의학석사 학위논문

Retrospective Investigation of Perioperative Upper Airway Complications after Anesthesia using Supraglottic Airway Devices in Children: Comparison of Desflurane and Sevoflurane

소아에서 후두 마스크를 이용한 마취 유지시 데스플루란과 세보플루란의 기도 관련 합병증 비교

2016년 1월

서울대학교 대학원

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노 현 정

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이 논문을 의학석사 학위논문으로 제출함

2015년 10월

서울대학교 대학원

의학과 마취통증의학 전공

노 현 정

노현정의 의학석사 학위논문을 인준함

2016년 1월

위 원 장 _____ (인)

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위 원 _____ (인)

Retrospective Investigation of Perioperative Upper Airway Complications after Anesthesia using Supraglottic Airway Devices in Children: Comparison of Desflurane and Sevoflurane

By

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A thesis submitted to the Department of Medicine in partial fulfillment of the requirement for the Degree of Master of Science in Medicine (Anesthesiology and Pain medicine) at Seoul National University College of Medicine

October 2015

Approved by Thesis Committee:

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Abstract

Retrospective Investigation of Perioperative Upper Airway Complications after Anesthesia using Supraglottic Airway Devices in Children: Comparison of Desflurane and Sevoflurane

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Background : Desflurane is known to be the most pungent of the currently used volatile anaesthetics. We aimed to assess wehether desflurane increases the incidence of perioperative upper airway complications in infants and children undergoing general anaesthesia using supraglottic airway devices compared with sevoflurane.

Methods : We retrospectively reviewed and analysed the electrical medical records of consecutive children aged 15 years or younger who underwent general anaesthesia under supraglottic airway devices using sevoflurane or desflurane as maintenance agents at Seoul National University Bundang Hospital between June 2013 and June 2015.

Results : In total, 3,511 patients were evaluated. The incidence of upper airway events was 0.46% (13/2,831) in patients maintained with sevoflurane and 0.74% (5/680) in those maintained with desflurane (P = 0.370). In a logistic regression model, after controlling for the effect of American Society of Anesthesiologist (ASA) class, the type and size of the supraglottic airways, as well as the type of surgery, the adjusted odds ratio was 0.99 (0.31-3.14), and there was no significant difference between sevoflurane and desflurane.

Conclusions : The incidence of perioperative upper airway complications after anaesthesia using supraglottic airway devices in children was not significantly different between sevoflurane and desflurane used as maintenance agents in infants and children.

Keywords : Airway-complications, Anesthetics volatile-desflurane, Anesthetics volatile-sevoflurane, Children, Infants

Trial registration number: NCT02644226.

Student number : 2014-21143

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Introduction

Since their introduction in 1990s, desflurane and sevoflurane have been widely used in paediatric anaesthesia. Desflurane has the lowest solubility in blood and other body tissues among inhalational anaesthetics, and this low solubility is associated with the rapid induction of anaesthesia and faster recovery compared with other inhalational anaesthetics.[1] In addition, the *in vivo* metabolism of desflurane is also the lowest among the currently used inhaled anaesthetics. This minimal metabolism of desflurane 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, the use of desflurane has been regarded as controversial for maintenance of anaesthesia via the supraglottic airways. Recent meta-analyses showed that desflurane is not different from other commonly used anaesthetics, such as sevoflurane, isoflurane, or propofol, in terms of upper airway adverse events in adult patients undergoing general anaesthesia using the laryngeal mask airway (LMA).[6,7] However, in children, such a large-scale study does not exist, and use of desflurane for maintenance of anaesthesia using the LMA remains controversial. In this retrospective cohort study, we aimed to assess whether desflurane increases the incidence of perioperative upper airway complications in infants and children undergoing general anaesthesia via the supraglottic airways compared with sevoflurane.

Methods

After obtaining approval from the Institutional Review Board of Seoul National University Bundang Hospital (Seongnam, Korea) and registering the trial at clinicaltrials.gov (NCT02644226), we retrospectively reviewed and analysed the electrical medical records of consecutive children aged 15 years or younger who underwent general anaesthesia via the supraglottic airways, with sevoflurane or desflurane used as maintenance agents, at Seoul National University Bundang Hospital between June 2013 and June 2015. Patients with known respiratory disease were excluded from the analysis. Data on the patients' age, sex, body mass index (BMI), American Society of Anesthesiologists (ASA) class, type and size of supraglottic airways, rocuronium or alfentanil use status, type of operations, duration of surgery, duration of anaesthesia, and occurrence of upper airway events were collected from the electronic medical records of the patients. The primary outcome variable was the incidence of perioperative upper airway events, which was defined as the occurrence of any one of a peripheral capillary oxygen saturation (SpO_2) of less than 90%, breathholding, laryngospasm, bronchospasm, or severe coughing.

Anaesthesia was induced with intravenous (IV) thiopental or the inhalation of sevoflurane and was maintained with sevoflurane or desflurane with 60% N_2O. Intraoperative rocuronium and alfentanil were used at the discretion of the attending anaesthesiologists. The supraglottic airway devices available for children at our

institution are i-gel® (Intersurgical Ltd., Berkshire, UK), LMA Supreme™ (Teleflex, Morrisville, NC, USA), LMA Flexible™ single use (Teleflex, Morrisville, NC, USA), and LarySeal™ Flexi (Flexicare Medical Ltd., Mid Glamorgan, UK), and the choice was determined by the attending anaesthesiologists. The ventilation was controlled to maintain an end-tidal CO_2 of 4 to 4.6 kPa. At the end of surgery, the supraglottic airways were removed in the operating room after the return of spontaneous ventilation and consciousness.

Statistical Analysis

To evaluate the effect of the anaesthetics used on the incidence of upper airway complications, we first assessed the unadjusted relationship with the type of anaesthetic (sevoflurane *vs.* desflurane) and potential confounders using Student's t-test, chi-squared test, or Fisher's exact test according to the data. We calculated the crude odds ratio for respiratory events according to type of anaesthetics used instead of the relative risk, so it could be compared with the adjusted odds ratio generated by the logistic regression model. Logistic regression was used to describe the effect of type of anaesthetic on upper airway complications after adjusting for potential confounders. Potential confounding variables were those that met the following criteria: (1) a statistically significant relationship with outcome ($P < 0.05$) and (2) included in the Hosmer-Lemeshow test in the logistic regression model. All of the variables included in the tables or described in the data collection section of the

article were evaluated for inclusion. The adjusted odds ratios are presented. The odds ratio for anaesthetics *vs*. upper airway complications was calculated, with a 95% confidence interval.

Results

Initially, 3,522 patient records were retrieved when we collected the data of consecutive paediatric patients aged less than 15 years who underwent general anaesthesia via the supraglottic airways. Among them, eight patients were maintained with propofol and three patients who underwent bronchoscopy were excluded from the analysis. Finally, 3,511 patients were evaluated. Among these patients, 2,831 (80.6%) were maintained with sevoflurane, and 680 (19.4%) were maintained with desflurane. The patient characteristics according to anaesthetic used are shown in Table 1. The incidence of upper airway events was 0.46% (13/2,831) in patients maintained with sevoflurane and 0.74% (5/680) in those maintained with desflurane (P = 0.370). The clinical characteristics and univariate relationship with the upper airway events are shown in Table 2.

Table 1 Patients' characteristics by anaesthetic used. Data are means (SD) or number of patients (%). Others: include ENT, neurosurgery and thoracic surgery.

	Sevoflurane (n = 2,831)	Desflurane (n = 680)	P value
Age (yr)	5.8 (3.3)	6.5 (3.8)	< 0.0001
Sex (M:F)	1,515:1316 (53.5:46.5)	401:279 (59.0:41.0)	0.011
ASA 1 / 2 / 3 (n, %)	2,519/305/7 (89.0/10.8/0.2)	603/74/3 (88.7/10.9/0.4)	0.624
BMI (kg m^{-2})	17.7 (3.3)	17.2 (3.1)	0.682
Duration of Surgery (min)	23.8 (15.7)	24.5 (19.6)	0.408
Duration of Anesthesia (min)	40.4 (20.9)	43.9 (27.3)	0.002

Rocuronium (n, %)	856 (30.2)	368 (54.1)	< 0.0001
Alfentanil (n, %)	2,206 (81.0)	519 (76.3)	0.198
Supraglottic airway (n, %)			< 0.0001
I-gel	365 (12.9)	235 (34.6)	
LMA Flexible	1,293 (45.7)	190 (27.9)	
LMA Supreme	90 (3.2)	53 (7.8)	
LarySeal	1,083 (38.3)	202 (29.7)	
Supraglottic airway size (n, %)			0.008
1.0	5 (0.2)	3 (0.4)	
1.5	84 (3)	28 (4.1)	
2.0	1,333 (47.1)	308 (45.3)	
2.5	924 (32.6)	173 (25.4)	
3.0	419 (14.8)	135 (19.9)	
4.0	62 (2.2)	33 (4.9)	
5.0	4 (0.1)	0 (0)	
Type of surgery (n, %)			< 0.0001
Ophthalmic	2,232 (78.8)	365 (53.7)	
General Surgery	211 (7.5)	158 (23.2)	
Orthopedic	235 (8.3)	77 (11.3)	
Urology	109 (3.9)	45 (6.6)	
Plastic	22 (0.8)	26 (3.8)	
Others	22 (0.8)	9 (1.3)	

Table 2 Clinical characteristics of the patient and univariate relationship with upper airway events. Data are number of patients as event/total (%). Others: include ENT, neurosurgery and thoracic surgery.

		Upper Airway Event (%)	*P*-value	Odds Ratio (95% CI)
Age (yr)	≥ 7	5/1,367 (0.4)	†	Baseline
	1 – 7	9/2,072 (0.4)	0.757	1.19 (0.40 – 3.55)
	< 1	4/72 (5.6)	< 0.0001	16.024 (4.21 – 61.02)

Sex	M	12/1,916 (0.6)		
	F	6/1,595 (0.4)	0.350	0.60 (0.22 - 1.60)
BMI (kg m^{-2})	< 25	16/3,144 (0.5)		
	≥ 25	1/98 (1.0)	0.407	2.02 (0.27 – 15.35)
ASA	1	13/3,122(0.4)		
	≥ 2	5/389 (1.3)	0.041	3.11 (1.10 – 8.78)
Anaesthetic	Sevoflurane	13/2,831 (0.50)		
	Desflurane	5/680 (0.7)	0.370	1.61 (0.57 - 4.52)
Rocuronium	No	8/2,287 (0.3)		
	Yes	10/1,224 (0.8)	0.082	2.35 (0.92-5.96)
Alfentanil	No	2/786 (0.3)		
	Yes	16/2,725 (0.6)	0.394	2.32 (0.53 – 10.09)
Supraglottic	LarySeal	3/1,285 (0.2)		Baseline
airway type	I-gel	7/600 (1.2)	0.019	5.04 (1.30 – 19.58)
	LMA Flexible	6/1,483 (0.4)	0.436	1.74 (0.43 – 6.96)
	LMA Supreme	2/143 (1.4)	0.049	6.06 (1.00 – 36.58)
Supraglottic	1.0	2/8 (25.00)	< 0.001	68.04 (11.89 – 389.43)
airway size	1.5	2/112 (1.8)	0.099	3.71 (0.779 – 17.69)
	2.0	8/1,641 (0.5)		Baseline
	2.5	2/1,097 (0.2)	0.212	0.37 (0.79 -1.76)
	3.0	4/554 (0.7)	0.520	1.49 (0.45 – 4.95)
	4.0	0/95 (0)	0.997	0
	5.0	0/4 (0)	0.999	0
Type of	Ophthalmic	9/2,597(0.3)		Baseline
surgery	General Surgery	6/369 (1.6)	0.003	4.75 (1.68 – 13.43)
	orthopedic	1/312 (0.3)	0.941	0.93 (0.12 – 7.32)
	Urology	1/154 (0.6)	0.551	1.88 (0.24 – 14.93)
	Plastic	1/48 (2.1)	0.089	6.12 (0.76 - 49.27)
	Others	0/31 (0)	0.998	0

The patients' age, ASA class, type and size of supraglottic airways, and type of surgery were regarded as potential confounding variables related to upper airway

events. The incidence of upper airway events was higher in patients aged less than 1 year (5.6%, P =0.001), with an ASA class of 2 or more (1.3%, P = 0.041), in whom i-gel (1.2%, P = 0.019) or LMA-Supreme (1.4%, P = 0.049) was used, with an SGA size of 1.0 (25%, P < 0.001), and who were in general surgery (1.6%, P = 0.003).

ASA class, the effect of the type and size of the supraglottic airways, and type of surgery were included in the final logistic regression model. After controlling for these variables, the adjusted odds ratio was 0.99 (0.31-3.14), and there was no significant difference according to anaesthetic used-sevoflurane or desflurane. The details of the upper airway events are described in Table 3.

Table 3 Details of upper airway events. ASD, atrial septal defect; bpm, beat per minute; GA, gestational age; ICU, intensive care unit; OR, operating room; PACU, postanaesthesia recovery unit; POD, postoperative day; SGA, supraglottic airway; s/p, status post.

No.	Sex/age/ASA/Anesthetics/SGA Operation Comorbidities	Clinical signs	Clinical courses
1	M/3 mo/1/ Sevo/i-gel Repair of inguinal hernia None	Not crying well, breathholding and dyspnea after the removal of SGA	1 day at ICU with O_2, discharged at POD 2
2	F/3 mo/3/ Des/i-gel Repair of inguinal hernia Preterm infant born at GA 34+1 wks, 1,050 g	Breathholding after removal of SGA at the end of surgery	Endotracheal intubation at OR, extubation after 3 hr at ICU, 1 day at ICU, discharged at POD 2
3	M/3 mo/3/ Des/ i-gel Cut-back anoplasty Imperforated anus, patent ductus arteriosus	Laryngospasm intraoperatively. Desaturation to 47%	SpO_2 was recovered immediately, transferred to PACU, discharged at POD1

4	M/6 mo/2/ Des/ i-gel Division of anal sphincter Hirschsprung's disease s/p Soave's op	Desaturation to 55% at recovery	SpO_2 was recovered after removal of SGA and mask ventilation, schedule changed from day surgery to admission, discharged POD 1
5	M/1 yr/1/ Sevo/LMA Supreme Orchiopexy None	Desaturation to 60% after removal of SGA	Endotracheal intubation done, extubation at OR, discharged POD 1
6	F/2 yr/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
7	M/2 yr/1/ Sevo/ i-gel Repair of inguinal hernia None	Bronchospasm and desaturation to 66% after induction of anesthesia	Endotracheal intubation done, extubation at OR, discharged without admission
8	F/3 yr/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
9	F/3 yr/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
10	M/3 yr/1/ Des/ i-gel Repair of inguinal hernia None	Laryngospasm, desaturation to 22%	Endotracheal intubation done, extubation at OR, discharged without admission
11	M/5 yr /1/ Sevo/ i-gel Repair of inguinal hernia None	Laryngospasm during induction of anesthesia	Recovered with mask ventilation, discharged without admission
12	F/5 yr/3/ Sevo/ LMA Flexible Epiblepharon repair Cerebral palsy, epilepsy	Breathholding after removal of SGA at the end of surgery	Endotracheal intubation done, extubation at OR, discharged without admission
13	M/6 yr/1/ Sevo/ LarySeal Strabismus surgery None	Laryngospasm during induction of anesthesia	Recovered with mask ventilation, discharged without admission

14	F/9 yr/1/ Sevo/ LMA Flexible Strabismus surgery None	Laryngospasm after induction of anesthesia	Endotracheal intubation done, extubation at OR, discharged without admission
15	M/11 yr/1/ Sevo/ LMA Flexible Strabismus surgery None	Laryngospasm after induction of anesthesia	Recovered after reinsertion of SGA, removal of SGA at OR, discharged without admission
16	M/12 yr/1/ Sevo/ LarySeal Strabismus surgery None	Laryngospasm during induction of anesthesia	Endotracheal intubation done, extubation at OR, discharged without admission
17	M/12 yr/1/ Des/ LMA Supreme Closed reduction None	Bronchospasm, desaturation to 50% after induction of anesthesia	Endotracheal intubation done, extubation at OR, discharged without admission
18	M/13 yr/1/ Sevo/ LMA Flexible Foreign body removal None	Laryngospasm after induction of anaesthesia	Recovered after IV rocuronium and reinsertion of SGA, discharged without admission

Discussion

In this retrospective cohort study, we evaluated 3,511 consecutive paediatric patients aged less than 15 years who underwent general anaesthesia via the supraglottic airways. The overall incidence of perioperative upper airway events was 0.51% (18/3,511), and there was no significant difference between sevoflurane and desflurane.

Desflurane, known to be the most pungent of the currently used volatile anaesthetics, induces coughing, salivation, breathholding, 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] Under these conditions, the manufacturer of desflurane still does not recommend its use for induction and maintenance of anaesthesia in non-intubated infants and children. However, our clinical impression is that this warning is somewhat exaggerated, and most of the children anaesthetised with desflurane within the range of clinical does do not present with 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 anaesthesia in non-intubated adult patients, a meta-analysis of 13 randomised controlled trials found no evidence of increased airway complications

compared with sevoflurane, isoflurane, or propofol anaesthesia, but concluded that emergence from general anaesthesia with desflurane was significantly faster than with all of the other anaesthetics.[7] However, in paediatric patients, no such large-scale dataset exists. There was one meta-analysis comparing use of desflurane and sevoflurane in paediatric anaesthesia, but it mainly concerned intubated patients and did not mention upper airway events; its conclusion was that desflurane might be associated with rapid recovery and fewer adverse effects, such as agitation, compared with sevoflurane.[10]

There was also a report by Lerman et al. regarding the greater incidence and severity of airway events after maintenance of anaesthesia with desflurane compared with isoflurane in children with LMA complications (9% *vs*. 4%).[8] However, the incidence of major airway events in that study was higher than in ours for both agents. We assume several factors were involved in our lower incidence of airway events compared with this previous 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 less than 30 min in the majority of cases. It is known that the recovery from desflurane is relatively unaffected by the duration of anaesthesia.[11] However, the effect of the duration of anaesthesia 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. included patients whose LMA was removed at a deep level of anaesthesia. Regarding the timing of LMA removal, awake removal is known to be favourable in the context of airway complications

compared with deep removal.[12] The third factor concerns the use of IV opioids. Among the analysed 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.

Our study had several limitations. The possibility exists 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-min 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. Another limitation stems from the characteristics of the retrospective study design, that is, we could not control the factors affecting the airway events. Indeed, the patients' age, type and size of supraglottic airways, medical status, and type of surgery appeared to be related to the incidence of airway complications. Further study is needed to fully elucidate these factors.

In our patients, the incidence of perioperative upper airway complications was higher in infants compared with that in children, but there was no difference between patients aged 1-6 years and those aged 7-15 years. This is in contrast to the results of Bordet et al., which showed that an age of less than 6 years was a risk factor for airway complications.[14] However, they did not subdivide the infants, and

only divided the patients into two overall groups: those aged less than 6 years and those aged 6-18 years. We also showed that the incidence of perioperative upper airway complications was higher in patients with a higher ASA physical status than in patients with an ASA physical status of 1. A previous report stated that the presence of respiratory infections before the procedure was a risk factor for perioperative airway complications in children, but we found no previous report describing the relationship between ASA physical status and airway complications.[14] The reasons for the high incidence of perioperative upper airway complications when using specific supraglottic airway devices, such as i-gel or LMA-Supreme-in the contest of a specific procedure such as general surgery- are not clear. Our assumption is that a higher proportion of patients using those devices and undergoing general surgery might be infants instead of children. After controlling for all these confounding variables using a logistic regression model, we found that the risk of perioperative airway complications in infants and children undergoing general anaesthesia using supraglottic airway devices was not higher with desflurane than with sevoflurane.

In conclusion, the incidence of perioperative upper airway complications after anaesthesia using suparglottic airway devices in children was not different between sevoflurane and desflurane used as maintenance agents.

초록

소아에서 후두 마스크를 이용한 마취 유지시 데스플루란과 세보플루란의 기도 관련 합병증 비교

연구배경 : 데스플루란은 기도 자극성이 심한 것으로 알려져 있어, 기도 삽관되지 않은 소아에게 마취 유지 약제로 사용하는 것이 기피되어 왔다. 본 연구의 목적은 소아에서 후두 마스크를 이용한 마취 유지시 데스플루란을 사용했을 경우와 세보플루란을 사용했을 경우 기도 관련 합병증의 발생 빈도에 차이가 있는지 비교하는 것이다.

연구방법 : 본 연구는 후향적 의무기록 연구로, 분당 서울대병원에서 2013년 6월부터 2015년 6월까지 후두마스크를 사용하여 전신 마취를 받은 15세 이하의 환아의 전자의무기록을 연구대상으로 하였다.

연구결과 : 총 3,528명의 환아가 분석 대상이 되었다. 세보플루란을 사용한 환자군에서 상기도 이벤트의 빈도는 0.60% (13/2,831), 데스플루란을 사용한 환자군에서는 1.17% (5/680)로 나타났다 (p = 0.370). 후두 마스크의 크기, 수술의 종류, 미국마취과학회의 신체등급분류를 로지스틱 회귀분석으로 보정한 결과, 보정된 위험비는 0.99 (0.31-3.14) 이었으며, 세보플루란과 데스플루란 사이에 유의한 차이는 없었다.

결론 : 후두 마스크를 사용하여 전신마취를 받는 소아에서, 데스플루란과 세보플루란을 마취 유지 약제로 사용했을 때에 상기도 합병증의 빈도에는 유의한 차이가 없었다.

주요어 : 기도 합병증, 흡입마취제 – 데스플루란, 흡입마취제 – 세포플루란, 소아, 영아

학번 : 2014-21143