

# Desflurane versus sevoflurane in pediatric anesthesia with a laryngeal mask airway

## A randomized controlled trial

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### Abstract

**Background:** Desflurane with a laryngeal mask airway may have advantages during ambulatory anesthesia. However, desflurane-induced airway irritability makes the use of desflurane challenging, especially in children. This study compared desflurane with sevoflurane maintenance anesthesia in terms of respiratory events and the emergence characteristics in children with a laryngeal mask airway.

**Methods:** This randomized controlled trial evaluated 200 children undergoing strabismus surgery allocated to desflurane or sevoflurane groups. After inducing anesthesia with sevoflurane and thiopental sodium 5 mg kg<sup>-1</sup>, the anesthetic agent was changed to desflurane in the desflurane group, whereas sevoflurane was continued in the sevoflurane group. Respiratory events, emergence time, recovery time, and emergence agitation were compared between the groups.

**Results:** The overall respiratory events did not differ between the groups. However, the incidence of mild desaturation (90% ≤ SpO<sub>2</sub> < 97%) was significantly higher in the desflurane group (7%) than in the sevoflurane group (0%) (*P* = .007). Emergence was significantly faster in the desflurane group (6.6 ± 3.9 vs 8.0 ± 2.2 min, *P* = .003). The recovery time and emergence agitation in the postanesthesia care unit were comparable between groups. Laryngospasm developed in 5 children (1 in the sevoflurane group and 4 in the desflurane group, *P* = .365); of these, 4 patients were younger than 3 years.

**Conclusion:** Desflurane maintenance anesthesia in children with a laryngeal mask airway shows a similar rate of overall respiratory events compared with sevoflurane anesthesia. However, anesthesiologists should be cautious of using desflurane in younger children concerning desaturation events during emergence.

**Abbreviations:** CI = confidence interval, LMA = laryngeal mask airway, MAC = minimum alveolar concentration, PACU = postanesthesia care unit, SpO<sub>2</sub> = peripheral oxygen saturation, URI = upper respiratory infection.

**Keywords:** desflurane, laryngeal mask airway, pediatrics

## 1. Introduction

Desflurane has a low solubility in blood, which enables more rapid awakening from anesthesia. Desflurane has faster emergence with a comparable incidence of emergence agitation compared with sevoflurane and isoflurane, even in children.<sup>[1,2]</sup> However, its pungency can provoke airway irritation, causing

secretions, breath-holding, cough, and laryngospasm.<sup>[3,4]</sup> Therefore, desflurane is contraindicated for inhalation induction in children and infants. The use of desflurane is considered safe in terms of airway irritability only with an endotracheal tube and during anesthesia maintenance.<sup>[5,6]</sup>

The manufacturer has warned that children, particularly those aged 6 years or younger, who are under anesthetic maintenance with desflurane delivered via an laryngeal mask airway (LMA), are at an increased risk for adverse respiratory reactions based on the report of Lerman et al. This study reported the incidence and severity of adverse airway events was higher in children under anesthetic maintenance with desflurane, via an LMA or a facemask, than in those under isoflurane anesthesia.<sup>[1]</sup> Furthermore, the Pediatric Advisory committee of the US Food and Drug Administration recommended that desflurane labeling be “revised to clearly state that the use of maintenance of non-intubated pediatric patients be contraindicated.”<sup>[7]</sup>

Nevertheless, there is increasing evidence that desflurane has a similar incidence of respiratory events as sevoflurane when both are given via an LMA. A retrospective investigation revealed that desflurane did not increase the risk of respiratory events in children with LMA.<sup>[8]</sup> Also, a meta-analysis by Stevanovic et al<sup>[9]</sup> concluded that, in adults, there is no difference in adverse upper airway events between anesthesia achieved with desflurane via an LMA, sevoflurane, isoflurane, or propofol anesthesia. However,

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no randomized controlled study has compared desflurane and sevoflurane use in children aged 6 years or younger, via an LMA, in terms of airway events.

Therefore, this randomized controlled trial compared the respiratory events and emergence characteristics of desflurane versus sevoflurane during ambulatory anesthesia, via an LMA, in children. The primary outcome was the overall incidence of respiratory adverse events, and the secondary outcomes were the emergence time and incidence of emergence agitation according to inhalation agents.

## 2. Methods

This study used a double-blind, randomized controlled, parallel group design and was conducted at a tertiary care children's hospital. The study was approved by the Institutional Review Board of Seoul National University Hospital (Ref. H-1504-116-668) and is registered at ClinicalTrials.gov (Ref. NCT02470442) on June 8, 2015. The first participant was enrolled on June 25, 2015. After obtaining written informed consent from the children's parents, the study enrolled 200 pediatric patients from 2 to 6 years of age who underwent general anesthesia for strabismus surgery from June 2015 to February 2016. We excluded patients who had an upper respiratory infection (URI) within the previous 2 weeks, any respiratory disease, known susceptibility to malignant hyperthermia, or a history of moderate-to-severe hepatic dysfunction following anesthesia with desflurane not otherwise explained.

### 2.1. Study protocol

We randomly allocated the pediatric patients to 1 of 2 parallel groups (1:1 allocation) using website-based randomization (www.randomization.org). The random permuted block method with a block size of 4 was used. A trained researcher generated the random allocation sequence, prepared sealed opaque envelope, opened an envelope immediately before the start of anesthesia, and assigned participants to the trial groups (S group, sevoflurane maintenance anesthesia; D group, desflurane maintenance anesthesia). Although the anesthesiologists assigned to the intervention group were aware of the group allocation, the patients, data analysts, and outcome assessors were blinded to the allocation. Standard monitoring with noninvasive blood pressure, electrocardiography, and peripheral oxygen saturation (SpO<sub>2</sub>) was performed. Anesthesia was induced with 5 mg kg<sup>-1</sup> thiopental sodium, atropine 0.01 mg kg<sup>-1</sup>, and 6 to 8 vol% sevoflurane under 100% O<sub>2</sub> mask ventilation, followed by 0.3 mg kg<sup>-1</sup> rocuronium to facilitate LMA placement. The Flexible LMA and standard insertion technique was used. Opioids were not administered in any patient. Immediately after the anesthetic induction, the inhalation agent was switched depending on the group allocation. Anesthesia was maintained with 2 to 3 vol% sevoflurane using an oxygen/air mixture in the S group and 7 to 8 vol% desflurane using an oxygen/air mixture in the D group. The minimum alveolar concentration (MAC) during the maintenance period was 0.8 to 1.2 MAC in both groups, as determined by the child's age.

All surgical procedures for strabismus in this study were performed by 1 surgeon. Before the end of surgery, the inhalation agents were slowly decreased and discontinued, 100% oxygen with 6 L/min was administered. Neostigmine and atropine were administered after confirming 4 twitches on train-of-4 stimulation to facilitate the recovery of residual muscular blockage, and the LMA was removed in the operating room after confirming

that the child was fully awake (i.e., the grimacing, regular respiration, gag reflex, and purposeful movement of the extremities). Then, the child was monitored in the postanesthesia care unit (PACU) until the modified Aldrete score reached 8.

A blinded investigator recorded perioperative events in the operating room. A blinded nurse recorded any adverse events and emergence agitation during recovery in the PACU until discharge.

The primary outcome was the overall number of respiratory adverse events during maintenance anesthesia and emergence. The events included breath-holding (> 15 s), bronchospasm (bilateral wheezing), coughing, laryngospasm, secretions (require suctioning), mild desaturation (90% ≤ SpO<sub>2</sub> < 97% that lasted for > 15 s), and severe desaturation (SpO<sub>2</sub> < 90% that lasted for > 15 s). The secondary outcomes were the emergence time (the time interval between discontinuation of inhaled anesthetics and LMA removal after confirming the awake state of children), recovery time (the PACU stay time), and emergence agitation. Emergence agitation was evaluated at 15 minutes after admission to the PACU using the 4-point agitation scale for emergence delirium, on which emergence delirium is defined by a score of 3 or 4 at any time (1, calm; 2, not calm but could be easily calmed; 3, not easily calmed, moderately agitated, restless; and 4, excited or disoriented).<sup>[10]</sup> The scale is simple to use and provides a meaningful and clear end point for the dichotomous outcome of emergence agitation.<sup>[11]</sup>

### 2.2. Statistical analysis

Data on patient characteristics are presented as means ± SD, medians (range), or absolute numbers as appropriate. The Kolmogorov–Smirnov test was used to test the normality of the data. We calculated the sample size based on a study by Saros et al.<sup>[12]</sup> They reported that respiratory complications occurred in 14% (5/35) and 2% (1/35) of their desflurane and sevoflurane groups, respectively. With an α-error of 0.05 and a power of 0.8, considering an attrition rate of 10%, a total sample of 200 patients was required to detect a difference in the incidence of overall respiratory adverse events between groups. Differences between the S and D groups were evaluated using Student's *t*-test or the Mann–Whitney *U* test, as appropriate. The incidence of respiratory adverse events and emergence agitation were assessed by chi-square or Fisher's exact test. Statistical significance was accepted for *P*-values < .05. All statistical analyses were performed using SPSS for Windows (ver. 21.0; IBM, Armonk, NY) and MedCalc (ver. 15.2.2; MedCalc, Mariakerke, Belgium).

## 3. Results

In total, 200 patients completed the study. The patient characteristics are listed in Table 1. The gender ratio, age, height, and weight were comparable between the groups. The anesthesia time, defined as the time interval between the initiation

**Table 1**  
The patient characteristics.

	S group (n=100)	D group (n=100)
Female:male	66:34	66:34
Age, y	4.0 (2.0–6.9)	3.8 (2.0–6.9)
Height, cm	104.6 ± 12.2	103.6 ± 14.5
Weight, kg	17.4 ± 4.4	17.3 ± 5.9
Anesthesia time, min	24.7 ± 5.4	26.2 ± 5.8

Values are expressed mean (range), mean ± SD, or absolute number of patients.  
S group = sevoflurane group, D group = desflurane group.

**Table 2****The detailed incidence of respiratory adverse events during emergence.**

	S group (n = 100)	D group (n = 100)	P	Relative risk	95% CI
Overall respiratory events, n	39	41	.885	1.05	0.74–1.47
Breath holding, n	10	16	.293	1.60	0.76–3.35
Coughing, n	28	30	.876	1.07	0.69–1.65
Secretion require suctioning, n	12	13	1.000	1.08	0.52–2.25
Laryngospasm, SpO <sub>2</sub> < 90%, n	1	4	.365	4.00	0.45–35.15
Bronchospasm, n	0	0	1.000		
Mild desaturation, 90% ≤ SpO <sub>2</sub> < 97%, n	0	7	.007		

Data are absolute values.

95% CI = 95% confidence interval, S group = sevoflurane group, D group = desflurane group.

*P* < .05 was considered to be significant.

of inhalation induction and discontinuation of the inhaled anesthetic agents, was longer in the D group than in the S group with statistical significance (mean difference 1.4 min and 95% confidence interval [CI]: 0.1–3.0 min). During the maintenance anesthesia, there were no respiratory adverse events in any patient.

The incidence of overall respiratory adverse events was comparable between the groups during emergence. Table 2 provides details of the respiratory adverse events. The incidence of coughing, secretion, breath-holding, and laryngospasm was similar in both groups. No patient developed bronchospasm during emergence. However, the incidence of mild desaturation (90% ≤ SpO<sub>2</sub> < 97%) was significantly higher in the D group. The cause of mild desaturation (n = 7 in the D group) was breath-holding and coughing. All patients (i.e., in both groups) who experienced laryngospasm eventually developed desaturation (SpO<sub>2</sub> range: 77–89%). The duration of desaturation did not exceed 30 seconds; all patients recovered promptly with an oxygen supply, stimulation of the laryngospasm notch, and positive airway pressure. None of the cases of laryngospasm had any negative outcome. Of the 5 children who experienced laryngospasm, 4 were aged < 3 years, and the other was a 5-year-old child in the D group. The incidence of laryngospasm was significantly higher (*P* = .0217) in the patients aged under 3 years (n = 48), compared with the older pediatric patients (n = 152) with a relative risk of 12.6 and 95% CI 1.45–110.62.

Table 3 shows the emergence characteristics of both groups. The emergence time was significantly shorter in the D group (mean difference 1.4 min and 95% CI: 0.5–2.3 min). There were no group differences in recovery time (mean difference 0.4 min and 95% CI: –2.1 to 1.2 min), the incidence of vomiting, and the incidence of overall respiratory adverse events (relative risk 1.05

and 95% CI: 0.74–1.47). The incidence of emergence delirium in the PACU was comparable in the 2 groups (52% and 51% in the S and D groups, respectively).

#### 4. Discussion

In this study, desflurane anesthesia following sevoflurane induction had a similar incidence of overall respiratory adverse events. In addition, desflurane anesthesia following sevoflurane induction showed slightly faster emergence and a comparable incidence of emergence delirium to that of sevoflurane anesthesia.

We assumed that the less airway irritability of LMA counteracts the effect of the desflurane on airway irritability when using the maintenance of anesthesia. A meta-analysis of LMA usage in pediatric anesthesia concluded that the incidence of desaturation, laryngospasm, cough, and breath-holding during recovery from anesthesia was lower than with tracheal intubation.<sup>[13]</sup> Even in pediatric patients with an upper respiratory infection which may increase the airway resistance, the LMA usage considered feasible alternative to the tracheal tube.<sup>[14,15]</sup>

It should be noted, however, that the degree of airway irritability due to inhalation agents differs between normal and susceptible airways.<sup>[16]</sup> Known risk factors for perioperative respiratory adverse events include a history of recent URI, age less than 6 years,<sup>[1]</sup> and airway surgery.<sup>[17,18]</sup> We controlled these variables by limiting the age of the children (2–6 years old) and excluding morbid patients. Interestingly, 4 of the 5 patients who developed laryngospasm were small children aged 2 to 3 years old. Perioperative respiratory adverse events during pediatric ambulatory anesthesia are increased in children younger than 3 years regardless of the anesthetic regimen, such as LMA or desflurane anesthetics.<sup>[19]</sup> Therefore, the interpretation of our results must specifically consider the patient age. In this prospective study, less than half of the patients were aged 2 to 3 years. Accordingly, we emphasize meticulous attention when using desflurane maintenance anesthesia with an LMA in pediatric patients aged ≤ 3 years.

The secondary outcomes of this study were the emergence time and incidence of emergence agitation according to the inhalation agent. Desflurane maintenance anesthesia resulted in faster emergence from anesthesia. However, faster emergence does not guarantee fast recovery and hospital discharge. Some authors concluded that faster emergence from anesthesia is associated with a higher incidence of postoperative agitation and even a delay in recovery.<sup>[20,21]</sup> Nevertheless, in this study, desflurane during maintenance anesthesia shortened the emergence time but was similar to sevoflurane with respect to emergence agitation and recovery time.

**Table 3****Emergence and recovery characteristics.**

	S group (n = 100)	D group (n = 100)	P
Emergence time, min	8.0 (2.2)	6.6 (3.9)	.003
Recovery time, min	33.1 (5.6)	33.5 (6.1)	.732
Vomiting, n	2	5	.441
Four points agitation score			.449
1	40	36	
2	8	13	
3	43	46	
4	9	5	

Values are expressed mean (range), mean (SD), or absolute number of patients (n), as appropriate.

S group = sevoflurane group, D group = desflurane group.

*P* < .05 was considered to be significant.

We examined whether the incidence of emergence agitation changes when different anesthetics are used to control contributing or confounding factors, such as pain intensity and surgical time, by enrolling children undergoing the same surgery for strabismus performed by a single operator. We found no difference in the incidence of emergence agitation between sevoflurane and desflurane. Consistent with our results, a systematic review of risk factors for emergence agitation showed that there is no difference in emergence agitation according to the inhalation agent.<sup>[22]</sup> However, the incidence of emergence agitation with both agents was very high in this study. Emergence agitation may affect the postoperative course,<sup>[23]</sup> and a multimodal approach to reducing the emergence agitation is needed.<sup>[11]</sup>

We should consider many factors when we choose an inhalation agent for anesthesia, including drug effectiveness, patient safety, costs, and environmental impact.<sup>[24]</sup> The operating room is a major source of perioperative costs and the anesthesiologist can affect the efficiency of the operating room by choosing anesthetic options that are cost-effective, safe, and facilitate rapid emergence.<sup>[25]</sup> Clinicians must consider the risks and benefits of desflurane anesthesia with an LMA in children. Careful patient selection and an optimal anesthetic technique are required.

This study had several limitations. First, the sample size was calculated based on the study performed in adult population under self-respiration. However, considering of adverse respiratory events in 2 groups (39% vs 41%) in this study, our study was under-powered to draw conclusions. Second, we used a muscle relaxant in all patients during the induction and maintenance of anesthesia, so the generalizability of our findings in patients with spontaneous ventilation supported by an LMA requires confirmation. Also, the muscle relaxant could increase the perioperative respiratory adverse events, especially after short surgical procedure. Third, our study population comprised children with normal airways and 111 of the 200 patients were aged > 3 years. Therefore, our results should be applied to the younger high-risk group carefully. Fourth, exposure to sevoflurane in both groups during the induction of anesthesia could have influenced the results. Lastly, the pediatric anesthesia emergence delirium scale is currently regarded as the standard evaluation tool for emergence agitation, but there is no consensus regarding an appropriate cut off for the presence of emergence agitation.<sup>[26]</sup> The scoring system also includes an evaluation of “eye contact,” which cannot not be assessed in pediatric patients undergoing strabismus surgery. Therefore, we attempted to determine whether emergence agitation is present by using Aono’s 4-point scale.

In conclusion, desflurane maintenance anesthesia in children with an LMA might be a possible alternative to sevoflurane during ambulatory anesthesia with respect to the rapid emergence and similar incidence of overall respiratory adverse events. However, anesthesiologists should pay more attention to desaturation during emergence when using LMAs with desflurane especially in small children younger than 3 years.

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