended effects of these three analgesics. Furthermore, only the optimal dosage of each analgesic was investigated according to reports but no different dosages of each drug evaluated in this study.

In conclusion, the administration of sufentanil induced more effective analgesia than tramadol and dezocine for postoperative pain management after thyroidectomy. Sufentanil transiently depressed respiratory and delayed the extubation compared with dezocine. No differences on consciousness recovery and other side effects were observed between the three groups.

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Disclosure of conflicts of interest

None.

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