

The influence of high-dose intraoperative remifentanyl on postoperative sore throat: a prospective randomized study

A CONSORT compliant article

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Abstract

Background: Endotracheal intubation for general anesthesia causes postoperative sore throat (POST). This study is designed to evaluate the effect of high-dose remifentanyl on the incidence of POST in patients after general anesthesia.

Methods: Ninety-two patients scheduled for orthopedic lower extremity surgery under general anesthesia were randomly assigned into 1 of 2 groups. In the high-dose remifentanyl (HR) group (n=46), remifentanyl was infused at a rate of 0.25 µg/kg/min and subsequently increased or decreased by 0.05 µg/kg/min per clinical demand. In the low-dose remifentanyl (LR) group (n=46), remifentanyl was infused at a rate of 0.05 µg/kg/min. The incidence of POST was monitored at 0, 2, 4, and 24 hours postoperatively. Complications regarding opioids were compared between groups.

Results: The overall incidence of POST was higher in the HR group compared with that in the LR group [33 (72%) vs 18 (39%), $P = .022$]. The incidence of POST at 0, 2, and 24 hours after surgery was higher in the HR group compared with that in the LR group ($P < .001$, $P = .001$, and $P = .001$, respectively). The incidence of postoperative nausea, vomiting, drowsiness, and headache was similar between the groups. The incidence of postoperative shivering was higher in the HR group than in the LR group [10 (22%) vs 2 (4%), difference 17%, 95% CI 2%–33%, $P = .027$].

Conclusion: A relatively large dose of intraoperative remifentanyl increased the incidence of POST in patients for orthopedic surgery under general anesthesia.

Trial Registration: Clinicaltrials.gov Identifier: NCT03173339.

Abbreviations: ETT = endotracheal tube, HR = high-dose remifentanyl, IQR = interquartile range, LR = low-dose remifentanyl, MAC = minimum alveolar concentration, POST = postoperative sore throat.

Keywords: intubation, pain, pharyngitis, postoperative, remifentanyl

1. Introduction

Postoperative sore throat (POST) is a common and undesirable occurrence after general anesthesia with orotracheal intubation.^[1] POST may decrease the quality of life.^[2,3] The reported incidence of POST ranges from 7% to 90%.^[3,4] Various intraoperative factors such as the size of endotracheal tube

(ETT), the cuff pressure, and the time and manipulations of ETT are related to the incidence of POST.^[3]

Remifentanyl is a short-acting opioid that has rapid onset and rapid recovery.^[5] The infusion of remifentanyl is popular to induce a potent intraoperative analgesia and a fast postoperative recovery. The exceptionally high clearance of remifentanyl by esterases is appropriate for the exposure to high cumulative doses and the rapid titration.^[6] A high-dose infusion of remifentanyl is related to acute tolerance and hyperalgesia.^[6] Its effect on the incidence of POST has not been investigated.

We hypothesized that a high-dose infusion of remifentanyl may increase the incidence of POST for 24 hours postoperatively compared with a low-dose infusion of remifentanyl. This investigation aimed to compare the effects of high-dose remifentanyl on the POST incidence in patients following orthopedic surgery.

2. Methods

2.1. Study population

The Institutional Review Board approved this investigation (Document no.: 2017-04-012). The study was registered at ClinicalTrials.gov (registration no.: NCT03173339) before enrollment. This was a prospective, randomized, double-blind, single-center, placebo-controlled, and parallel group study. A

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total of 92 patients with American Society of Anesthesiologists physical status I, II, and III and aged between 18 and 80 years who were scheduled to undergo orthopedic surgery of the lower extremity under general anesthesia were recruited. Patients with a history of a pre-existing sore throat, previous neck surgery, anticipated difficult intubation, a Mallampati grade greater than 2, more than 1 attempt at intubation, known allergies to remifentanyl, recent upper respiratory infection, pregnancy, friable teeth, use of dexamethasone, use of gastric tube, or severe cardiorespiratory, and hepatic disease were excluded from this study.

2.2. Study procedures and anesthesia

Patients were allocated to 1 of 2 groups: the high-dose remifentanyl (HR) group and low-dose remifentanyl (LR) group. A random number table was generated using the Random Allocation Software (ver. 1.0.0; Isfahan University of Medical Sciences, Isfahan, Iran). The sealed envelope method was applied to conceal the assignments.

The patients were monitored with electrocardiography, noninvasive blood pressure, pulse oximetry, acceleromyography (TOF-watch SX; MSD BV, Oss, the Netherlands), and a bispectral index monitor (A-2000 XP; Aspect Medical Systems, Newton, MA). Propofol of 2 mg/kg and remifentanyl of 1 μ g/kg was administered for the induction of anesthesia. Rocuronium of 0.8 mg/kg was infused to facilitate ETT intubation. An experienced and blinded anesthesiologist (HCK) inserted an ETT (Unomedical, Kedah, Malaysia) while train-of-four counts were monitored with acceleromyography at the adductor pollicis muscle. ETTs that had internal diameters of 7.5 and 7.0 mm were used for males and females, respectively. Laryngoscope with a Macintosh blade with either size 3 or 4 was used for ETT intubation. The ETT was inserted to locate the vocal cords between the 2 black marks on the proximal part of the ETT. Intubation was confirmed by an end-tidal capnography. The ETT cuff was inflated with air. The ETT cuff pressure was set to 20 mm Hg using a manual cuff manometer (VBM Medizintechnik, Sulz, Germany) intraoperatively. A sevoflurane inhalation and continuous remifentanyl infusion was used for the maintenance of anesthesia. Nitrous oxide was not used as part of the anesthetic agents. The ETT cuff pressure was maintained to 20 mm Hg intraoperatively.

In the HR group, a remifentanyl was infused at a rate of 0.25 μ g/kg/min and subsequently titrated by 0.05 μ g/kg/min to maintain the mean blood pressure within $\pm 20\%$ from the baseline and bispectral index in a range of 40 to 60, respectively. The end-tidal concentration of the sevoflurane was maintained at 0.6 minimum alveolar concentration (MAC). In the LR group, remifentanyl was infused at a rate of 0.05 μ g/kg/min. The sevoflurane end-tidal concentration was started at 0.6 MAC and subsequently titrated by 0.5% to 1% increments according to the clinical demand. Attending anesthetists could not be blinded. The average intraoperative sevoflurane concentrations were recorded as the mean age-adjusted MAC to compare the sevoflurane concentration between the groups. The Mapleson method ($MAC^{age} = MAC_{40} \times 10^{[-0.00269 \times (age-40)]}$, MAC_{40} : MAC value at 40 years old) was used to calculate the age-adjusted MAC.^[7]

When the muscle layer was sutured completely, 5 mg of morphine was injected intramuscularly. A total of 100 mL of ropivacaine HCL 1.5 mg/mL was injected into the wound. At the beginning of skin closure, 25 mg of pethidine was infused intravenously. Pyridostigmine (0.3 mg/kg) with glycopyrrolate (0.01 mg/kg) were infused to reverse residual neuromuscular relaxation after the surgery. Oropharyngeal suction was gently

performed under direct vision for the avoidance of the tissue trauma before extubation. Extubation was done after the train-of-four ratio was greater than 90% and response to verbal commands and adequate spontaneous breathing were confirmed. Postoperative pain management was completed with supplemental rescue analgesics such as diclofenac, pethidine, and tramadol. When patients complained of moderate-to-severe pain, 75 mg of diclofenac sodium was infused. When pain did not subside, 25 mg of pethidine was injected also. An addition of 50 mg of tramadol was injected when the pain did not subside after the pethidine and diclofenac sodium injections.

2.3. Outcomes measurements

The Mallampati grade was recorded before the surgery by the investigator who was blinded to the study protocol. The Cormack and Lehane grade was recorded by the anesthesiologist that performed the ETT intubation (HCK). The time-to-intubation was measured as the time between inserting the laryngoscope blade into the mouth of patient and confirming the end-tidal CO₂ >30 mm Hg. The mean arterial blood pressure and heart rate were recorded immediately before intubation and 2 minutes after intubation. The duration of tracheal intubation was measured.

The incidences of POST and hoarseness were assessed by a blind examiner (JHP) at 0, 2, 4, and 24 hours after surgery. POST was assessed at rest (without coughing or deglutition). A POST was assessed on a 4-point scale (0–3) where 0 indicated no POST; 1 denoted a mild POST (complaints of POST only when asked); 2 signified a moderate POST (complaints of POST by oneself); and 3 indicated a severe POST (change in voice or hoarseness that is associated with throat pain). Hoarseness was assessed on a 4-point scale (0–3): 0 denoted no complaint of hoarseness; 1 signified minimal hoarseness (minimal change in quality of speech of which patient answers in the affirmative only when asked); 2 indicated moderate hoarseness (moderate change in quality of speech of which the patient complains by oneself); and 3 signified severe hoarseness (gross change in the quality of voice recognized by the examiner). Postoperative cough was assessed on a 4-point scale (0–3): 0 signified no cough; 1 denoted a mild cough; 2 indicated a moderate cough; and 3 denoted a severe cough. Postoperative wound pain at rest was evaluated using a numerical rating scale of 11 points (0: no pain, 10: worst imaginable pain) at the same time point. Sedation was graded on a 4-point scale (0–3): 0 indicated fully awake; 1 specified somnolent and responsive to verbal commands; 2 denoted somnolent and responsive to tactile stimulation; and 3 signified asleep and responsive to painful stimulation. Shivering was graded on a 5-point scale (0–4): 0 indicated no shivering; 1 denoted peripheral vasoconstriction without visible muscular activity; 2 signified visible muscular activity confined to 1 muscle group; 3 specified visible muscular activity in more than 1 muscle group; and 4 indicated gross muscular activity involving the entire body. Side-effects such as postoperative nausea and vomiting were recorded. A cumulative diclofenac, pethidine, and tramadol requirements were noted at postoperative 24 hours. The number of patients who required additional rescue analgesics was recorded.

The primary endpoint was the incidence of POST during the 24 hours following surgery. The secondary endpoints were the incidence of POST, hoarseness, and cough at postoperative 0, 2, 4, and 24 hours, as well as nausea, vomiting, sedation, shivering, cumulative rescue analgesics requirements, the number of patients who required rescue analgesics and postoperative pain scores during the 24 hours after surgery.

2.4. Statistical analysis

A previous investigation showed that the incidence of POST was about 43% during the 24 hours after general anesthesia with endotracheal intubation.^[8] Assuming that this incidence would increase to 73% in the HR group, 41 patients would be necessary in each group ($\alpha=0.05$ and $\beta=0.20$). Considering a 100% compliance rate and a 10% dropout rate, 46 patients per group were included.

Statistical analyses were performed using the IBM SPSS Statistics software (ver. 22.0; IBM CORP, Armonk, NY). The incidence of POST, hoarseness, cough, nausea, vomiting, shivering, sedation, and the number of patients with the use of additional rescue analgesics were assessed using a χ^2 test, or if there were 5 or less values per cell, the Fisher exact test. Continuous variables were compared using a Mann–Whitney *U* test or Student *t* test after a normality test (Kolmogorov–Smirnov test). The alpha value was adjusted with Bonferroni correction to

compare the incidence of POST, hoarseness, cough, and pain scores between groups at each time point. The *P* values were compared to adjust the alpha values. Otherwise, a *P* value of less than .05 was considered statistically significant. Data are presented as mean \pm standard deviation or number (percentage).

3. Results

A total of 102 patients from June 2017 to September 2017 were screened and 10 patients were excluded: 4 patients for multiple laryngoscopy, 2 patients for history of neck surgery history, 2 patients for a Mallampati grade greater than 2, and 2 patients for having hepatic disease. The data of 92 patients were analyzed in the final analysis (Fig. 1). There were no statistically significant differences in the patients' baseline characteristics between the groups (Table 1).

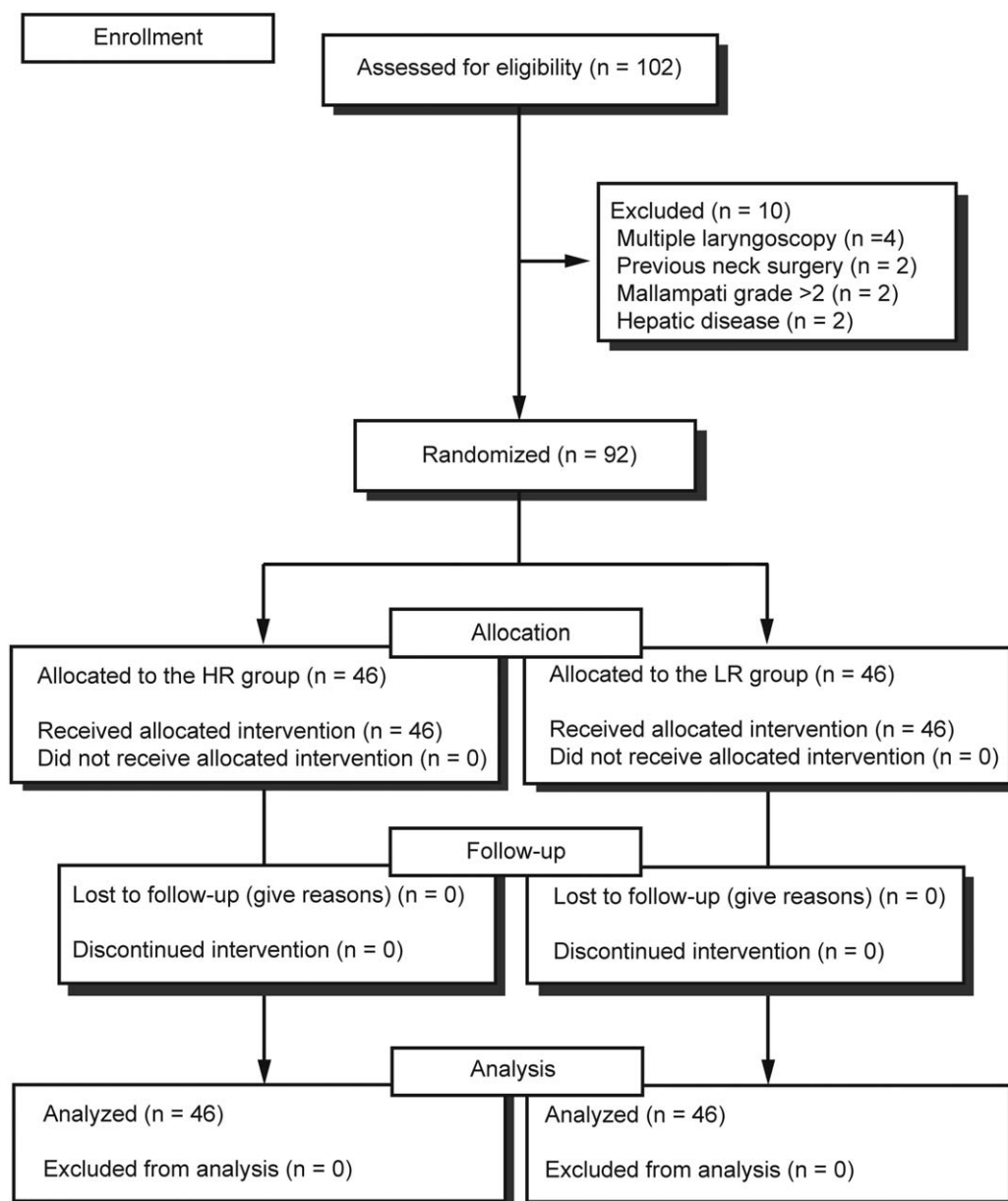


Figure 1. CONSORT diagram for the investigation. Ninety-two patients were randomized and included into final analysis.

Table 1**Patient and anesthetic characteristics.**

	HR (n = 46)	LR (n = 46)	P
Age, yrs	65 ± 9	63 ± 12	.380
Female/male	28 (61%)/18 (39%)	27 (59%)/19 (41%)	.832
Weight, kg	59 ± 12	58 ± 12	.821
Height, cm	158 ± 10	159 ± 10	.736
Body mass index, kg/m	23.5 ± 4.0	22.9 ± 3.1	.411
ASA-PS, I/II/III	14 (30%)/30 (65%)/2 (5%)	14 (30%)/30 (65%) 2 (5%)	1.000
Type of surgery			.470
Total hip replacement	36 (78%)	33 (72%)	
Femur, open reduction and fixation	10 (22%)	13 (28%)	
Time to intubation, s	34 ± 11	34 ± 10	.968
Duration of tracheal intubation, min	177 ± 52	167 ± 41	.268
Mallampati grade, I/II	17 (37%)/29 (63%)	18 (39%)/28 (61%)	.830
C-L grading scale, I/II/III	19 (41%)/26 (57%)/ 1 (2%)	17 (37%)/ 27 (59%)/ 2 (4%)	.793
Mean arterial pressure, mm Hg			
Before intubation	82 ± 16	79 ± 15	.352
2 min after intubation	114 ± 23	113 ± 25	.781
Heart rate, beats/min			
Before intubation	83 ± 14	82 ± 15	.762
2 min after intubation	102 ± 18	100 ± 17	.580

Values are presented as the mean ± SD or the number (%) of patients.

ASA-PS = American Society of Anesthesiologists physical status, C-L = Cormack-Lehane, HR = high-dose remifentanyl group, LR = low-dose remifentanyl group.

The overall incidence of POST was higher in the HR group compared with the LR group [33 (72%) vs 18 (39%), difference 33%, 95% confidence interval (CI) 11% to 51%, $P = .002$, Table 2, Fig. 2]. The incidence of POST at 0, 2, and 24 hours after surgery was higher in the HR group compared with that in the LR group [$P < .001$, $P = .001$, and $P = .001$ respectively]. The incidence of POST at postoperative 4 hours was comparable. The incidence of moderate to severe POST was comparable between groups at all time points. The incidence of hoarseness and cough was comparable between groups at all time points.

The postoperative wound pain scores at 0, 2, 4, and 24 hours postoperatively were comparable (Fig. 3). The number of patients who require rescue analgesics was higher in the HR group compared with that in the LR group [37 (80%) vs 24 (52%), difference 28%, 95% CI 7 to 46%, $P = .004$]. The postoperative diclofenac sodium, pethidine, and tramadol requirements were higher in the HR group than that in the LR group ($P = .001$, $P = .008$, and $P < .001$, respectively, Table 3).

The incidence of nausea [15 (33%) vs 10 (22%), difference 11%, 95% CI -9% to 30%, $P = .241$], vomiting [3 (7%) vs 2

Table 2**Incidence and severity of postoperative sore throat, hoarseness, and cough.**

	HR (n = 46)	LR (n = 46)	Difference (95% CI)	P
Sore throat				
Overall incidence	33 (72%)	18 (39%)	33% (11% to 51%)	.002
Postoperative 0 h (none/mild/moderate/severe)	23 (23/17/3/3)	5 (41/2/3/0)	39% (19% to 55%)	<.001
Postoperative 2 h (none/mild/moderate/severe)	26 (20/21/2/3)	10 (36/9/0/1)	35% (13% to 52%)	.001
Postoperative 4 h (none/mild/moderate/severe)	18 (28/15/1/2)	11 (35/8/2/1)	15% (-5% to 34%)	.116
Postoperative 24 h (none/mild/moderate/severe)	16 (30/13/2/1)	4 (42/4/0/0)	26% (8% to 43%)	.001
Hoarseness				
Overall incidence	20 (44%)	14 (30%)	13% (-8% to 33%)	.195
Postoperative 0 h (none/mild/moderate/severe)	11 (35/9/2/0)	8 (38/5/3/0)	7% (-12% to 24%)	.440
Postoperative 2 h (none/mild/moderate/severe)	13 (33/12/1/0)	9 (37/7/2/0)	9% (-10% to 27%)	.328
Postoperative 4 h (none/mild/moderate/severe)	13 (33/12/1/0)	6 (40/6/0/0)	15% (-3% to 32%)	.071
Postoperative 24 h (none/mild/moderate/severe)	12 (34/11/1/0)	5 (41/5/0/0)	15% (-2% to 32%)	.060
Cough				
Overall incidence	3 (7%)	5 (11%)	4% (-10% to 19%)	.714
Postoperative 0 h (none/mild/moderate/severe)	0 (46/0/0/0)	0 (46/0/0/0)	0% (-10% to 10%)	1.000
Postoperative 2 h (none/mild/moderate/severe)	1 (45/1/0/0)	2 (44/2/0/0)	2% (-9% to 14%)	1.000
Postoperative 4 h (none/mild/moderate/severe)	1 (45/1/0/0)	1 (45/1/0/0)	0% (-11% to 11%)	1.000
Postoperative 24 h (none/mild/moderate/severe)	1 (45/1/0/0)	4 (42/4/0/0)	7% (-6% to 20%)	.361

Values are presented as the number (%) of patients. P value was adjusted to .0125 with Bonferroni correction to compare the postoperative sore throat between the 2 groups at each time point.

CI = confidence interval, HR = high-dose remifentanyl group, LR = low-dose remifentanyl group.

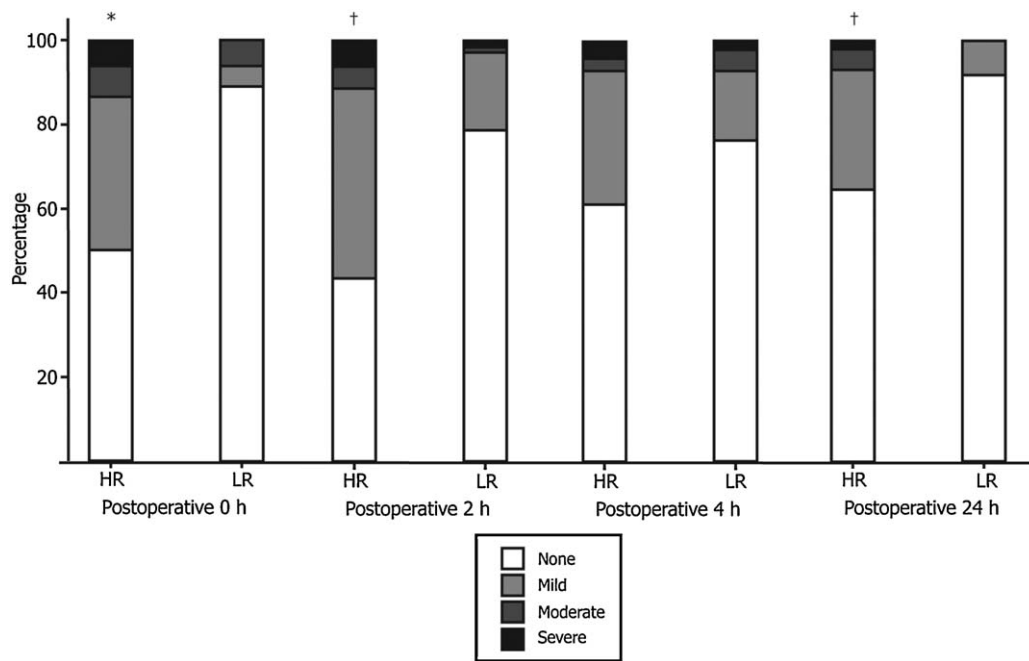


Figure 2. Percentage incidence and severity of postoperative sore throat. * $P < .001$ versus low-dose remifentanyl group, † $P < .05$ versus low-dose remifentanyl group. HR=high-dose remifentanyl group, LR=low-dose remifentanyl group.

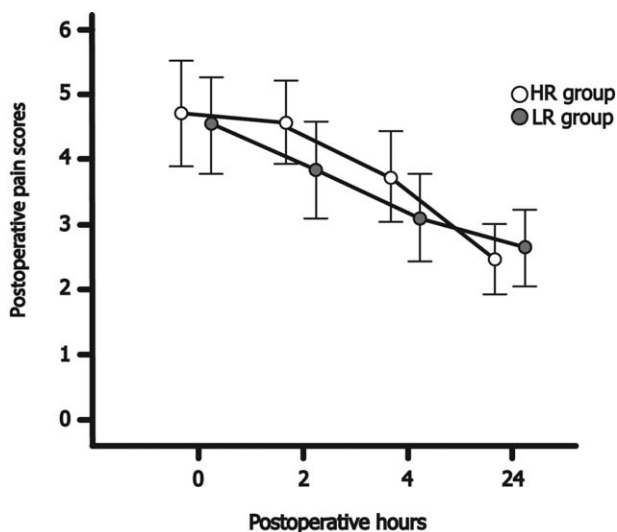


Figure 3. Mean scores of numerical wound pain scores (0: no pain, 10: worst imaginable pain). Error bar shows 95% confidence interval for mean. HR=high-dose remifentanyl group, LR=low-dose remifentanyl group.

(4%), difference 2%, 95% CI -10% to 15%, $P=1.000$], and sedation [20 (44%) vs 20 (44%), difference 0%, 95% CI -21% to 21%, $P=1.000$] was comparable during the entire investigation period. The incidence of shivering was higher in the HR group compared with that in the LR group [10 (22%) vs 2 (4%), difference 17%, 95% CI 2% to 33%, $P=.027$].

4. Discussion

This investigation showed that the high-dose remifentanyl during surgery increased the overall POST incidence. The detrimental effect of high-dose remifentanyl lasted for 24 hours following surgery. The high-dose remifentanyl increased the number of patients requiring rescue analgesics for 24 hours, as well as the rescue analgesic requirements. The high-dose remifentanyl also increased the incidence of shivering postoperatively.

Patients after general anesthesia with airway instrumentation often complain of POST, although it is regarded as a minor complication. The cause of POST might be an inflammation through the injury of the pharyngeal and tracheal mucosa during airway manipulation.^[2,9] Remifentanyl is known to increase pain by central sensitization of nociceptive pathways and descending

Table 3
Perioperative anesthetic and analgesic requirements.

	HR (n=46)	LR (n=46)	Difference (95% CI)	P
Age adjusted MAC	0.6 (0.0)	0.9 (0.2)	0.9 (-1.5 to 3.2)	<.001
Intraoperative remifentanyl, $\mu\text{g}/\text{kg}/\text{min}$	4.9 (2.4)	2.7 (1.1)	2.3 (1.5 to 3.1)	<.001
Diclofenac sodium, mg	75 (0)	75 (75)	31 (10 to 52)	.001
Pethidine, mg	25 (25)	0 (25)	9 (1 to 16)	.008
Tramadol, mg	0 (50)	0 (0)	21 (5 to 11)	<.001

Values are presented as the median (interquartile range). Age-adjusted MAC was calculated using Mapleson method ($\text{MAC}_{\text{age}} = \text{MAC}_{40} \times 10^{[-0.00269 \times (\text{age}-40)]}$), MAC_{40} : MAC value at 40-yr old).^[7] CI=confidence interval, HR=high-dose remifentanyl group, LR=low-dose remifentanyl group, MAC=minimum alveolar concentration.

pain modulatory system.^[10,11] Sore throat pain due to submucosal tear,^[12] may be enhanced by these mechanisms of pain enhancement of remifentanyl in our investigation. Intraoperative variables such as the use of a smaller endotracheal tube, low intracuff pressure, and cuffs filled with lidocaine are the common methods for the prevention of POST.^[12–16] The effect of intraoperative anesthetic agents such as inhalational agents or opioids on POST, however, has not been studied. The factors regarding intubation such as the time to intubation, the duration of intubation, and the difficulty of intubation may influence the incidence of POST.^[12,17] The adequate dose of remifentanyl is known to improve conditions for intubation.^[18] We controlled for the variables regarding intubation to investigate the effect of high-dose remifentanyl on the incidence of POST. In this investigation, the infusion of high-dose remifentanyl increased the incidence of POST by 33% for postoperative 24 hours.

Previous investigations demonstrated that remifentanyl increases postoperative pain for up to 4 hours following surgery.^[19,20] In our study, however, a high-dose infusion of remifentanyl increased the incidence of POST for up to 24 hours. Joly et al^[21] demonstrated that a high-dose of remifentanyl decreases tactile pain thresholds adjacent to the wound up to 48 hours postoperatively. A high-dose infusion of remifentanyl increases the verbal numerical rating scale of pain in patients undergoing thyroidectomy at 48 hours postoperatively.^[22] Whether a long duration of detrimental effects of intraoperative high-dose remifentanyl on POST is related to the tolerance of acute opioids or hyperalgesia needs to be investigated.

The incidence of POST in this investigation was relatively lower than that in the previous reports.^[16,23,24] POST can be influenced by factors such as younger age,^[25] ETT cuff pressure,^[26] and type of surgery.^[12] In our investigation, relatively older patients were included. The intraoperative nitrous oxide is known to diffuse into the ETT cuff and results in the increase of the ETT cuff pressure.^[27] Nitrous oxide was not used and the ETT cuff pressure was maintained at 20 mm Hg in our investigation. We enrolled patients for lower extremity surgery to minimize the influence on the airway. These variables may explain the relatively lower POST incidence in this study.

High-dose remifentanyl infusion is known to increase postoperative surgical pain.^[6,19] The wound pain scores, however, were similar between the 2 groups in our investigation. The number of patients included in this study may not have been adequate to detect the statistical differences in postoperative wound pain scores. Patients in which high-dose remifentanyl was infused required more diclofenac sodium, pethidine, and tramadol in our investigation. Those postoperative supplemental analgesics may reduce the wound pain scores. Intravenous diclofenac sodium has no effect on the prevention of POST;^[28] although, the topical approach of diclofenac sodium decreased the incidence of POST.^[29] The effect of parenteral pethidine or tramadol on the prevention or treatment of POST has not been studied. In this study, higher requirements of pethidine or tramadol in the patients with high-dose remifentanyl infusion failed to reduce the incidence of POST. The influence of additional rescue analgesics on the incidence of POST needs to be further investigated.

The high-dose remifentanyl infusion increased the incidence of shivering in this investigation. The investigation by Nakasuji et al^[30] demonstrated that intraoperative high-dose remifentanyl increased postanesthetic shivering in patients undergoing gynecological laparotomy. The incidence of shivering in our study, however, is lower than that of the previous investigation. A younger age is the most important risk factor for postoperative

shivering.^[31] Pethidine is known to decrease postoperative shivering.^[32] In our protocol, relatively older patients were enrolled and pethidine was infused for surgical pain management. The difference in the population and postoperative pain management protocol may contribute to differences of the postoperative shivering incidence.

The current study had some limitations. First, the test that can differentiate POST, wound pain from hyperalgesia or acute opioids tolerance was not performed. Application of a quantitative sensory test of the mechanical pain threshold using von Frey filament may be necessary in the future reports. Second, patients were enrolled following total hip replacement or open reduction and fixation of the femur. The duration of total hip replacement is usually longer than that of open reduction and fixation of the femur. The duration of intubation and postoperative surgical pain may affect the incidence and severity of POST. The distribution of surgery type, however, was similar between groups. Third, POST and wound pain score are subjective variables. Moreover, airway instrumentation including oral suctioning and extubation may cause airway injury which is related to the incidence and severity of POST. To minimize bias, our study applied a double-blind randomized controlled design. Fourth, using low-dose remifentanyl may negatively impact on stress response. Remifentanyl is known to counteract cortisol response during laparoscopic cholecystectomy.^[33] Monitoring stress response in anesthesia using remifentanyl may be necessary to infuse the adequate dose of remifentanyl.^[34] Fifth, we failed to figure out the mechanism regarding POST and high-dose remifentanyl. Further investigation in mechanism of action of remifentanyl which may lead to sore throat is necessary. Sixth, the dose of remifentanyl for induction was controlled between groups. The adequate dose of remifentanyl enhances the conditions of the intubation.^[18] The influence of high-dose remifentanyl at anesthetic induction on the incidence of POST needs to be studied.

5. Conclusions

This investigation found the adverse effect of using the high-dose remifentanyl infusion for patients following general anesthesia with ETT intubation. The infusion of high-dose remifentanyl increased the POST incidence for 24 hours following surgery. We recommend the preventative treatment for POST in patients under general anesthesia using high dose of remifentanyl infusion.

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