BRITISH JOURNAL OF HOSPITAL MEDICINE

ARTICLE

Impact of Propofol Administered before Extubation on Respiratory Adverse Events in Pediatric Patients Undergoing Tonsillectomy and Adenoidectomy: A Randomized Controlled Trial

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Abstract

Aims/Background Perioperative respiratory adverse events (PRAEs) are common in pediatric anesthesia, especially in otolaryngology procedures. In this randomized controlled trial, we investigated the impact of administering propofol before extubation on PRAEs in pediatric patients undergoing tonsillectomy and adenoidectomy.

Methods We enrolled children aged 3 to 8 years old, of American Society of Anesthesiologists (ASA) classes I to III, scheduled for tonsillectomy, and randomly divided them into propofol and control groups. The subjects in the propofol group received multiple small doses of propofol (0.5 mg/kg per dose, total 1–2 mg/kg) until the patient resumed regular spontaneous breathing and exhibited no bodily movements. The subjects in the control group received 0.15 mL/kg of saline. The primary outcome was the rate of PRAEs, such as laryngospasm, bronchospasm, breath-holding spell, severe coughing, desaturation, and airway obstruction, post-extubation. The secondary outcomes were the extubation time, pre-extubation Richmond Agitation-Sedation Scale (RASS) score, end-tidal sevoflurane concentration at extubation, incidence of postoperative agitation, time to consciousness, and Face, Legs, Activity, Cry, and Consolability (FLACC) pain score in the recovery room. Results were reported with risk ratios (RR) and their 95% confidence intervals (CI), as well as the *p*-values indicating statistical significance.

Results A total of 239 patients were included, including 119 in the propofol group and 120 in the control group. Our findings indicated no significant difference in the rate of PRAEs between the two groups (5.9% vs 10.8%, RR: 0.54, 95% CI: 0.23 to 1.31, $p = 0.17$). However, the propofol group showed a notable decrease in moderate to severe coughs (13.4% vs 60.0%, RR: 0.22, 95% CI: 0.14 to 0.36, $p < 0.001$) and postoperative agitation (4.2% vs 60.8%, RR: 0.07, 95% CI: 0.03 to 0.17, $p < 0.001$).

Conclusion This trial demonstrated that while administering repeated small doses of propofol before extubation does not significantly reduce respiratory adverse events in children undergoing tonsillectomy and adenoidectomy, it does significantly reduce the incidence of severe coughing, improving postoperative recovery and clinical outcomes. Moreover, propofol helps reduce postoperative agitation, enhancing the safety and effectiveness of postoperative care, and maintaining its valuable clinical role in postoperative management.

Clinical Trial Registration ClinicalTrials.gov (NCT05769842).

Key words: perioperative respiratory adverse events; propofol; children; extubation

Submitted: 15 July 2024 Revised: 12 September 2024 Accepted: 14 September 2024

How to cite this article:
Liao R, Zhou Z, Wang X, Shao H. Impact of Propofol Administered before Extubation on Respiratory Adverse Events in Pediatric Patients Undergoing Tonsillectomy and Adenoidectomy: A Randomized Controlled Trial. Br J Hosp Med. 2024. https://doi.org/10.12968/hmed.2024.0431

Introduction

Perioperative respiratory adverse events (PRAEs) are among the most common complications in pediatric anesthesia, with an increased incidence during tracheal

extubation, leading to severe hypoxia and aspiration, elevated chances of unplanned intensive care unit (ICU) admissions, prolonged hospital stays, and more economic burden for patients (Egbuta and Mason, 2020). These adverse effects, primarily including laryngospasm, bronchospasm, breath-holding spell, severe coughing, desaturation, and airway obstruction, account for 30% of cardiac arrests in pediatric patients during the perioperative period (Bhananker et al, 2007). It has been reported that the rate of PRAEs in children undergoing tonsillectomy and adenoidectomy with at least one relevant risk factor was as high as 62% (von Ungern-Sternberg et al, 2013). The occurrence of PRAEs is closely associated with heightened airway reactivity, with high-risk factors including asthma, eczema, and an upper airway infection occurring within two weeks leading up to the onset of PRAEs (von Ungern-Sternberg et al, 2010).

Several studies have compared the effects of deep anesthesia extubation and awake extubation on PRAEs, revealing that deep anesthesia extubation was unable to reduce the incidence of PRAEs in children (Baijal et al, 2015; von Ungern-Sternberg et al, 2013). Furthermore, another study has indicated that preoperative use of salbutamol also failed to reduce the risk of PRAEs in school-age children (Ramgolam et al, 2017). Nevertheless, a recent study has shown that preoperative intranasal dexmedetomidine effectively reduces the incidence of PRAEs (Shen et al, 2022). This finding sparks a new question on whether there are any other drugs that are equally effective in reducing the occurrence of PRAEs.

Propofol, a general anesthetic, primarily exerts its inhibitory effects on the central nervous system by enhancing the neurotransmitter gamma-aminobutyric acid (GABA) (Chidambaran et al, 2015). Propofol has been demonstrated to lower the occurrence of laryngospasm compared to sevoflurane (Li and Zhu, 2024) . Moreover, intravenous maintenance has also been associated with a lower occurrence of PRAEs compared to inhalation maintenance (von Ungern-Sternberg et al, 2010). Nevertheless, inhalation anesthesia is widely used due to its convenience. This has prompted the next question of whether the advantages of both inhalation and intravenous anesthesia approaches can be integrated to maximize the chances of PRAEs reduction during extubation. All of these requirements led us to hypothesize that administering repeated small doses of propofol before extubation could reduce the occurrence of PRAEs.

Methods

Data Collection

This study was conducted in accordance with the principles outlined in the Declaration of Helsinki and was approved by the Ethics Committee of the Children's Hospital of Fudan University (Approval No. 2022-259). The parents of all participants had given their informed consent before allowing their children to take part in the study. This study was registered on clinicaltrials.gov (NCT05769842, https://clinicaltrials.gov/study/NCT05769842), before patient enrollment. Additionally, the study was conducted and reported in adherence to the CONSORT reporting guidelines (Schulz et al, 2010).

This single-center randomized controlled trial was conducted at the Children's Hospital of Fudan University between November 2023 and December 2023. The flowchart is depicted in Fig. 1. The inclusion criteria for this study are as follows: (1) children aged 3 to 8 years; (2) subjects classified as American Society of Anesthesiologists (ASA) classes I to III (Mayhew et al, 2019); (3) subjects scheduled for tonsillectomy and adenoidectomy; and (4) subjects whose parents had given their informed consent for study participation. The exclusion criteria are as follows: (1) patients with congenital heart disease; (2) patients with tumors, severe pulmonary diseases, hepatic or renal dysfunction; (3) patients with neurological or coagulation disorders; and (4) patients unwilling to participate in the experiment. No sedatives were administered on the day before the surgery. The patients were randomly assigned to the propofol group and the control group. Routine monitoring was conducted on the patients, including examinations of their blood pressure, heart rate, pulse oxygen saturation, end-tidal carbon dioxide and concentration of anesthetic gases. The intravenous induction for intubation was conducted using propofol at a dose of 3 mg/kg, remifentanil at a dose of 3–5 μg/kg, and atropine at a dose of 0.01 mg/kg. During surgery, the patient was mechanically ventilated via endotracheal intubation. Anesthesia maintenance during the procedure involved a combination of 2.5% sevoflurane and 50% nitrous oxide. Dexamethasone was administered at a dose of 0.3 mg/kg (up to a maximum of 8 mg) for anti-inflammatory and antiemetic effects. Postoperative analgesia was administered with propacetamol at a dose of 30 mg/kg and hydromorphone, which was given at a dose of 5 μg/kg prior to extubation and supplemented with an additional 3–5 μg/kg, as needed, post-extubation depending on the anesthesiologist's experience as well as the patient's respiratory rate and level of pain they could endure. In the propofol group, sevoflurane administration was stopped and oxygen flow was increased to 10 L/min at the end of the surgery. When the patients showed spontaneous but irregular breathing, we administered an initial dose of 0.5 mg/kg of propofol. Additional 0.5 mg/kg doses were given as needed if the patient exhibited involuntary movements. These dose adjustments were set to achieve optimal sedation to facilitate smooth extubation while maintaining respiratory function (0.5 mg/kg for each dose, up to 1–2 mg/kg in total). In the control group, sevoflurane administration was ceased at the conclusion of the surgery. Subsequently, the patients received high-flow oxygen administered at a rate of exceeding 10 liters per minute and saline infusion at 0.15 mL/kg. We performed lung expansion maneuvers and oropharyngeal suctioning on the patient before extubation. The extubation was only performed in the subjects of the propofol group if the following criteria were fulfilled: (1) patient showed stable breathing, with no signs of respiratory depression; and (2) patient's tidal volume >5 mL/kg. The endotracheal tube was gently removed upon the cessation of spontaneous breathing in the patient, to avoid causing irritation or discomfort to the patient during the extubation process. On the other hand, the extubation was only conducted in the subjects of the control group if the following criteria were met: (1) patient exhibiting body movements or opening eye; and (2) patient's tidal volume >5 mL/kg without showing signs of respiratory depression. The endotracheal tube was gently removed when the spontaneous breathing stopped (Veyckemans, 2020).

Both groups received oxygen via face mask post-extubation and were monitored for agitation (defined as purposeless movements or restlessness that are difficult to soothe). If agitation occurred, propofol at a dose of 0.5–1 mg/kg was administered for sedation.

Randomization and Blinding

After excluding two cases, an aggregate of 239 children were ultimately recruited. A total of 241 numbers were randomly generated using a computer, and each of the generated numbers was sealed in an envelope. The anesthesiologist would administer one of the two agents to each patient depending on the number he revealed when he/she met the patient. In a blinded procedure, saline solution would be administered to patients in the control group if an odd number was revealed, whereas propofol solution was given to those in the propofol group if an even number was obtained. During extubation, another researcher recorded the data. The patients, data recorders, nurses, and other staff were all unaware of the group assignments.

Outcome Definitions

Primary Outcome

The PRAEs that occurred during the period from extubation to the time in the recovery room include laryngospasm, bronchospasm, breath-holding spell, severe coughing, desaturation, and airway obstruction. Laryngospasm is defined as reduced or absence of airflow under the chin and absence of breathing sounds upon auscultation of the throat, necessitating mask ventilation with positive pressure or administration of anesthetic agents such as propofol or succinylcholine for relief. Bronchospasm is defined as decreased tidal volume and audible wheezing upon lung auscultation, accompanied by a decrease in oxygen saturation. Breath-holding spell refers to the cessation of breathing for more than 5 seconds. Coughing is divided into 4 categories corresponding to the level of severity: 0 = no cough; 1 = 1–2 episodes of coughing; 2 = non-continuous coughing for 3 or more episodes; 3 = continuous and strong coughing lasting more than 10 seconds. Grade 3 coughing is considered a PRAE. Desaturation is defined as post-extubation oxygen saturation (SpO_2) of $<92\%$ and unresponsiveness to oxygen supplementation delivered through a mask, which lasts for more than 10 seconds. Airway obstruction reflects the need for jaw support for relief. The presence of any one or more of the mentioned conditions indicates the occurrence of PRAEs (Ramgolam et al, 2018).

Secondary Outcomes

In addition to the main outcomes, we also compared the following indicators:

Extubation time (the time from the end of sevoflurane closure to extubation), pre-extubation Richmond Agitation-Sedation Scale (RASS) score (Kerson et al, 2016), end-tidal sevoflurane concentration at extubation, the incidence of postoperative agitation, time to consciousness (the time from extubation to eye opening and being able to respond coherently), and Face, Legs, Activity, Cry, and Consola-

bility (FLACC) pain score (stands for Face, Legs, Activity, Cry, and Consolability, representing the five domains assessed to determine pain intensity) in the recovery room (Merkel et al, 1997).

Sample Size Calculation

In our preliminary experiment, we observed that the incidence of PRAEs was 16% (3/18) in the control group, which was higher than 5% (1/20) in the propofol group. To allow for an 80% chance of detecting a significant difference between the groups using a two-sided test with a significance level of 0.05, this study was designed with a sample size of 119 children per group.

Statistical Analysis

The data in this study were analyzed using IBM SPSS Statistics 25.0 (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY, USA). We employed the Shapiro–Wilk test to confirm the normality of the distribution and then used Student's *t*-test to compare data of continuous variables between the two groups. For continuous data with a non-normal distribution, the Wilcoxon Mann–Whitney test was used for analysis. Categorical variables were compared using the Chi-square test or Fisher's exact test. Results are presented as risk ratio (RR) and 95% confidence intervals (CI), along with the associated *p*-value denoting statistical significance. The two-sided *p*-value less than or equal to 0.05 was considered statistically significant.

Results

A total of 241 pediatric patients were enrolled. One case was excluded from the control group due to post-tonsillectomy bleeding requiring re-intubation. In another case, sudden agitation from a patient of the propofol group caused bending of the cannula needle, which impeded the smooth flow of propofol into the body, leading to its exclusion from the study. Therefore, data for the present study were collected from a total of 239 patients, which comprised 119 patients in the propofol group (49 patients received a dose of 1 mg/kg of propofol, 52 received 1.5 mg/kg, and 18 received 2 mg/kg) and 120 individuals in the control group (Fig. 1).

The demographic and clinical data of the patients are presented in Table 1. No significant differences were observed between the control and propofol groups in asthma, eczema, recent cold symptoms, ASA classification, anesthesia time, or surgical duration ($p > 0.05$). Table 2 summarizes the incidence of PRAEs after extubation in the two groups of children. The propofol group showed a decreased incidence of PRAEs compared to the control group (a difference of 4.9%), but this difference was not statistically significant (propofol group vs control group: 5.9% vs 10.8%, RR: 0.54, 95% CI: 0.23–1.31, $p = 0.17$).

However, conspicuous differences in the proportions of patients in the two groups across the different severity levels of coughing were observed (Fig. 2). Table 3 provides the specific data regarding the varying degrees of coughing between the two groups. The incidence of grades 2–3 cough in the propofol group was sig-

Table 1. Demographic and clinical data of the patients in control and propofol groups.

	Control group	Propofol group	*t*-value, χ^2 or Z-value	*p*-value
	n = 120	*n* = 119		
Age (y), Mean ± SD	4.75 ± 1.49	4.50 ± 1.33	1.35	0.18
Gender			0.05	0.83
(Male), *n* (%)	72 (60.0%)	73 (61.3%)		
(Female), *n* (%)	48 (40.0%)	46 (38.7%)		
Weight (kg), Mean ± SD	20.39 ± 5.42	19.77 ± 4.61	0.96	0.34
ASA, *n* (%)			0.51	0.78
Class I	81 (67.5%)	77 (64.7%)		
Class II	36 (30.0%)	40 (33.6%)		
Class III	3 (2.5%)	2 (1.7%)		
Anesthesia duration (min), Median (IQR)	21.50 (16.25 to 30.00)	24.00 (16.00 to 32.00)	0.71	0.48
Surgery duration (min), Median (IQR)	16.00 (11.00 to 25.00)	18.00 (11.00 to 27.00)	0.64	0.52
Presence of asthma, *n* (%)	0 (0.0%)	1 (0.8%)	-	0.50
Presence of eczema, *n* (%)	5 (4.2%)	3 (2.5%)	0.12	0.73
Recent cold symptoms in the past two weeks, *n* (%)	38 (31.7%)	39 (32.8%)	0.03	0.86

ASA, American Society of Anesthesiologists; SD, standard deviation; IQR, interquartile range.

nificantly lower than that in the control group (13.4% vs 60.0%, RR: 0.22, 95% CI: 0.14–0.36, $p < 0.001$). Fig. 3 displays the number of cases across different severity levels of cough after extubation in the two groups of patients, who were further stratified based on their history of upper respiratory tract infection within the preceding two weeks. Among patients with such a history, the incidence of grade 2–3 cough in the propofol group was also lower compared to the control group (23.1% vs 63.2%, RR: 0.37, 95% CI: 0.20–0.68, $p < 0.001$) (Table 4).

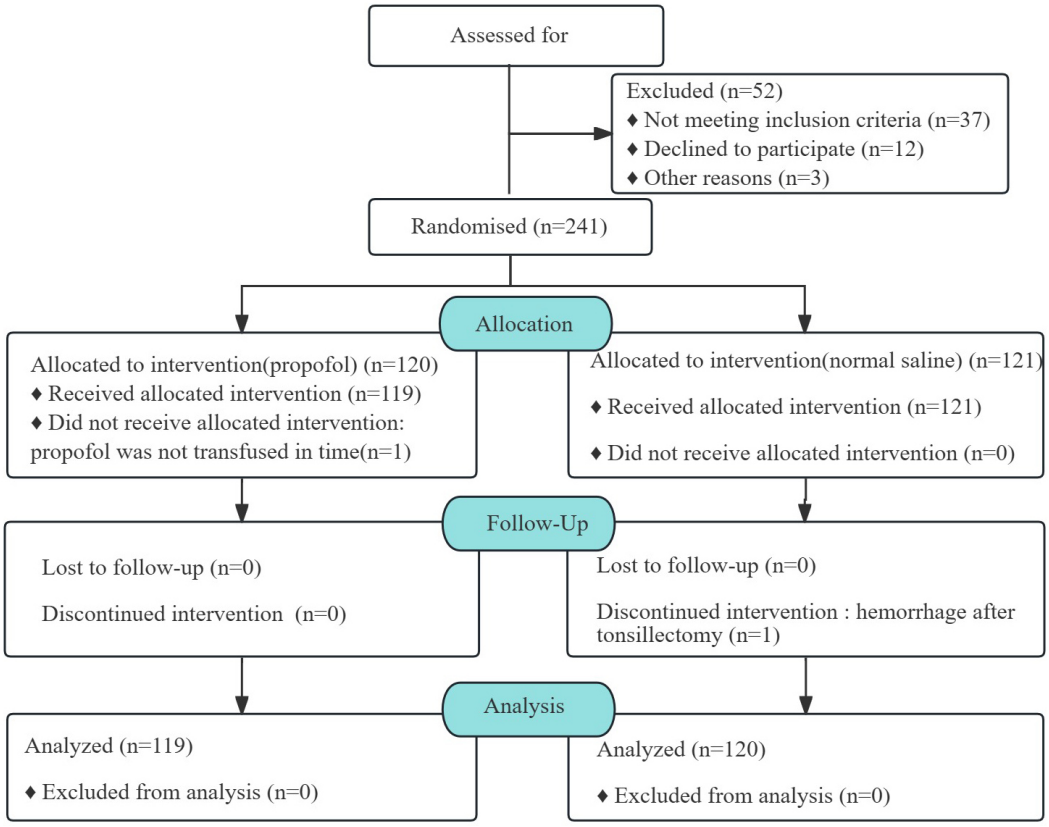

Fig. 1. Flowchart of selecting and including patients for this study.

Extubation time was prolonged in the propofol group with an average of 1.31 minutes, as compared to the control group (mean ± SD, 11.72 ± 2.40 vs 10.41 ± 2.01, 95% CI: –1.88 to –0.75, $p < 0.001$). Nevertheless, statistically speaking, the difference was held with little clinical significance because the 95% CI of the difference in means had crossed 1, although the p-value was <0.001. The end-tidal concentration of sevoflurane at extubation was 0.22% in the control group and 0.28% in the propofol group; however, this difference was clinically the same in the two groups even if statistically significant ($p < 0.01$). The incidence of postoperative agitation in the propofol group was significantly lower than that in the control group (4.2% vs 60.8%, RR: 0.07, 95% CI: 0.03 to 0.17, $p < 0.001$). Separately, the pre-extubation RASS score of the propofol group was lower than that of the control group (median [interquartile range (IQR)], –3 [–4 to 1] vs 2 [2 to 3], $p < 0.001$). There were no significant differences in awakening time and postoperative FLACC pain scores between the two groups (Table 5).

Table 2. Comparison of the incidence of PRAEs between the control and propofol groups.

	Control group	Propofol group	RR	95% CI	*p*-value
	n = 120	*n* = 119			
Laryngospasm	0 (0.0%)	0 (0.0%)	-	-	-
Bronchospasm	0 (0.0%)	0 (0.0%)	-	-	-
Breath-holding spell	2 (1.7%)	0 (0.0%)	-	-	0.48
Severe coughing	10 (8.3%)	0 (0.0%)	-	-	<0.01
Desaturation <92%	7 (5.8%)	7 (5.9%)	1.01	0.37–2.79	0.99
Airway obstruction	0 (0.0%)	5 (4.2%)	-	-	0.07
Overall complications	13 (10.8%)	7 (5.9%)	0.54	0.23–1.31	0.17

The data are presented as *n* (%). Severe coughing = Grade 3 (continuous and strong coughing lasting more than 10 seconds). Overall complications: the presence of any one or more of the mentioned conditions indicates the occurrence of PRAEs. PRAEs, perioperative respiratory adverse events; RR, risk ratio; CI, confidence interval.

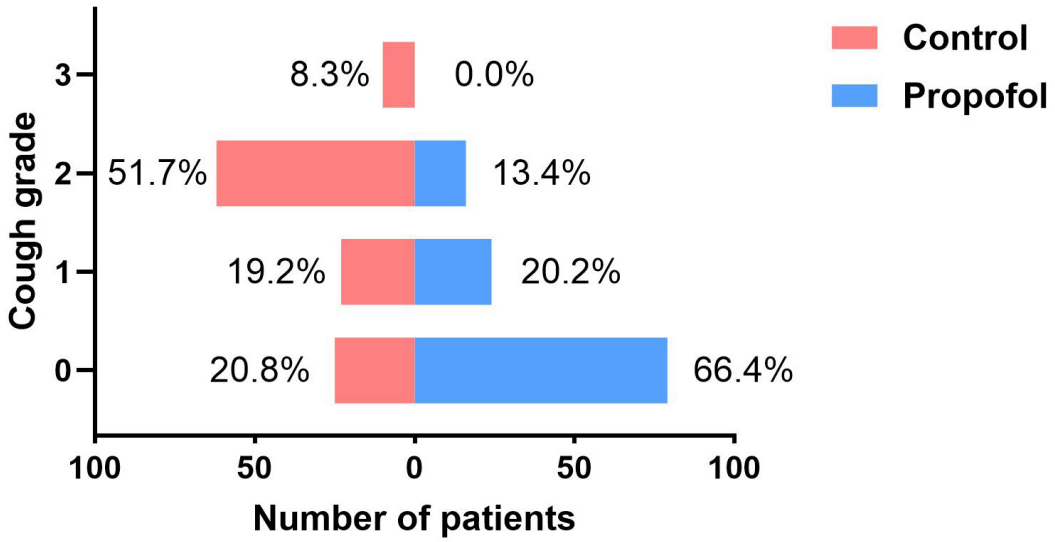

Fig. 2. Distribution of patients of the control and propofol groups across the different severity levels of cough.

Discussion

The current study found that it is safe to utilize propofol, or not, before extubation, given that the risk of laryngospasm and bronchospasm after extubation in children is very low. Although administering propofol in repeated small doses before extubation did not reduce the incidence of PRAEs in children undergoing tonsillectomy and adenoidectomy, it could significantly reduce the incidence of coughing after extubation, making the extubation process smoother and more comfortable for the patients. Furthermore, through the observation from our analysis, we notice that laryngospasm or bronchospasm may occur by chance. According to the statistical rule of 3/N for estimating the upper 95% CI of a complication that did not occur in a sample of patients (Ho et al, 2018), we found that the overall incidence

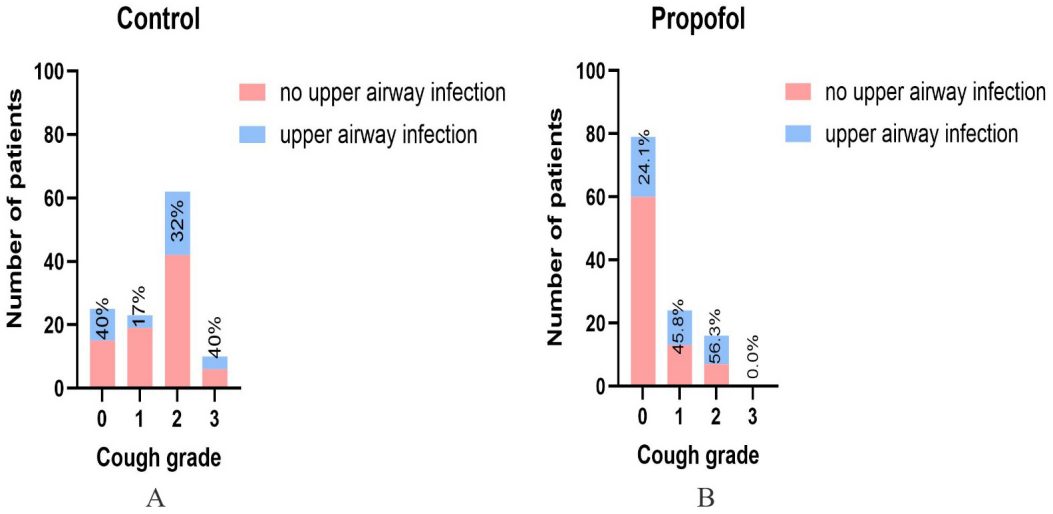

Fig. 3. Distribution of patients of the control (A) and propofol (B) groups, with or without a history of upper airway infection, across the different severity levels of cough.

Table 3. Incidence and severity of coughing in patients of the control and propofol groups after extubation.

Cough grade	Control group	Propofol group	RR	95% CI	*p*-value
	n = 120	*n* = 119			
0	25 (20.8%)	79 (66.4%)			
1	23 (19.2%)	24 (20.2%)			
0–1	48 (40.0%)	103 (86.6%)	2.16	1.72–2.72	<0.001
2	62 (51.7%)	16 (13.4%)			
3	10 (8.3%)	0 (0.0%)			
2–3	72 (60.0%)	16 (13.4%)	0.22	0.14–0.36	<0.001

The data are presented as *n* (%). Cough grades: 0 = no cough; 1 = 1–2 episodes of coughing; 2 = non-continuous coughing of 3 or more episodes; 3 = continuous and strong coughing lasting more than 10 seconds.

of laryngospasm or bronchospasm was 1.3% (3/239) in this study, resembling the average incidence reported in the APRICOT data (Habre et al, 2017).

Previously, Hosseini et al (2022), investigated the effects of pre-extubation single-dose propofol (0.5 mg/kg) on post-extubation respiratory complications in 70 children undergoing tonsillectomy, realizing that low-dose propofol could suppress the occurrence of laryngospasm (control group vs propofol group, 0 vs 14.3%) but no significant difference in coughing rates between the two groups was detected. It is important to note that our experimental design and anesthetic approach are distinct from theirs. In our study, a higher total dose of propofol (>0.5 mg/kg) effectively reduced coughing. Furthermore, differences in extubation proficiency between the two anesthesiologists likely contributed to the significant disparity in laryngospasm incidence observed in the two trials.

The endotracheal tube to the airway stimulation is the main cause of cough after general anesthesia. Coughing may result in throat injury, causing swelling

Table 4. Incidence and severity of coughing after extubation in patients of the control and propofol groups who had an upper airway infection within the preceding two weeks.

Cough grade	Control group	Propofol group	RR	95% CI	*p*-value
	n = 38	*n* = 39			
0	10 (26.3%)	19 (48.7%)			
1	4 (10.5%)	11 (28.2%)			
0–1	14 (36.8%)	30 (76.9%)	2.09	1.33–3.28	<0.001
2	20 (52.6%)	9 (23.1%)			
3	4 (10.5%)	0 (0.0%)			
2–3	24 (63.2%)	9 (23.1%)	0.37	0.20–0.68	<0.001

The data are presented as *n* (%). Cough grades: 0 = no cough; 1 = 1–2 episodes of coughing; 2 = non-continuous coughing of 3 or more episodes; 3 = continuous and strong coughing lasting more than 10 seconds.

and hoarseness, and it may exacerbate asthmatic symptoms or lead to complications such as pneumothorax or subcutaneous emphysema. Coughing can also cause wound dehiscence, impair healing, and intensify pain (Irwin, 2006). Therefore, alleviating post-extubation coughing is crucial for enhancing postoperative comfort and reducing the risk of complications in patients. Our results align with a study by Hohlrieder et al (2007), which revealed a significant reduction in the incidence of coughing at extubation through total intravenous anesthesia as compared to combined anesthesia. In the same vein, Karam et al (2023) found that total intravenous anesthesia significantly reduced the occurrence of PRAEs compared to sevoflurane maintenance, indicating propofol's superior ability to suppress laryngeal reflex responses. On the one hand, propofol, at hypnotic concentrations, significantly reduces pharyngeal constriction and suppresses laryngeal reflexes, thereby attenuating the intense stimulation of the airway during extubation (Sundman et al, 2001). On the other hand, as a general anesthetic, propofol may downregulate cough reflex pathways associated with the central nervous system (Widdicombe and Singh, 2006). Therefore, administering propofol may alleviate the occurrence of irritative coughing post-extubation, enhancing overall postoperative comfort. Another study in 2023 showed that administering a single dose of 0.5 mg/kg propofol at the end of surgery did not effectively reduce the incidence of emergence coughing (Ouellet et al, 2023). This was likely due to the short half-life of propofol, which is not potent enough to maintain sufficient blood levels of propofol to suppress airway stimulation. In our trial, multiple additional doses of propofol were administered to maintain a certain blood concentration of propofol, extending the duration of propofol's action and effectively alleviating the incidence of post-extubation cough.

Our research yielded results similar to those of deep anesthesia extubation, indicating that while it could not reduce the incidence of PRAEs, it significantly lowered the occurrence of post-extubation coughing (Baijal et al, 2015; von Ungern-Sternberg et al, 2013). Therefore, both sevoflurane and propofol are general anesthetic agents that are capable of suppressing airway reflexes (Chidambaran et al, 2015; Ramgolam et al, 2018).

Table 5. Comparison of several parameters at extubation between the control and propofol groups.

	Control group	Propofol group	*t*-value, χ^2 or Z-value	Mean difference or RR (95% CI)	*p*-value
	n = 120	*n* = 119			
Extubation time (minutes), Mean ± SD	10.41 ± 2.01	11.72 ± 2.40	–4.59	–1.31 (–1.88 to –0.75)	<0.001
End-tidal sevoflurane concentration at extubation (%), Median (IQR)	0.22 (0.12 to 0.29)	0.28 (0.20 to 0.32)	3.58	–0.05 (–0.08 to –0.02)	<0.01
Postoperative agitation, *n* (%)	73 (60.8%)	5 (4.2%)	87.16	0.07 (0.03 to 0.17)	<0.001
FLACC pain score, Median (IQR)	2 (1 to 3)	2 (0 to 3)	0.65	0 (0 to 0)	0.51
Pre-extubation RASS score, Median (IQR)	2 (2 to 3)	–3 (–4 to 1)	12.63	5 (4 to 5)	<0.001
Time to wakefulness (minutes), Median (IQR)	16.50 (11.00 to 24.00)	18.00 (11.00 to 25.00)	0.63	–1.00 (–3.00 to 2.00)	0.53

RASS, Richmond Agitation-Sedation Scale; FLACC, Face, Legs, Activity, Cry, and Consolability.

In addition, research conducted by von Ungern-Sternberg et al (2013), suggested that the incidence of PRAEs during emergence from anesthesia with sevoflurane in children undergoing adenotonsillectomy was 62%, which was significantly higher than the 10.8% in our control group. This substantially increased incidence in their study is attributed to the inclusion of children carrying at least one high-risk factor for PRAEs, which greatly increases the incidence of PRAEs during extubation. Moreover, the age range of the children recruited in the two experiments was different, as were the anesthesia plans, contributing to the natural variance in the outcomes of the two studies.

Our secondary outcomes revealed that pre-extubation administration of propofol significantly reduced the occurrence of postoperative agitation in pediatric patients. This aligns with findings from the study by Miyake et al (2023). Agitation is a relatively common phenomenon during the postoperative awakening period, and potential risk factors include patient age, personality, preoperative anxiety, pain, surgical type, and anesthesia strategy (Kanaya, 2016). Moreover, sevoflurane is more likely to cause emergence agitation compared to other anesthetics (Costi et al, 2014). Administering propofol before extubation effectively prolongs the postoperative state of neural suppression, reducing the likelihood of excessive excitement and agitation during the awakening period in pediatric patients. Propofol inhibits emergence agitation for the following reasons: first, propofol acts by agonizing gamma-aminobutyric acid (GABA) receptors, enhancing inhibitory signals and producing a central sedative effect, which helps reduce emergence agitation (Sahinovic et al, 2018). Second, it non-competitively antagonizes N-methyl-D-aspartate (NMDA) receptors, lowering the activity of excitatory neurotransmitters, and thereby helping to suppress neural pathways associated with anxiety and ag-

itation (Vasileiou et al, 2009). Additionally, during the emergence from sevoflurane anesthesia, transitioning to propofol facilitates the elimination of sevoflurane, which can more effectively reduce postoperative agitation and allow the patient to more smoothly transition to a wakeful state (Xiao et al, 2022).

We chose propofol in this study for the following advantages: Firstly, propofol was a commonly used, easily accessible intravenous induction agent. Secondly, propofol has a short half-life, allowing for rapid metabolism, thereby reducing the occurrence of prolonged sedation and other adverse reactions (Chidambaran et al, 2015). Additionally, pre-extubation administration of propofol effectively decreased postoperative agitation, increasing the safety of extubation procedures.

In the propofol group, 5 patients experienced airway obstruction after extubation. Although there was no statistically significant difference between the two groups of children, this is indeed a concern for all patients who are extubated before regaining full consciousness. If a patient does not regain consciousness immediately after extubation, it is essential to continuously assess whether the child's airway is clear to avoid the occurrence of hypoxemia.

Being prospective and randomized controlled are the two major strengths of the current study. Administering propofol in small doses multiple times after the resumption of spontaneous breathing allows for better control of drug concentration, thereby reducing potential adverse reactions. Our experiment did not use neuromuscular blocking agents, eliminating the impact of these agents on the experimental results.

Several limitations of this study should be highlighted. The primary limitation of this trial was the lack of monitoring of sedation levels in pediatric patients during extubation. Different levels of sedation could lead to varying respiratory responses, potentially affecting the trial results. Additionally, we did not classify the severity of obstructive sleep apnea syndrome (OSAS) in the patients, which could result in varying degrees of airway obstruction. In future trials, we hope to include Bispectral Index (BIS) monitoring to assess anesthesia depth and perform polysomnography for pediatric patients with OSAS.

Conclusion

In conclusion, repeatedly administering propofol in small doses before extubation does not reduce the incidence of PRAEs following tonsillectomy and adenoidectomy in pediatric patients, but it can decrease the rate of coughing. Additionally, propofol also reduces the incidence of postoperative agitation. This finding highlights a potential approach to safe extubation in patients. However, further research and validation are needed to determine the exact effectiveness and safety of propofol in other age groups and in patients undergoing different surgical procedures.

Key Points

- Children undergoing tonsillectomy and adenoidectomy have an increased incidence of perioperative respiratory adverse events (PRAEs) during extubation, compared with those undergoing other surgeries.
- Currently, methods available to treat PRAEs are limited.
- In our trial, administering propofol in repeated small doses before extubation does not reduce respiratory adverse events in children undergoing tonsillectomy and adenoidectomy.
- However, such propofol administration protocol significantly reduces coughing and postoperative agitation, improving overall patient comfort and smoothness during extubation.

Availability of Data and Materials

Raw datasets are available from the corresponding author upon reasonable request, subject to compliance with applicable data protection regulations and ethical standards.

Author Contributions

RTL and ZJZ designed the study. RTL, ZJZ, XW, and HYS conducted the study. RTL collected and analyzed the data. RTL participated in drafting the manuscript, and all authors contributed to the critical revision of the manuscript for important intellectual content. All authors gave final approval of the version to be published. All authors participated fully in the work, took public responsibility for appropriate portions of the content, and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or completeness of any part of the work were appropriately investigated and resolved.

Ethics Approval and Consent to Participate

This study received approval from the Ethics Committee of the Children's Hospital of Fudan University (Approval No. 2022-259), and the parents of all participants had given their informed consents before allowing their children to take part in the study.

Acknowledgement

The authors would like to express their sincere gratitude to all the children who participated in the study and their families. We also thank the doctors and nurses involved in recording data.

Funding

This research received no external funding.

Conflict of Interest

The authors declare no conflict of interest.

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