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Retrospective cohort investigation of perioperative upper respiratory events in children undergoing general anesthesia via a supraglottic airway

A comparison of sevoflurane and desflurane

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Abstract

Desflurane is the most pungent of the currently used volatile anesthetics. We assessed whether the incidence of perioperative upper respiratory events in children undergoing general anesthesia via a supraglottic airway is higher with desflurane than with sevoflurane as maintenance anesthetic.

We retrospectively reviewed and analyzed the electronic medical records of consecutive children 1 to 15 years of age who underwent general anesthesia via a supraglottic airway at Seoul National University Bundang Hospital between June 2013 and June 2015. The patients were assigned to the sevoflurane or desflurane group according to the anesthetic used. The characteristics of the patients were compared. The primary outcome variable was the incidence of upper respiratory events.

The incidence of upper respiratory events in the 3439 evaluated patients was 0.43% (12/2777) in the sevoflurane group and 0.30% (2/662) in the desflurane group ($P=0.75$; odds ratio=0.69 [95% confidence interval=0.16–3.13]). The difference between the 2 groups was not significant.

Compared with sevoflurane, desflurane does not increase the risk of perioperative upper respiratory events in children receiving general anesthesia via a supraglottic airway.

Abbreviations: ASA = American Society of Anesthesiologist, BMI = body mass index, IV = intravenous, LMA = laryngeal mask airway, MAC = minimum alveolar concentration, SpO_2 = peripheral capillary oxygen saturation.

Keywords: children, desflurane, sevoflurane, supraglottic airways, upper respiratory events

1. Introduction

Since their introduction in 1990s, desflurane and sevoflurane have been widely used in pediatric anesthesia. Desflurane has the lowest solubility in blood and other body tissues among inhalational anesthetics. This is associated with a faster induction of anesthesia and a faster recovery than obtained with other inhalational anesthetics.[1] In addition, the in vivo metabolism of desflurane is also the lowest among the currently used inhaled anesthetics. This is associated with a minimal risk of metabolic hepatocellular injury and postoperative immune hepatitis.[2] However, airway irritation has been reported when desflurane is inhaled at a high concentration.[3–5] Hence, its use in the maintenance of anesthesia via a supraglottic airway is controversial. Recent meta-analyses have shown that desflurane is not different from other commonly used anesthetics, such as sevoflurane, isoflurane, or propofol, in terms of upper respiratory adverse events in adult patients undergoing general anesthesia using the laryngeal mask airway (LMA).[6,7] However, no large-scale study on this has been conducted in children, and the use of desflurane in the maintenance of anesthesia via the LMA in this population remains a matter of debate. Thus, we assessed whether the incidence of perioperative upper respiratory complications in children undergoing general anesthesia via a supraglottic airway is higher with desflurane than with sevoflurane.

2. Materials and methods

Approval was obtained from the Institutional Review Board of Seoul National University Bundang Hospital (Seongnam, Korea). The trial was registered at clinicaltrials.gov (NCT02644226). The study was based on a retrospective review and analysis of the

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electronic medical records of consecutive children 1 to 15 years of age who underwent general anesthesia via a supraglottic airway, with sevoflurane or desflurane used as the maintenance agent. All patients were seen at the Seoul National University Bundang Hospital between June 2013 and June 2015. Data on age, sex, body mass index (BMI), American Society of Anesthesiologists (ASA) class, supraglottic airway type and size, rocuronium or alfentanil use status, type and duration of surgery, duration of anesthesia, and occurrence of upper respiratory events were collected from the electronic medical records of the patients.

The primary outcome variable was the incidence of perioperative upper respiratory events, defined as the occurrence of peripheral capillary oxygen saturation (SpO_2) <90%, breath-holding, laryngospasm, bronchospasm, or severe coughing either intraoperatively or in the immediate postoperative period, during the patient's stay in the postanesthesia recovery unit. To detect perioperative upper respiratory events, the patients' electronic medical records were searched using the words saturation, desaturation, SpO_2, breath-holding, laryngospasm, bronchospasm, spasm, cough, and event. Then records containing these words were manually searched.

Anesthesia was administered by anesthesiologists with >2 years of clinical experience; all medical residents involved in the procedures were under the supervision of a pediatric anesthesiologist. Anesthesia was induced with intravenous (IV) thiopental or the inhalation of sevoflurane and was maintained with sevoflurane or desflurane. In patients in whom anesthesia was induced with IV thiopental, inhalation of sevoflurane or desflurane was started just after confirming the loss of consciousness and before the insertion of a supraglottic airway. Intraoperative rocuronium and alfentanil were used at the discretion of the attending anesthesiologist. The supraglottic airway devices available for children at our institution are i-gel (Intersurgical Ltd., Berkshire, UK), LMA Supreme (Teleflex, Morrisville, NC), LMA Flexible single use (Teleflex, Morrisville, NC), and LarySeal Flexi (Flexicare Medical Ltd., Mid Glamorgan, UK). The choice of airway device was determined by the attending anesthesiologist and according to the product guidelines. Ventilation was controlled to maintain an end-tidal CO_2 of 4 to 4.6 kPa. At the end of surgery, the supraglottic airway was removed in the operating room after the return of spontaneous ventilation and consciousness was confirmed in the patient.

2.1. Statistical analysis

IBM SPSS Statistics version 22 (IBM Corp., Armonk, NY) was used for the statistical analysis. A P value <0.05 was considered to indicate statistical significance. The effects of the anesthetics used on the incidence of upper respiratory events was determined by first assessing the unadjusted relationship between the type of anesthetic (sevoflurane vs desflurane) and potential confounders using Student's t test, the χ^2 test, or Fisher exact test according to the data. The crude odds ratio for upper respiratory events was calculated according to type of anesthetic used and potential confounders. The odds ratio and 95% confidence interval (95% CI) for the anesthetic type and potential confounders versus upper respiratory events were calculated as well.

3. Results

The records of 3450 patients were retrieved during the collection of data on consecutive pediatric patients 1 to 15 years of age who underwent general anesthesia via a supraglottic airway. Among them, 8 patients were maintained with propofol and 3 patients who underwent bronchoscopy were excluded from the analysis. Thus, 3439 patients were evaluated. The main anesthetic used in these patients was sevoflurane in 2777 (80.8%) and desflurane in 662 (19.2%) patients. The patients' characteristics according to anesthetic used are shown in Table 1. The incidence of upper respiratory events was not significantly different between the 2 groups: 0.43% (12/2777) and 0.30% (2/662) in those maintained with sevoflurane and desflurane, respectively ($P=0.75$). The clinical characteristics and univariate relationship with upper respiratory events are shown in Table 2. The odds ratio for the incidence of upper respiratory events was 0.69 (95% CI: 0.16–3.13). There were no significant differences between the sevoflurane group and the desflurane group. The patients in the 2 groups differed significantly in their age and sex distribution, duration of anesthesia, the use of rocuronium, type and size of supraglottic airway, and type of surgery (Table 1). However, a univariate analysis of these factors showed that none were related to the incidence of upper respiratory events (Table 2). There was also no significant relationship between the patients' BMI, ASA class, and use of alfentanil and upper respiratory events (Table 2). The nature of the upper respiratory events recorded in the 2 groups is described in Table 3.

4. Discussion

In this retrospective cohort study, 3439 consecutive pediatric patients 1 to 15 years of age who underwent general anesthesia

Table 1

Patients' characteristics by anesthetic used.

	Sevoflurane (n=2777)	Desflurane (n=662)	P
Age (y)	5.9 (3.2)	6.7 (3.8)	<0.001
Sex (M:F)	1475:1302 (53.1:46.9)	387:275 (58.5:41.5)	0.013
ASA 1/2/3 (n, %)	2475/296/6 (89.1/10.7/0.2)	596/70/1 (89.3/10.6/0.2)	1.00
BMI (kg m^{-2})	17.1 (3.2)	17.2 (3.2)	0.31
Duration of surgery (min)	23.7 (15.5)	24.6 (19.8)	0.27
Duration of anesthesia (min)	40.2 (20.7)	43.9 (27.4)	0.002
Rocuronium (n, %)	832 (30.0)	359 (54.2)	<0.001
Alfentanil (n, %)	2173 (78.2)	506 (76.4)	0.32
Supraglottic airway (n, %)			<0.001
I-gel	332 (12.0)	220 (33.2)	
LMA Flexible	1286 (46.3)	189 (28.5)	
LMA Supreme	88 (3.2)	52 (7.9)	
LarySeal	1071 (38.5)	201 (30.4)	
Supraglottic airway size (n, %)			0.002
1.5	57 (2.1)	17 (2.6)	
2.0	1311 (47.2)	304 (45.9)	
2.5	924 (33.3)	173 (26.1)	
3.0	419 (15.1)	135 (20.4)	
4.0	62 (2.2)	33 (5.0)	
5.0	4 (0.1)	0 (0)	
Type of surgery (n, %)			<0.001
Ophthalmic	2212 (79.7)	363 (54.8)	
Surgery	188 (6.8)	145 (21.9)	
Orthopedic	234 (8.4)	76 (11.5)	
Urology	100 (3.6)	44 (6.6)	
Plastic	21 (0.8)	25 (3.8)	
Others*	22 (0.8)	9 (1.4)	

Data are means (SD) or number of patients (%).
* Others include ENT, neurosurgery, and thoracic surgery.

Table 2

Clinical characteristics of the patient and univariate relationship with upper respiratory events.

		Upper airway event (%)	P	Odds ratio (95% CI)
Age (y)	≥7	5/1367 (0.4)		Baseline
	1–6	9/2072 (0.4)	1.00	1.19 (0.40–3.55)
Sex	M	9/2072 (0.4)		
	F	5/1577 (0.5)	0.59	.65 (0.22–1.96)
BMI (kg m^{-2})	<25	13/3094 (0.4)		
	≥25	1/94 (1.1)	0.34	2.55 (0.33–19.69)
ASA	1	12/3066 (0.4)		
	≥2	2/373 (0.5)	0.66	1.37 (0.31–6.15)
Anesthetic	Sevoflurane	12/2777 (0.4)		
	Desflurane	2/662 (0.3)	0.75	0.69 (0.16–3.13)
Rocuronium	No	6/22448 (0.3)		
	Yes	8/1191 (0.7)	0.09	2.53 (0.88–7.30)
Alfentanil	No	2/760 (0.3)		
	Yes	12/2679 (0.4)	0.75	1.71 (0.38–7.30)
Supraglottic airway type	LMA Flexible	6/1475 (0.4)		Baseline
	LarySeal	3/1272 (0.2)	0.44	0.58 (0.14–2.32)
	I-gel	3/552 (0.5)	0.68	1.34 (0.33–5.37)
	LMA Supreme	2/140 (1.4)	0.12	3.55 (0.71–17.75)
Supraglottic airway size				
	1.5	0/74 (0.00)	0.997	0
	2.0	8/1615 (0.5)		Baseline
	2.5	2/1097 (0.2)	0.205	0.37 (0.78–1.73)
	3.0	4/554 (0.7)	0.537	1.49 (0.44–4.87)
	4.0	0/95 (0)	0.997	0
	5.0	0/4 (0)	0.999	0
Type of surgery	Ophthalmic	8/2575 (0.3)		Baseline
	General surgery	3/333 (0.9)	0.12	2.92 (0.77–11.05)
	Orthopedic	1/310 (0.3)	0.97	1.04 (0.13–8.33)
	Urology	1/144 (0.7)	0.45	2.24 (0.28–8.06)
	Plastic	1/46 (2.2)	0.07	7.13 (0.87–58.21)
	Others*	0/31 (0)	0.99	0

Data are number of patients as event/total (%).
* Others include ENT, neurosurgery, and thoracic surgery.

via a supraglottic airway were evaluated. The overall incidence of perioperative upper respiratory events was 0.41% (14/3439), without a significant difference between the sevoflurane and desflurane groups.

Desflurane, one of the most pungent of the currently used volatile anesthetics, induces coughing, salivation, breath-holding, and laryngospasm when administered at a high concentration.[3–5,8] Sites responding to an increasing concentration of desflurane are located in both the upper and lower airways. These responses induce direct irritation of the airway mucosa and sympathetic activation, leading to a significant increase in heart rate and mean arterial pressure.[9] For this reason, the manufacturer of desflurane does not recommend its use for the induction and maintenance of anesthesia in nonintubated infants and children. However, our clinical impression is that this warning is somewhat exaggerated, and most of the children anesthetized with desflurane at a clinical dose do not develop significant airway complications. Indeed, previous studies reporting an increased incidence of respiratory adverse events used a high concentration of desflurane, up to 2 minimum alveolar concentration (MAC), which is seldom used in clinical practice. Regarding the use of desflurane for the maintenance of anesthesia in nonintubated adult patients, a meta-analysis of 13 randomized, controlled trials found no evidence of increased airway complications compared with sevoflurane, isoflurane, or propofol anesthesia, but concluded that the emergence from general anesthesia was significantly faster with desflurane than with any of the other anesthetics.[7] However, in pediatric patients, no such large-scale dataset exists. The focus of a meta-analysis comparing the use of desflurane and sevoflurane in pediatric anesthesia was intubated patients; upper respiratory events were not mentioned. The conclusion of that study was that, compared with sevoflurane, desflurane was associated with a faster recovery and fewer adverse effects, such as agitation.[10]

Lerman et al[8] reported a higher incidence and greater severity of airway events after maintenance anesthesia with desflurane than with isoflurane in children with LMA complications (9% vs 4%). However, the incidence of major airway events in that study was higher than in ours for both agents. Several factors may explain the lower incidence of airway events in our study. First, the mean duration of surgery was shorter in our patients. Most of our patients were undergoing ophthalmic surgery, primarily strabismus surgery, the duration of which was <30 minutes in the majority of cases. Recovery from desflurane is relatively unaffected by the duration of anesthesia.[11] However, the effects of the duration of anesthesia on airway complications is not clear. Second, there was a difference in the strategy of LMA removal. Our strategy was to remove the LMA after the patient was fully awake but Lerman et al[8] included patients whose LMA was removed during a deep level of anesthesia. Regarding the timing of LMA removal, awake removal is favorable in the context of airway complications compared with deep removal.[12] The third factor concerns the use of IV opioids. Among the analyzed patients, IV alfentanil was used in 77.6% of our patients. There was a report that IV opioids reduced airway irritability significantly during inhalational induction with desflurane in adults.[13] Fourth, in patients maintained with desflurane, we seldom used more than 8% of desflurane, possibly further lowering the incidence of airway events.

In our patients, the incidence of perioperative upper respiratory events was not different between patients 1 to 6 years of age and those 7 to 15 years of age. This is in contrast to the results of Bordet et al,[14] who showed that age <6 years was a risk factor for airway complications. However, those authors did not subdivide the group of infants, although they have the highest rate of adverse incidents. Instead, the patients were divided into 2 overall groups: age <6 years and age 6 to 18 years.[15]

In our patients, there were no differences in the incidence of perioperative upper respiratory events according to ASA physical status. This is in contrast to previous reports in which a higher ASA physical status was identified as a risk factor for perioperative adverse events.[15] The majority of our patients had an ASA physical status of 1 and there were too few patients with a higher ASA class to detect a potential effect on perioperative upper respiratory events.

Our study had several limitations. First, it may be that we did not capture all of the airway events. Our routine setting of the electronic medical system is to import the vital signs from the monitor at 2.5-minute intervals, and we could record specific events as text. Some minor events, such as a brief period of minor desaturation or mild coughing, could have been missed. However, meaningful events such as major airway complications must have been recorded. Second, because of the retrospective study design, we could not control the factors affecting the airway events. However, none of the factors evaluated in this study, that is, patient age, type and size of the supraglottic airway, medical

Table 3

Details of upper respiratory events.

No.	Sex/age/ASA/anesthetics/SGA operation comorbidities	Clinical signs	Clinical courses
1	M/1 y/1/ Sevo/LMA Supreme orchiopexy none	Desaturation to 60% after removal of SGA	Endotracheal intubation done, extubation at OR, discharged POD 1
2	F/2 y/1/ Sevo/LMA Flexible strabismus surgery none	Laryngospasm and desaturation to 80% after removal of SGA	Endotracheal intubation done, extubation at OR, discharged without admission
3	M/2 y/1/ Sevo/ i-gel Repair of inguinal hernia none	Bronchospasm and desaturation to 66% at 10 min after insertion of SGA	Endotracheal intubation done, extubation at OR, discharged without admission
4	F/3 y/3/ Sevo/ LMA Flexible epiblepharon repair moderate to large ASD	Laryngospasm after induction of anesthesia, desaturation to 80% at PACU	Endotracheal intubation done, extubation at OR, schedule changed from day surgery to admission, discharged POD 1
5	F/3 y/1/ Sevo/LarySeal strabismus surgery none	Laryngospasm, desaturation to 53%, and bradycardia to 70 bpm during induction of anesthesia	SpO_2 was recovered after mask ventilation, IV atropine was used for bradycardia, discharged without admission
6	M/3 y/1/ Des/ i-gel Repair of inguinal hernia none	Laryngospasm and desaturation to 22% during emergence from anesthesia	Endotracheal intubation done, extubation at OR, discharged without admission
7	M/5 y /1/ Sevo/ i-gel Repair of inguinal hernia none	Laryngospasm after failure to insert SGA	Recovered with mask ventilation, discharged without admission
8	F/5 y/3/ Sevo/ LMA Flexible epiblepharon repair cerebral palsy, epilepsy	Breath-holding after removal of SGA at the end of surgery	Endotracheal intubation done, extubation at OR, discharged without admission
9	M/6 y/1/ Sevo/ LarySeal strabismus surgery none	Laryngospasm during induction of anesthesia	Recovered with mask ventilation, discharged without admission
10	F/9 y/1/ Sevo/ LMA Flexible strabismus surgery none	Laryngospasm after insertion of SGA	Endotracheal intubation done, extubation at OR, discharged without admission
11	M/11 y/1/ Sevo/ LMA Flexible strabismus surgery none	Laryngospasm after insertion of SGA	Recovered after reinsertion of SGA, removal of SGA at OR, discharged without admission
12	M/12 y/1/ Sevo/ LarySeal strabismus surgery none	Laryngospasm after insertion of SGA	Endotracheal intubation done, extubation at OR, discharged without admission
13	M/12 y/1/ Des/ LMA Supreme closed reduction none	Bronchospasm, desaturation to 50% at 10 min after insertion of SGA	Endotracheal intubation done, extubation at OR, discharged without admission
14	M/13 y/1/ Sevo/ LMA Flexible foreign body removal none	Laryngospasm after insertion of SGA	Recovered after IV rocuronium and reinsertion of SGA, discharged without admission

ASD = atrial septal defect, bpm = beat per minute, Des = desflurane, GA = gestational age, ICU = intensive care unit, OR = operating room, PACU = postanesthesia recovery unit, POD = postoperative day, Sevo = sevoflurane, SGA = supraglottic airway, s/p = status post.

status, and type of surgery, were related to the incidence of upper respiratory events. Third, only relatively healthy children undergoing relatively short and uncomplicated procedures were evaluated. Thus, our results remain to be validated in further studies.

In conclusion, the incidence of perioperative upper respiratory events did not differ in children administered sevoflurane versus desflurane after anesthesia via a supraglottic airway.

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