Tracheal Extubation of Anesthetized Pediatric Patients with Heart Disease Decreases the Incidence of Emergence Agitation: A Retrospective Study

Abstract

Background: Emergence agitation for pediatric patients after general anesthesia is one of the postoperative complications. The relationship between consciousness at tracheal extubation and emergence agitation is not clear. **Aim:** The aim of the present study was to determine whether tracheal extubation of anesthetized pediatric patients with heart disease by propofol decreases the incidence of emergence agitation. **Settings and Design:** This was a retrospective case-control study conducted at a children's hospital. **Materials and Methods:** Pediatric patients with heart disease aged 0-14 years who underwent cardiac catheterization under general anesthesia by propofol between October 2014 and September 2018 were enrolled. The incidence of emergence agitation by anesthetized extubation was compared with that by awake extubation. **Statistical Analysis Used:** Logistic regression analysis was performed. **Results:** Anesthetized extubation was performed in 202 patients and awake extubation was performed in 56 patients. The incidence of emergence agitation was significantly lower in patients who underwent anesthetized extubation than in patients who underwent awake extubation (25.2% vs. 69.6%, $P = 0.000$). In logistic regression analysis, anesthetized extubation [odds ratio (OR): 0.075, 95% confidence interval (CI): 0.034-0.165, $P = 0.000$] and older age (OR: 0.808, 95% CI: 0.728-0.897, $P = 0.000$) were associated with a decreased incidence of emergence agitation, and preoperative anxiety (OR: 2.220, 95% CI: 1.060-4.660, $P = 0.03$) was associated with an increased incidence of emergence agitation. **Conclusions:** Tracheal extubation under anesthesia by propofol decreases the incidence of emergence agitation in pediatric patients with heart disease.

Keywords: *Cardiac catheterization, emergence agitation, general anesthesia, heart disease, pediatric*

Tatsuya Kunigo, Yuko Nawa[1], Yusuke Yoshikawa[2], Michiaki Yamakage[2]

Department of Anesthesiology, Hokkaido P.W.F.A.C. Obihiro Kosei General Hospital, Obihiro, Hokkaido 080-0024, [1]Department of Anesthesiology, Hokkaido Medical Center for Child Health and Rehabilitation, [2]Department of Anesthesiology, Sapporo Medical University School of Medicine, Hokkaido, Japan

Introduction

Emergence agitation of pediatric patients is defined "a disturbance in a child's awareness of and attention to his or her environment with disorientation and perceptual alterations including hypersensitivity to stimuli and hyperactive motor behavior in the immediate post anesthesia period".[1]

The reported incidence of emergence agitation varies widely from 10% to 80% depending on the evaluation scale or method.[2-6] Although most children soon recover by themselves from emergence agitation without sequelae, it may be harmful to pediatric patients with heart disease.

Rapid emergence was reported to be a risk factor for emergence agitation.[6] Sevoflurane and desflurane, inhalational anesthetics with low solubility, have been reported to be associated with a high incidence of emergence agitation because of the rapid emergence from general anesthesia induced by these drugs.[2,5,7,8] However, Cohen *et al.* reported that only sevoflurane was associated with a high incidence of emergence agitation, although both sevoflurane and propofol allow for rapid emergence from general anaesthesia.[9] Thus, rapid emergence might not be the only cause of emergence agitation.

The aim of this study, which was a single-center retrospective case-control study, was to determine the relationship between consciousness at tracheal extubation and emergence agitation. Our primary study hypothesis was that tracheal extubation of anesthetized pediatric patients with heart disease decreases emergence agitation. We also investigated other risk factors associated with the incidence of emergence agitation and complications.

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Materials and Methods

This study was approved by the Institutional Review Board of a children's hospital and was conducted in accordance with the Declaration of Helsinki and EQUATOR guidelines. The Institutional Review Board waived the requirement for written informed consent from the patients and their parents because this was a retrospective observational study and the data were analyzed anonymously. This research was carried out without funding. The approval from the ethics committee is obtained. The date of the approval is December 3, 2018.

Medical records of the children's hospital between October 2014 and September 2018 were retrospectively reviewed. Pediatric patients (0-14 years old) with American Society of Anesthesiologists physical status (ASA PS) 1 or 2 who had undergone elective cardiac catheterization under general anesthesia by propofol were enrolled in this study. Exclusion criteria were over 15 years of age, ASA PS of 3 or more, emergency cases, general anesthesia with an anesthetic agent other than propofol, not extubated after general anesthesia and not awake or drowsy during a 3-hour rest period. For patients who had undergone cardiac catheterization more than twice during the study period, we used only the most recent data for the patient because we considered the most recent data to be the most reliable.

Most of the patients were pre-medicated with triclofos sodium, chloral hydrate, midazolam, thiamylal, brotizolam or zolpidem tartrate before general anesthesia. After a peripheral venous line had been inserted, thiamylal (4-5 mg/kg) or propofol (2-3 mg/kg) was administered for induction of anesthesia. The patients were intubated after administration of rocuronium (0.6-1.0 mg/kg) and remifentanil (0.3-0.5 mcg/kg/minute). Anesthesia was maintained by propofol (step down from 10 to 6 mg/kg/hour in 30-40 minutes), rocuronium (0.1-0.3 mg/kg every 20-30 minutes) and remifentanil (0.1-0.5 mcg/kg/minute). Some patients were administered fentanil, flurbiprofenaxetil and acetaminophen during general anesthesia by the decision of each anesthesiologist. Cardiac catheterization was performed from the femoral vein and artery, and some patients received cardiac catheter treatment in addition to examination. After cardiac catheterization, anesthetized extubation or awake extubation was performed in all patients following administration of sugammadex (2-4 mg/kg) and stop infusion of propofol and remifentanil at the same time. Anesthetized extubation was defined as extubation when the patients' spontaneous respiratory rate reached 70%-80% of normal according to their age and the end-tidal CO_2 was between 45 and 60 mmHg without spontaneous opening eye and moving. Mild respiratory depression is evidence of adequate level of anesthesia for anesthetized extubation. Awake extubation was defined as extubation when the patients opened their eyes and moved spontaneously with enough spontaneous breathing. After extubation, all patients went straight back to the general ward (our hospital did not have post anesthesia care unit or recovery room) and needed to be in the supine position without bending their hip joints for 3 hours for hemostasis of the puncture site. The patients were monitored by nurses with electrocardiogram, noninvasive blood pressure and pulse oximetry. For patients who could not keep resting due to emergence agitation, sedative or analgesic medication including propofol, thiamylal, midazolam or fentanil was administered.

Data obtained from medical records included data for age, sex, ASA PS, general anesthetic agents (propofol or others), state of 3-hour rest (whether the patient had awakened up within 3 hours or been sleeping for 3 hours after extubation), anesthesia history, premedication, preoperative anxiety, main disease and state (no surgery, after palliative surgery, after radical surgery), global developmental delay (or diseases related to it), transesophageal echocardiography examination, cardiac catheter treatment, use of fentanil, anesthesia time, operation time, prophylactic postoperative analgesia, type of tracheal extubation (anesthetized extubation or awake extubation), incidence of emergence agitation and complications. Preoperative anxiety was assessed by nurses and anesthesiologists at the time of induction of anesthesia using the pediatric anesthesia behavior score (PAB score) as follows: 1, happy: calm and controlled, compliant with induction; 2, sad: tearful and/or withdrawn but compliant with induction; and 3, mad: loud vocal resistance (screaming or shouting) and/or physical resistance to induction requiring physical restraint by staff and/or parents.[10] We considered that a PAB score of 2 or 3 indicates preoperative anxiety. Emergence agitation was assessed by nurses and anesthesiologists using the four-point emergence agitation scale (Watcha scale) as follows: 1, asleep or calm; 2, crying, but can be consoled; 3, crying, cannot be consoled; and 4, agitated and thrashing around.[11] We considered that a Watcha scale of 3 or 4 indicates emergence agitation. The association the type of tracheal extubation with the incidence of emergence agitation is the primary outcome in this study. Age, sex, preoperative anxiety, global developmental delay (or diseases related to it), transesophageal echocardiography examination, cardiac catheter treatment, use of fentanil, and prophylactic postoperative analgesia were also considered to be variables associated with emergence agitation without collinearity among the variables. The variables and complications (airway obstruction, re-bleeding and laryngeal spasm) were surveyed as secondary outcomes.

The Kolmogorov-Smirnov test and F test were used to determine whether continuous variables followed a normal distribution and the homogeneity of variance. Continuous variables were expressed as means with standard deviation (SD) or medians with interquartile range (IQR),

and they were compared using Student's *t* test or the Mann–Whitney test. Frequencies were expressed as absolute numbers and percentages, and they were compared using the Chi-square test. Multivariate logistic regression analysis was performed to evaluate the independent associations between variables and incidence of emergence agitation. The *P* value <0.05 was considered statistically significant. Statistical analysis was performed using EZR version 1.37.[12]

Results

A total of 590 patients were enrolled in this study, and data for 258 patients including 202 anesthetized extubated patients and 56 awake extubated patients were analyzed [Figure 1]. There were no missing data. Emergence agitation occurred in 90 children (34.9%) and all cases were treated by the sedative drugs including propofol, thiamylal, midazolam or fentanil. The number of emergence agitation in patients who were administered fentanil, flurbiprofenaxetil and acetaminophen during general anesthesia was respectively 58 (35.8%), 6 (22.2%) and 62 (34.8%). All of children with Watcha scale 1 or 2 were treated by TV program or their parent's lullaby and so on without drugs. The rate of premedication in the anesthetized extubated patients was higher than that in the awake extubated patients, but the anesthetized extubated patients were younger and had a lower incidence of emergence agitation [Table 1]. Atrial septal defect (ASD) and ventricular septum defect (VSD) were the major diseases targeted by cardiac catheterization and there were few cases after palliative surgery [Table 2]. Age was included in multivariate logistic regression analysis as not a categorical variable but a continuous variable because there was a linear relation between the incidence of emergence agitation and age [Figure 2]. In multivariate logistic regression analysis, there was no collinearity among variables as all variance inflation factors were less than 2. Anesthetized extubation [odds ratio (OR): 0.075, 95% confidence interval (CI): 0.034-0.165, *P* = 0.000] and older age (OR: 0.808, 95% CI: 0.728-0.897, *P* = 0.000) were associated with a significantly decreased incidence of emergence agitation, and preoperative anxiety (OR:
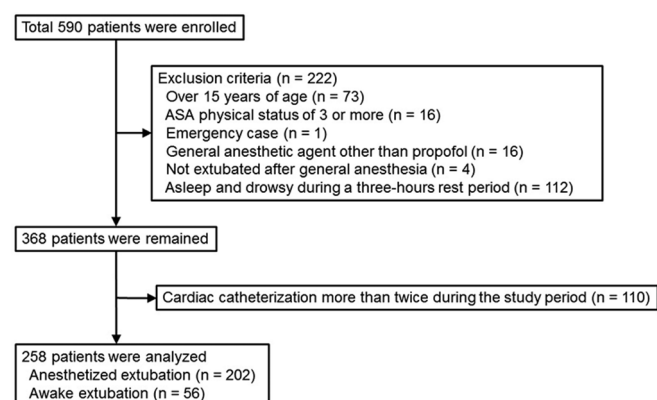
2.220, 95% CI: 1.060–4.660, *P* = 0.03) was associated with a significantly increased incidence of emergence agitation [Table 3]. There were two cases of airway obstruction that needed a nasal airway in the anesthetized extubated patients (0.99%) and one such case in the awake extubated patients (1.79%). In addition, there were two cases of re-bleeding (3.57%) and one case of laryngeal spasm (1.79%) in the awake extubated patients. All patients with complications recovered without sequelae.

Discussion

In this study, we found that anesthetized extubation by propofol decreased the incidence of emergence agitation for pediatric patients with heart disease. Young age and preoperative anxiety associated with an increased incidence of emergence agitation.

Although it has been shown that propofol decreases the incidence of emergence agitation there has been no study in which anesthetized extubation was compared with awake extubation in general anesthesia by propofol in terms of the incidence of emergence agitation.[3,8] Regarding tracheal extubation of anesthetized pediatric patients, Valley reported that the incidences of emergence agitation were 40% with isoflurane, 21-25% with sevoflurane and 46% with desflurane, but there were no statistically significant differences in the incidences.[13,14] Shen reported that low-dose remifentanil (average dose of 0.036 mcg/kg/minute) for extubation in deep sevoflurane anesthesia resulted in rapid recovery and less use of an oral airway but did not decrease the incidence of emergence agitation.[15] Children who were extubated under anesthesia woke up by their parents without uncomfortability by tracheal tube. That might have been the reason for the low incidence of emergence agitation in those children compared with that in awake extubated children.

Young age and preoperative anxiety were shown to be associated with a high incidence of emergence agitation,
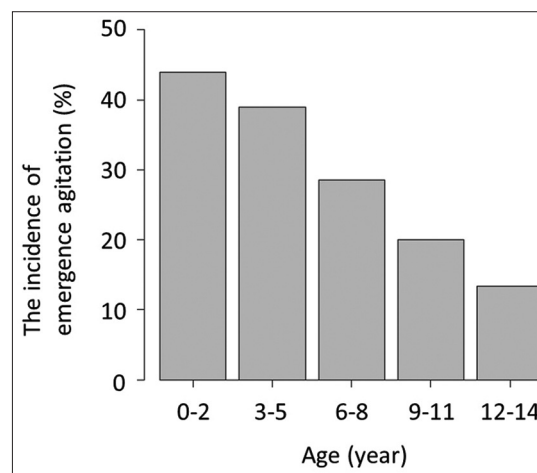

Figure 1: Flow chart. ASA: American Society of Anesthesiologists

Figure 2: Linear relation between emergence agitation and age. There was a linear relation between incidence of emergence agitation and age

Table 1: Patients' characteristics

Variables	Anesthetized extubation (*n*=202)	Awake extubation (*n*=56)	*P*
Age (year)	4 [1-6]	5 [2-9]	0.04
0-2	85 (42.1)	15 (26.8)	
3-5	43 (21.3)	16 (28.6)	
6-8	39 (19.3)	10 (17.9)	
9-11	26 (12.9)	9 (16.1)	
12-14	9 (4.5)	6 (10.7)	
Male	96 (47.5)	24 (42.9)	0.55
ASA physical status 1/2	91 (45.0)/111 (55.0)	26 (46.4)/30 (53.6)	0.88
First time anesthesia	72 (35.6)	22 (39.3)	0.64
Premedication	189 (93.6)	45 (80.4)	0.01
Triclofos sodium	29 (14.4)	2 (3.6)	
Midazolam	91 (45.0)	32 (57.1)	
Brotizolam	59 (29.2)	11 (19.6)	
Others	10 (5.0)	0 (0)	
Preoperative anxiety	42 (20.8)	6 (10.7)	0.12
PAB score			
1	160 (79.2)	50 (89.3)	
2	4 (2.0)	2 (3.6)	
3	38 (18.8)	4 (7.1)	
Global developmental delay	37 (18.3)	12 (21.4)	0.57
TEE	74 (36.6)	26 (46.4)	0.22
Catheter intervention	52 (25.8)	12 (21.4)	0.60
ASO	15 (7.4)	2 (3.5)	
ADO	12 (5.9)	4 (7.1)	
PTA	12 (5.9)	3 (5.4)	
Coil	10 (5.0)	2 (3.5)	
Others	3 (1.5)	1 (1.8)	
Use of fentanyl	123 (60.9)	39 (69.6)	0.28
Anesthesia time (minute)	151.2 (±29.1)	153.0 (±28.0)	0.68
Operation time (minute)	89.5 (±30.7)	96.5 (±30.0)	0.13
Postoperative analgesia	160 (79.2)	45 (80.4)	1.00
Acetaminophen	142 (70.3)	36 (64.3)	
Flurbiprofenaxetil	18 (8.9)	9 (16.1)	
Emergence agitation	51 (25.2)	39 (69.6)	0.000
Watcha scale			
1	115 (56.9)	15 (26.8)	
2	36 (17.8)	2 (3.6)	
3	14 (6.9)	4 (7.1)	
4	37 (18.3)	35 (62.5)	

Data were expressed as absolute numbers (percentage), means (±standard deviation) or medians [interquartile range]. ADO: Amplatzer duct occlude; ASA: American Society of Anesthesiologists; ASO: Amplatzer septal occlude; PAB score: The pediatric anesthesia behavior score; PTA: Percutaneous transluminal angioplasty; TEE: Transesophageal echocardiography

being consistent with results of previous reports.[6,16,17] It has been reported that global developmental delay is not associated with an emotional or unsociable personality as the risk factor of emergence agitation.[17] That is why global developmental delay did not increase the incidence of emergence agitation. Peripheral nerve block and administration of nonsteroidal antiinflammatory drugs (NSAIDs) reduce postoperative pain and the incidence of emergence agitation. As a result, catheter intervention and transesophageal echocardiography, which are procedures with little postoperative pain, were

not associated with emergence agitation. Postoperative analgesia drugs also were not associated with emergence agitation in this study. Previous studies showed that opioids prevent emergence agitation.[6,18] It was also shown that administration of 1.0 mcg/kg fentanyl near the end of surgery was effective for prevention of emergence agitation.[4] We did not considered the timing and dose of fentanyl in this study, and fentanyl was therefore not associated with emergence agitation in our study. Administration of midazolam around the end of surgery was also shown to be effective for prevention of emergence

Table 2: Main disease and state of patients

Variables	Anesthetized extubation (*n*=202)	Awake extubation (*n*=56)
Main disease		
ASD	54 (26.7)	19 (33.9)
VSD	23 (11.4)	7 (12.5)
AVSD	13 (6.4)	2 (3.6)
PDA	20 (9.9)	5 (8.9)
CoA/IAA	6 (3.0)	3 (5.4)
TOF	22 (10.9)	2 (3.6)
DORV	9 (4.5)	3 (5.4)
TGA	6 (3.0)	3 (5.4)
TAPVC/PAPVC	3 (1.5)	1 (1.8)
Ebstein	3 (1.5)	1 (1.8)
TA	2 (1.0)	0 (0)
SV	5 (2.5)	3 (5.4)
PS	11 (5.4)	1 (1.8)
AS	5 (2.5)	2 (3.6)
MR	3 (1.5)	0 (0)
CAVF	3 (1.5)	1 (1.8)
Kawasaki	7 (3.5)	2 (3.6)
Cardiomyopathy	2 (1.0)	0 (0)
Others	5 (2.5)	1 (1.8)
State of patients		
No surgery	101 (50.0)	29 (51.8)
After palliative surgery	19 (9.4)	3 (5.4)
After radical surgery	82 (40.6)	24 (42.9)

Data were expressed as absolute numbers (percentage). AS: Aortic stenosis; ASD: Atrial septal defect; AVSD: Atrioventricular septal defect; CAVF: Coronary arteriovenous fistula; CoA: Coactation of the aorta; DORV: Double outlet right ventricle; Ebstein: Ebstein's anomaly; IAA: Interruption of the aortic arch; Kawasaki: Kawasaki disease; MR: Mitral regurgitation; PAPVC: Partial anomalous pulmonary venous connection; PDA: Patent ductus arteriosus; PS: Pulmonary stenosis; SV: Single ventricle; TA: Tricuspid atresia; TAPVC: Total anomalous pulmonary venous connection; TGA: Transposition of the great arteries; TOF: Tetralogy of Fallot; VSD: Ventricular septal defect

Table 3: Logistic regression analysis with the incidence of emergence agitation

Variables	OR	95% CI	*P*
Age	0.808	0.728-0.897	0.000
Male	1.080	0.584-1.990	0.81
Preoperative anxiety	2.220	1.060-4.660	0.03
GDD	0.647	0.303-1.380	0.26
TEE	1.130	0.575-2.220	0.72
Catheter intervention	0.949	0.465-1.940	0.89
Use of fentanyl	0.659	0.345-1.260	0.21
Postoperative analgesia	0.788	0.379-1.640	0.53
Anesthetized extubation	0.075	0.034-0.165	0.000

CI: Confidence interval; MR: Mental retardation; OR: Odds ratio; TEE: Transesophageal echocardiography; GDD: Global developmental delay

agitation, but midazolam as premedication was not effective.[19,20] We used midazolam only as premedication and did not include it in logistic regression analysis. Ketamine and dexmedetomidine (intravenous or intranasal)

were also reported to be effective; however, they were not administered to the pediatric patients in our study.[21-24]

There are several limitations to this study. First, only children with heart disease were registered in this study. They might be different from healthy children in emergence agitation because of delayed growth due to heart failure, unique living environment with long or frequent hospitalization. That is why it is difficult to apply this study result to healthy children. Second, we used the Watcha scale without the pediatric anesthesia emergence delirium scale (PAED scale) as an elaborate tool. The children crying because of the uncomfortability by the mandatory supine position might have been over estimated as emergence agitation with the Watcha scale. However, Bajwa *et al.* reported that the Watcha score was superior to the PAED scale for assessment of pediatric emergence agitation.[25] Third, anesthetized extubated children were more likely to have received a premedication compared to awake extubated children. It is possible that the lower incidence of emergence agitation in the anesthetized group was due to preoperative anti-anxiety effects or residual sedative effects of the premedication. However, there were no significant difference in preoperative anxiety in both groups and asleep or drowsy cases were excluded. Fourth, midazolam as premedication does not affect emergence agitation, but triclofos sodium and brotizolamare not clear.[19,20] Although we excluded asleep or drowsy cases, different premedication agents have different effects on incidence of emergence agitation. Fifth, we decided the variables of multivariate logistic regression analysis based on previous reports respect to emergence agitation. It is the possible that unknown confounding factors caused bias. This is the limitation of all retrospective studies.

In conclusion, anesthetized tracheal extubation with propofol is associated with a decreased incidence of emergence agitation compared with awake extubation in pediatric patients with heart disease. Further prospective studies are needed.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

References

1. Sikich N, Lerman J. Development and psychometric evaluation of the pediatric anesthesia emergence delirium scale. Anesthesiology 2004;100:1138-45.

2. Cravero J, Surgenor S, Whalen K. Emergence agitation in paediatric patients after sevoflurane anaesthesia and no surgery: A comparison with halothane. Paediatr Anaesth 2000;10:419-24.

3. van Hoff SL, O'Neill ES, Cohen LC, Collins BA. Does a prophylactic dose of propofol reduce emergence agitation in children receiving anesthesia? A systematic review and meta-analysis. Paediatr Anaesth 2015;25:668-76.

4. Kim N, Park JH, Lee JS, Choi T, Kim MS. Effects of intravenous fentanyl around the end of surgery on emergence agitation in children: Systematic review and meta-analysis. Paediatr Anaesth 2017;27:885-92.

5. Kuratani N, Oi Y. Greater incidence of emergence agitation in children after sevoflurane anesthesia as compared with halothane: A meta-analysis of randomized controlled trials. Anesthesiology 2008;109:225-32.

6. Bong CL, Ng AS. Evaluation of emergence delirium in Asian children using the Pediatric Anesthesia Emergence Delirium Scale. Paediatr Anaesth 2009;19:593-600.

7. Uezono S, Goto T, Terui K, Ichinose F, Ishguro Y, Nakata Y, *et al.* Emergence agitation after sevoflurane versus propofol in pediatric patients. Anesth Analg 2000;91:563-6.

8. Sethi S, Ghai B, Ram J, Wig J. Postoperative emergence delirium in pediatric patients undergoing cataract surgery—A comparison of desflurane and sevoflurane. Paediatr Anaesth 2013;23:1131-7.

9. Cohen IT, Finkel JC, Hannallah RS, Hummer KA, Patel KM. Rapid emergence does not explain agitation following sevoflurane anaesthesia in infants and children: A comparison with propofol. Paediatr Anaesth 2003;13:63-7.

10. Beringer RM, Greenwood R, Kilpatrick N. Development and validation of the Pediatric Anesthesia Behavior score—An objective measure of behavior during induction of anesthesia. Paediatr Anaesth 2014;24:196-200.

11. Watcha MF, Ramirez-Ruiz M, White PF, Jones MB, Lagueruela RG, Terkonda RP. Perioperative effects of oral ketorolac and acetaminophen in children undergoing bilateral myringotomy. Can J Anaesth 1992;39:649-54.

12. Kanda Y. Investigation of the freely available easy-to-use software 'EZR' for medical statistics. Bone Marrow Transplant 2013;48:452-8.

13. Valley RD, Ramza JT, Calhoun P, Freid EB, Bailey AG, Kopp VJ, *et al.* Tracheal extubation of deeply anesthetized pediatric patients: A comparison of isoflurane and sevoflurane. Anesth Analg 1999;88:742-5.

14. Valley RD, Freid EB, Bailey AG, Kopp VJ, Georges LS, Fletcher J, *et al.* Tracheal extubation of deeply anesthetized pediatric patients: A comparison of desflurane and sevoflurane. Anesth Analg 2003;96:1320-4.

15. Shen X, Hu C, Li W. Tracheal extubation of deeply anesthetized pediatric patients: A comparison of sevoflurane and sevoflurane in combination with low-dose remifentanil. Paediatr Anaesth 2012;22:1179-84.

16. Aono J, Ueda W, Mamiya K, Takimoto E, Manabe M. Greater incidence of delirium during recovery from sevoflurane anesthesia in preschool boys. Anesthesiology 1997;87:1298-300.

17. Kain ZN, Caldwell-Andrews AA, Maranets I, McClain B, Gaal D, Mayes LC, *et al.* Preoperative anxiety and emergence delirium and postoperative maladaptive behaviors. Anesth Analg 2004;99:1648-54.

18. Tan Y, Shi Y, Ding H, Kong X, Zhou H, Tian J. μ-Opioid agonists for preventing emergence agitation under sevoflurane anesthesia in children: A meta-analysis of randomized controlled trials. Paediatr Anaesth 2016;26:139-50.

19. Chen J, Li W, Hu X, Wang D. Emergence agitation after cataract surgery in children: A comparison of midazolam, propofol and ketamine. Paediatr Anaesth 2010;20:873-9.

20. Viitanen H, Annila P, Viitanen M, Yli-Hankala A. Midazolam premedication delays recovery from propofol-induced sevoflurane anesthesia in children 1-3 yr. Can J Anaesth 1999;46:766-71.

21. Abu-Shahwan I, Chowdary K. Ketamine is effective in decreasing the incidence of emergence agitation in children undergoing dental repair under sevoflurane general anesthesia. Paediatr Anaesth 2007;17:846-50.

22. Patel A, Davidson M, Tran MC, Quraishi H, Schoenberg C, Sant M, *et al.* Dexmedetomidine infusion for analgesia and prevention of emergence agitation in children with obstructive sleep apnea syndrome undergoing tonsillectomy and adenoidectomy. Anesth Analg 2010;111:1004-10.

23. Yao Y, Qian B, Lin Y, Wu W, Ye H, Chen Y. Intranasal dexmedetomidine premedication reduces minimum alveolar concentration of sevoflurane for laryngeal mask airway insertion and emergence delirium in children: A prospective, randomized, double-blind, placebo-controlled trial. Paediatr Anaesth 2015;25:492-8.

24. Hauber JA, Davis PJ, Bendel LP, Martyn SV, McCarthy DL, Evans MC, *et al.* Dexmedetomidine as a rapid bolus for treatment and prophylactic prevention of emergence agitation in anesthetized children. Anesth Analg 2015;121:1308-15.

25. Bajwa SA, Costi D, Cyna AM. A comparison of emergence delirium scales following general anesthesia in children. Paediatr Anaesth 2010;20:704-11.