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ORIGINAL ARTICLE

Influence of intraoperative sevoflurane or desflurane on postoperative sore throat: a prospective randomized study

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Abstract

Purpose Tracheal intubation for general anesthesia causes postoperative sore throat. The purpose of this study was to evaluate the effect of sevoflurane and desflurane on prevalence of postoperative sore throat in patients after general anesthesia.

Methods Ninety-six patients scheduled for orthopedic lower extremity surgery under general anesthesia were assigned to sevoflurane group or desflurane group. In the sevoflurane group ($n=48$), sevoflurane was used as a maintenance anesthetic agent. In the desflurane group ($n=48$), desflurane was used. Prevalence of sore throat, number of patients with rescue analgesics, and analgesics requirements were evaluated.

Results The overall prevalence of postoperative sore throat in the sevoflurane group was lower than that in the desflurane group [21 (44%) vs. 32 (67%), $p=0.024$]. The prevalence of sore throat at postoperative 4 h in the sevoflurane group was lower than that in the desflurane group [6 (13%) vs. 18 (38%), $p=0.005$]. The number of patients requiring rescue analgesics was lower in the sevoflurane group [25 (52%) vs. 36 (75%), $p=0.020$]. The requirement of diclofenac was also lower in the sevoflurane group (30 ± 37 mg vs. 47 ± 40 mg, $p=0.031$).

Conclusions We have shown that sevoflurane was associated with less frequent sore throat than desflurane in patients undergoing orthopedic lower extremity surgery.

Keywords Sevoflurane · Desflurane · Pharyngitis · Intubation · Pain, postoperative

Introduction

Postoperative sore throat is a common complication in patients after general anesthesia with tracheal intubation, with prevalence ranging from 7 to 90% [1–3]. Sore throat may worsen the quality of recovery after surgery [2, 4]. The cause of postoperative sore throat is associated with inflammation and irritation by tracheal intubation [5]. Thermosoftening, magnesium, and steroids are known to prevent sore throat after surgery [6–8].

Sevoflurane and desflurane are the most commonly used inhalational anesthetic agents. Higher postanesthesia recovery score with desflurane after discontinuation of anesthesia compared with sevoflurane has been reported [9]. Compared with sevoflurane, desflurane is a more pungent and irritating agent to the airway [10]. Desflurane is related to higher prevalence of cough in patients after outpatient surgery [11]. Desflurane leads to higher prevalence of postoperative sore throat in patients using laryngeal mask undergoing minor ambulatory knee surgery than sevoflurane [12]. Previous investigation regarding standard anesthetic technique using sevoflurane or desflurane in patient undergoing middle ear microsurgery has shown that there is no difference in the prevalence of sore throat between the two groups [13].

Orthopedic lower extremity surgery including total hip replacement and fixation of femur fracture is a major operation with relatively long procedure time [14, 15]. Prolonged duration of anesthetic time and tracheal intubation are known risk factors of sore throat after surgery [16]. However, the influence of sevoflurane or desflurane on the prevalence of postoperative sore throat in patients undergoing tracheal intubation for major surgery with long procedure time has not been reported yet.

The hypothesis of this investigation was that intraoperative desflurane inhalation could increase the prevalence of sore throat related to tracheal intubation compared with

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intraoperative sevoflurane inhalation in patients undergoing major orthopedic lower extremity surgery. Thus, the objective of this study was to determine effects of intraoperative desflurane inhalation compared with sevoflurane inhalation on the prevalence of sore throat in patients after tracheal intubation for major orthopedic lower extremity surgery.

Methods

This study was approved by the Research Ethics Board (Document no. 2017-08-030) of Keimyung University in South Korea. Patients enrollment was conducted after registration at ClinicalTrials.gov (Registration no. NCT 03259672). This investigation was a single-center, prospective, randomized, double-blind, and parallel group study. Patients aged 18–80 years with American Society of Anesthesiologists physical statuses I–III who were scheduled to receive orthopedic lower extremity surgery under general anesthesia were included in the present investigation. Patients having a history of recent sore throat, recent upper respiratory infection, chronic cough, past neck surgery, anticipated difficult airway, friable teeth, a Mallampati grade > 2, multiple attempts at intubation, known allergies to sevoflurane or desflurane, malignant hyperthermia, pregnancy, use of dexamethasone, use of gastric tube, or severe cardiorespiratory and hepatic disorder were excluded.

Patients were allocated into sevoflurane group or desflurane group. Random Allocation Software version 1.0.0 (Isfahan University of Medical Sciences, Isfahan, Iran) was used to allocate patients. Opaque-sealed envelope with random number assignment was opened before patients entered the investigation. Patients and examiners of postoperative outcomes were blinded to allocations. The attending anesthetists could not be blinded.

Patients were monitored with pulse oximetry, electrocardiography, and non-invasive blood pressure. Bispectral index monitor A-2000 XP (Aspect Medical Systems, Newton, MA, USA) was used to measure the depth of anesthesia. Acceleromyography (TOF-watch SX; MSD BV, Oss, The Netherlands) was used to measure the degree of neuromuscular blockade. Preoxygenation was performed. Propofol of 2 mg/kg and remifentanil of 1 μg/kg were infused for the induction of anesthesia. After loss of consciousness, rocuronium of 0.8 mg/kg was infused to facilitate tracheal intubation. Direct laryngoscopy was performed with a Macintosh blade (size 3 or 4) for tracheal intubation. Tracheal intubation was performed by an anesthesiologist (SK) using tracheal tube (Unomedical, Kedah, Malaysia) with an internal diameter of 7.0 for female and 7.5 mm for male. The tracheal tube was positioned to place vocal cords between two depth marker lines on the tracheal tube. The cuff of tracheal tube was inflated with air. The cuff pressure of tracheal tube of 20 mmHg was maintained using a manual cuff manometer (VBM Medizintechnik, Sulz, Germany) intraoperatively. Intubation was confirmed by observing end-tidal capnography.

In the sevoflurane group, sevoflurane inhalation and continuous remifentanil infusion were applied for maintenance of anesthesia. In the desflurane group, desflurane was inhaled and remifentanil was infused continuously. The concentration of inhalational agents and the infusion rate of remifentanil were titrated by the attending anesthetists to maintain bispectral index between 40 and 60 and mean blood pressure within 20% of baseline values. Average intraoperative sevoflurane and desflurane concentrations were documented as the mean age-adjusted minimum alveolar concentration (MAC) to compare sevoflurane and desflurane concentrations between groups. Mapleson's method ($MAC^{age} = MAC_{40} \times 10^{[-0.00269 \times (age-40)]}$, MAC_{40}: MAC value at 40 years) was used to calculate age-adjusted MAC [17]. The average concentration of intraoperative remifentanil was recorded and compared. After completing the procedure, residual neuromuscular relaxation was reversed with pyridostigmine (0.3 mg/kg) and glycopyrrolate (0.01 mg/kg). Ramosetron 0.3 mg was administered to prevent postoperative nausea and vomiting. Oropharyngeal secretion was carefully aspirated to prevent tissue trauma before extubation. After the train-of-four ratio was greater than 90% with response to verbal commands and adequate spontaneous breathing, extubation was done.

Postoperative pain was managed with infiltration of local anesthetic agents and morphine as well as supplemental rescue pain medications. Morphine (5 mg) was injected intramuscularly after muscle layer repair. Ropivacaine HCL 150 mg (total volume 100 ml) was injected into the wound. Intravenous pethidine 25 mg was slowly infused when skin closure was started. Postoperative wound pain, while rest was evaluated by an 11-point verbal numerical rating scale (0 no pain, 10 worst imaginable pain). Supplemental rescue pain medication such as diclofenac, pethidine, or tramadol was used for moderate-to-severe pain (pain scores 4–10). When moderate-to-severe pain was present, 75 mg of diclofenac sodium was infused. When pain did not adequately disappear (pain score of 4–10) and patients asked for additional pain rescue analgesics, 25 mg of pethidine was injected additionally. Tramadol 50 mg was injected when pain did not subside after pethidine and diclofenac sodium injections (pain scores of 4–10).

The anesthesiologist (JHP) blinded to the study's protocol evaluated Mallampati grade preoperatively. The investigator (SK) who performed tracheal intubation assessed Cormack and Lehane grade. Time-to-intubation was determined as the time when the blade of laryngoscope was inserted into the mouth of the patient until end-tidal $CO_2 > 30$ mmHg was confirmed. Hemodynamic outcomes including heart rate

and mean blood pressure were recorded immediately before intubation and at 2 min after intubation.

Prevalences of airway complications such as sore throat, hoarseness, and cough were examined by a blind anesthesiologist (JL) at 0, 2, 4, and 24 h after surgery. Sore throat was evaluated while resting. Sore throat was recorded on a four-point scale (0–3): 3, severe sore throat (hoarseness or change in vocalization that is regarded as throat discomfort); 2, moderate sore throat (complaints of sore throat spontaneously); 1, mild sore throat (complaints of sore throat only when asking); and 0, no sign of sore throat. Hoarseness was recorded on a four-point scale (0–3): 3, severe hoarseness (severe change in the quality of speech observed by the investigator); 2, moderate hoarseness (moderate change in quality of voice of which the patient complained by oneself); 1, minimal hoarseness (minimal change in quality of voice of which patient replied only when being asked); and 0, no sign of hoarseness. Postoperative cough was assessed on a four-point scale (0–3): 3, severe cough (greater than noted with a cold); 2, moderate cough (as would be noted with a cold); 1, mild cough (less than noted with a cold); and 0, no cough [18].

The degree of sedation was evaluated as follows: 3, asleep and responsive to painful stimuli; 2, somnolent and responsive to tactile stimuli; 1, somnolent and responsive to verbal commands; and 0, fully awake. Shivering was evaluated as follows with a five-point scale: 4, massive muscular movement of the entire body; 3, obvious muscular movement in more than one muscle; 2, obvious muscular movement restricted to one muscle group; 1, peripheral vasoconstriction without visible muscular movement; and 0, no shivering. Side effects such as postoperative nausea and vomiting were assessed. Cumulative requirements of analgesics such as diclofenac, meperidine, and tramadol were evaluated at postoperative 24 h. The number of patients that required additional rescue analgesics was assessed.

The primary variable was the overall prevalence of sore throat during postoperative 24 h. Secondary variables were the prevalence of sore throat, hoarseness, and cough at 0, 2, 4, and 24 h postoperatively. Prevalences of nausea, vomiting, sedation, shivering, cumulative rescue analgesics requirements, and the number of patients who required rescue pain medications during 24 h after surgery were also compared.

Statistical analysis

A previous investigation showed that the prevalence of sore throat was 57% during 24 h after general anesthesia with tracheal intubation using sevoflurane as a maintenance anesthetic agent [19]. Assuming that this prevalence would increase to 87% in patients following general anesthesia using desflurane, 34 patients per group would be needed with 80% power and two-sided test 5%. Considering a compliance rate of 90% and a dropout rate of 20%, 48 subjects per group were enrolled.

IBM SPSS® Statistics software version 22.0 (IBM CORP., Armonk, NY, USA) was used for statistical all analyses. Prevalence of airway complications (sore throat, hoarseness, and cough), other complications (nausea, vomiting, shivering, and sedation), and the number of patients requiring additional rescue analgesics were analyzed using Chi-square test or Fisher's exact test when necessary. Student's *t* test or Mann–Whitney *U* test was used to compare continuous variables following Kolmogorov–Smirnov test. A *p* value of less than 0.05 was considered statistically different. Data are presented as mean ± standard deviation or number (percentage).

Results

A total of 105 patients were screened from September 2017 to February 2018. Nine patients were excluded including three patients with multiple laryngoscopy, three patients with Mallampati grade greater than 2, and three patients with chronic cough. Finally, 96 patients were recruited in this study (Fig. 1). Baseline characteristics of patients were similar between sevoflurane and desflurane groups (Table 1).

The overall prevalence of sore throat in the sevoflurane group was lower than that in the desflurane group [21 (44%) vs. 32 (67%), difference 23%, 95% confidence interval (CI) 2–42, $p = 0.024$, Table 2]. The prevalence of mild sore throat in the sevoflurane group was lower than that in the desflurane group [15 (31%) vs. 29 (60%), difference 29%, 95% CI 8–47, $p = 0.004$]. Prevalences of moderate-to-severe sore throat were comparable between the two groups. Prevalences of hoarseness and cough were also similar between the two groups.

Prevalences of nausea [15 (32%) vs. 12 (25%), difference 6%, 95% CI − 13 to 25, $p = 0.496$], vomiting [2 (4%) vs. 3 (6%), difference 2%, 95% CI − 10 to 15, $p = 1.000$], and sedation [29 (60%) vs. 27 (56%), difference 2%, 95% CI − 18 to 22, $p = 0.679$] were also similar between the two groups during the entire course of investigation.

The number of patients requiring rescue pain medicines in the sevoflurane group was lower compared with that in the desflurane group [25 (52%) vs. 36 (75%), difference 23%, 95% CI 2–41, $p = 0.020$, Table 3]. Total requirement for diclofenac was lower in the sevoflurane group (30 ± 37 mg vs. 47 ± 40 mg, mean difference 17 mg, 95% CI 2–33, $p = 0.031$). Requirements for pethidine and tramadol were comparable between the two groups ($p = 0.363$ and $p = 0.168$, respectively).

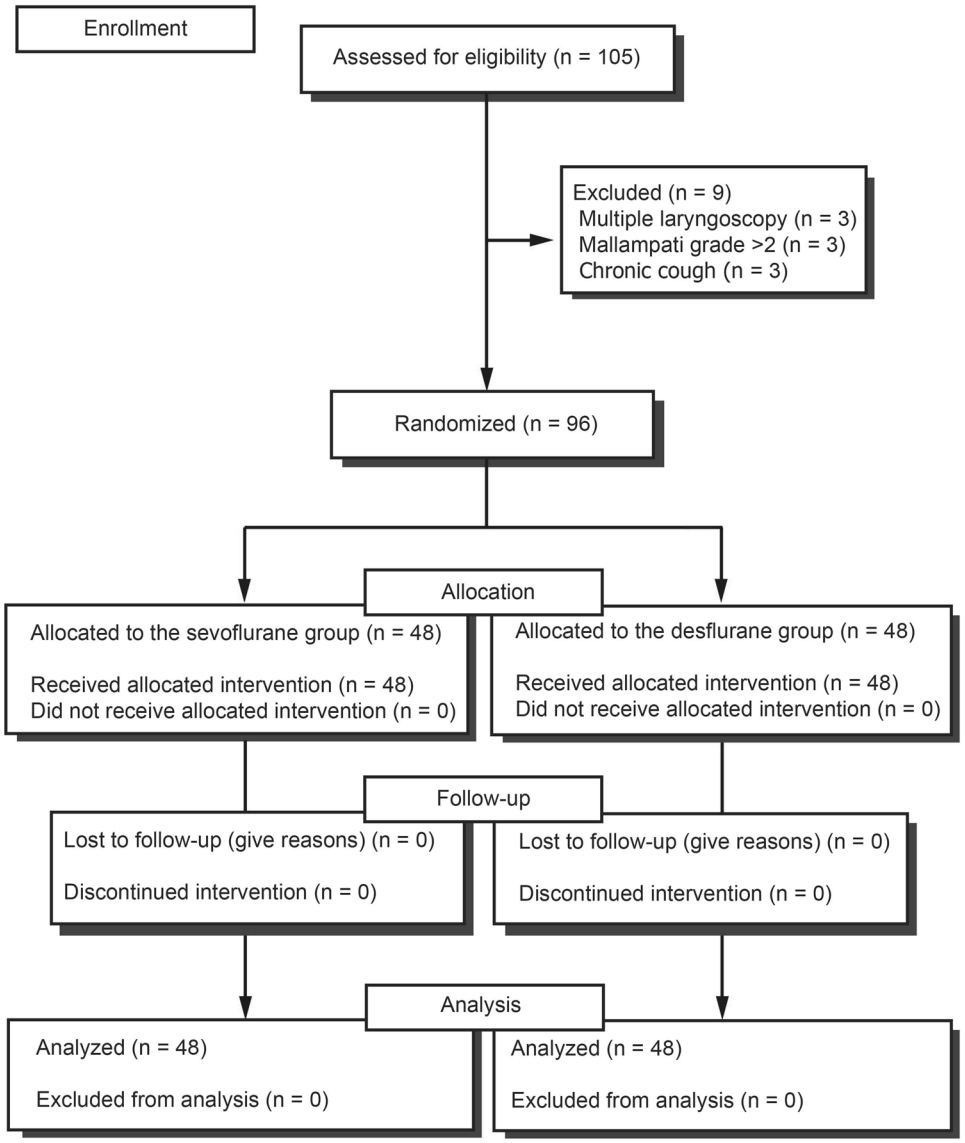

Fig. 1 CONSORT diagram

Discussion

Our investigation showed that sevoflurane was related to less frequent sore throat than desflurane in patients after major orthopedic lower extremity surgery. This is the first study to show that desflurane leads to higher prevalence of sore throat compared with sevoflurane in patients undergoing tracheal intubation. Compared with desflurane, sevoflurane resulted in less number of patients demanding rescue analgesics. It also resulted in less the total amount of analgesics required such as diclofenac required for postoperative 24 h.

Sevoflurane and desflurane have shown different effects on various postoperative outcomes [11, 20–22]. In the present investigation, the sevoflurane group demonstrated less prevalence of postoperative sore throat than the desflurane group. Higher irritation of desflurane may increase upper airway complications [23]. Sore throat is associated with inflammation [5]. Sevoflurane and desflurane can suppress inflammatory responses [24–26]. Desflurane shows greater systemic and intrapulmonary proinflammatory response compared with sevoflurane during anesthesia [27]. More irritation and inflammatory process of desflurane compared with sevoflurane might have resulted in higher prevalence of sore throat in patients undergoing orthopedic surgery under general anesthesia in our study. The faster recovery profiles of desflurane which makes patients complain pain more seriously [9] might have led to higher prevalence of postoperative sore throat in the desflurane group. Desflurane, however, does not affect the prevalence of sore throat for patients after outpatient surgery [28]. Different settings might have influenced the prevalence of sore throat after surgery. Laryngeal mask airway was applied in the previous study [28]. Laryngeal mask airway shows less prevalence of sore throat than tracheal intubation [29]. Less stimulus by

Table 1 Patient and anesthetic characteristics

	Sevoflurane ($n=48$)	Desflurane ($n=48$)
Age, years	62 ± 15	61 ± 14
Female/male	26 (54%)/22 (46%)	23 (48%)/25 (52%)
Weight, kg	62 ± 12	64 ± 13
Height, cm	161 ± 10	163 ± 10
Body mass index, kg/m	23.7 ± 3.1	24.1 ± 3.9
ASA-PS, I/II/III	19 (40%)/22 (46%)/7 (14%)	16 (33%)/29 (60%) 3 (7%)
Type of surgery		
Total hip replacement	36 (75%)	34 (71%)
Femur, open reduction and fixation	12 (25%)	14 (29%)
Time to intubation, s	38 ± 10	37 ± 14
Duration of tracheal intubation, min	169 ± 53	166 ± 51
Mallampati grade, I/II	11 (23%)/37 (77%)	15 (31%)/33 (69%)
C–L grading scale, I/II/III	13 (27%)/35 (73%)/0 (0%)	16 (33%)/31 (65%)/1 (2%)
Mean arterial pressure, mmHg		
Before intubation	81 ± 15	79 ± 13
2 min after intubation	105 ± 27	108 ± 25
Heart rate, beats/min		
Before intubation	80 ± 12	78 ± 16
2 min after intubation	97 ± 15	93 ± 21

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

ASA-PS American Society of Anesthesiologists physical status, *C–L* Cormack–Lehane

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

	Sevoflurane ($n=48$)	Desflurane ($n=48$)	Difference (%) (95% CI)	*p value*
Sore throat				
Postoperative 0 h (none/mild/moderate/severe)	14 (34/10/2/2)	22 (26/19/3/0)		
Postoperative 2 h (none/mild/moderate/severe)	13 (35/11/2/0)	24 (24/23/1/0)		
Postoperative 4 h (none/mild/moderate/severe)	6 (42/6/0/0)	18 (30/17/1/0)		
Postoperative 24 h (none/mild/moderate/severe)	7 (41/5/1/1)	6 (42/5/1/0)		
Overall incidence	21 (44%)	32 (67%)	23 (2 to 42%)	0.024
Hoarseness				
Postoperative 0 h (none/mild/moderate/severe)	19 (29/17/2/0)	18 (30/18/0/0)		
Postoperative 2 h (none/mild/moderate/severe)	19 (29/18/1/0)	22 (26/20/2/0)		
Postoperative 4 h (none/mild/moderate/severe)	10 (38/10/0/0)	17 (31/15/2/0)		
Postoperative 24 h (none/mild/moderate/severe)	7 (41/7/0/0)	11 (37/10/1/0)		
Overall incidence	24 (50%)	27 (56%)	6 (− 15 to 26%)	0.539
Cough				
Postoperative 0 h (none/mild/moderate/severe)	3 (45/3/0/0)	3 (45/3/0/0)		
Postoperative 2 h (none/mild/moderate/severe)	4 (44/4/0/0)	5 (43/5/0/0)		
Postoperative 4 h (none/mild/moderate/severe)	5 (43/5/0/0)	3 (45/3/0/0)		
Postoperative 24 h (none/mild/moderate/severe)	3 (45/3/0/0)	2 (46/2/0/0)		
Overall incidence	8 (17%)	7 (15%)	2 (− 14 to 18%)	0.779

Values are presented as the number (%) of patients

CI confidence interval

laryngeal mask airway compared with tracheal tube might have influenced the prevalence of sore throat. In our investigation, tracheal intubation was done to secure the airway, because total hip replacement and open reduction and fixation of femur required positional change of patients. Such positional change of patients might have influenced the

Table 3 Perioperative anesthetic and analgesic requirements

	Sevoflurane ($n=48$)	Desflurane ($n=48$)	Difference (95% CI)	p value
Age-adjusted MAC	1.0 (0.1)	1.0 (0.1)	0.0 (0.0 to 0.0)	0.316
Intraoperative remifentanil, μg/kg/min	0.04 (0.03)	0.05 (0.03)	0.01 (−0.01 to 0.02)	0.321
Number of patients requiring rescue pain medicines	25 (52%)	36 (75%)	23% (2 to 41%)	0.020
Diclofenac sodium, mg	30 (37)	47 (40)	17 (2 to 33)	0.031
Pethidine, mg	22 (33)	28 (29)	6 (−7 to 18)	0.363
Tramadol, mg	8 (19)	4 (9)	4 (−2 to 10)	0.168

Values are presented as the median (interquartile range) or the number (%) of patients. Age-adjusted MAC was calculated using Mapleson's method ($MAC_{age} = MAC_{40} \times 10^{[-0.00269 \times (age-40)]}$, MAC_{40}: MAC value at 40 years) [12]

CI confidence interval, *MAC* minimum alveolar concentration

optimal position of laryngeal mask airway and interfered with oxygenation and ventilation. The duration of surgery might have also influenced the prevalence of sore throat after surgery. Prolonged duration of anesthesia is also a known risk factor of sore throat after surgery [16]. The relatively longer duration of intubation in the present study compared with that in a previous study [28] might have contributed to the higher prevalence of postoperative sore throat in our investigation.

Desflurane can lead to higher prevalence of cough in patients after outpatient anesthesia compared with sevoflurane [11]. Cough can increase the development of sore throat. Pethidine was infused at the end of surgery to decrease acute wound pain in our investigation. Antitussive effect of meperidine might have contributed to the low prevalence of cough at immediate postoperative period in this study. Laryngeal mask airway was used in a previous study [28]. Insertion of laryngeal mask airway might have exposed desflurane or sevoflurane more to the upper airway than tracheal intubation with tracheal tube. Cuff sealing of tracheal tube in our study might have prevented exposure of vocal cords or epiglottis to inhalational agents. Although the prevalence of cough was comparable between the two groups, the prevalence of sore throat was still higher in the desflurane group in this investigation. This study suggests that irritating and inflammatory effects of desflurane rather than cough itself might be responsible for the higher prevalence of sore throat in the desflurane group.

Sevoflurane group showed less number of patients requiring rescue analgesics in our investigation compared with desflurane group. Sevoflurane group also had less diclofenac requirements. Difference in analgesic requirements might have influenced pain scores between the two groups in our study. Desflurane can lead to faster recovery profiles such as eye-opening, following commands, and orientation compared with sevoflurane [11]. A faster recovery and more rapid experience of pain in the desflurane group might have increased early analgesic requirements in this investigation. Nonsteroidal anti-inflammatory drugs such as diclofenac are related to kidney injury [30]. Considering that perioperative kidney injury is associated with considerable morbidity and mortality [31], sevoflurane might be more beneficial for patients undergoing orthopedic lower extremity surgery than desflurane. The power calculation of this investigation, however, was not designed to detect difference in wound pain scores or analgesic requirements between sevoflurane and desflurane groups. Future investigation regarding the effect of sevoflurane on postoperative pain and analgesic requirements is needed.

The current investigation had some limitations. First, the attending anesthesiologist was not blinded to maintenance anesthetic agents. Anesthetic depth was controlled using bispectral index monitor while maintaining stable hemodynamic variables. Age-adjusted MAC was comparable. The investigator who evaluated outcomes was blinded. Second, subjective outcomes such as sore throat, hoarseness, cough and wound pain scores were checked. To minimize bias, we applied randomization to minimize bias.

Conclusions

For patients undergoing orthopedic lower extremity surgery, sevoflurane group demonstrated less prevalence of sore throat compared with desflurane group. Thus, adequate preventive management may be recommended for patients using desflurane as a maintenance anesthetic agent. In addition, sevoflurane group showed less analgesic requirements and more number of patients demanding rescue analgesics compared with desflurane group.

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Compliance with ethical standards

Conflict of interest No external funding and no competing interests declared.

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