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ORIGINAL ARTICLE

Dexmedetomidine facilitates extubation in children who require intubation and respiratory support after airway foreign body retrieval: a case–cohort analysis of 57 cases

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Abstract

Purpose This study aimed to investigate whether dexmedetomidine had sedative weaning advantage for extubation after airway foreign body (FB) removal in children.

Methods A retrospective case–cohort comparison study with total of 57 critical children who required mechanical ventilation after rigid bronchoscopy was performed. After tracheal intubation, group D (received dexmedetomidine 1 μg/kg over 10 min, followed by an infusion of 0.8 μg/kg/h), and group RP (received remifentanil–propofol 6–10 μg/kg/h and 1–3 mg/kg/h, respectively). The primary outcome was successful extubation rate on first weaning trial. The minor outcomes included weaning time, emergency agitation, coughing score and the incidence of respiratory adverse complications on emergency.

Main results All 57 patients were included in the analysis, with 30 patients in group D and 27 controlled cases in group RP. The success rate of first weaning trial in the D group was 96.7 vs 77.8% in the RP group, risk ratio (RR) 1.56, 95% CI [0.78–1.98]. Time for resuming spontaneous breathing after termination infusion was shorter in the D group (median 8 min, IQR 15 min) vs RP group (median 12 min, IQR 19 min, $P = 0.02$, RR 0.56, 95% CI 0.14–6.57).

Conclusions In mechanical ventilation of pediatric patients following rigid bronchoscopy, in comparison to remifentanil–propofol, dexmedetomidine is proved to have high success rate for weaning strategy.

What is already known? Remifentanil is proved to be effective for weaning in ICU patients. Dexmedetomedine can provide similar rates of smooth extubation for pediatric patients who underwent airway surgery.

What this article adds? Invasive ventilation is used for patients with severe comorbidity after airway surgery, but the correct strategy for pediatric extubation after removal of airway foreign body remains unclear. For these patients with short-term mechanical ventilation, dexmedetomedine may improve the extubation rate, when compared with remifentanil–propofol.

Keywords Foreign body · Extubation · Weaning

Introduction

Aspiration of foreign body is a common and critical emergency in preschool children [1]. The risk during emergency includes apnea and hypoxemia that requires tracheal intubation and mechanical ventilation in some life-threatening cases. Ensuring uneventful extubation without deteriorating outcomes is challenging for anesthetists and intensive care physicians. Outcomes following weaning failure vary in critical patients, including hypoxemia, cardiac arrest and even death. In pediatric patients who need mechanical ventilation supportive therapy postoperatively, a mutually beneficial weaning strategy should be recommended for both.

Recent studies have shown that sedatives such as midazolam and propofol facilitate weaning from long-term ventilation [2, 3]. Dexmedetomidine is a selective α_2-adrenoceptor agonist with sedative, anxiolytic and analgesic effects, and is useful in facilitating extubation in patients with prolonged mechanical ventilation [4, 5]. It also increases tolerance to surgical intervention of the airway, and is used in fiber-optic bronchoscopy, as well as in facilitating extubation in pediatric airway surgery [6]. However, there are very few reports from short-term ventilation, especially in pediatric patients with fundamental airway

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pathological change caused either by foreign body aspiration or iatrogenic injury.

The airway is extremely sensitive to stimulation after foreign body aspiration, and the underlying problem of hypoxemia exists even after foreign body removal due to pathological changes (preoperative airway compromise such as segmental atelectasis or pneumonia) and iatrogenic damages (hypercapnia due to manual jet ventilation) [7]. Several studies have evaluated the efficacy of remifentanil–propofol or sevoflurane to achieve successful extubation of patients from mechanical ventilation [1, 8]. However, there is no standardized weaning protocol for pediatric patients who require intubation and respiratory support after airway foreign body removal.

The present study was performed to evaluate the weaning efficacy of dexmedetomidine in comparison with remifentanil–propofol in critical pediatric patients who needed mechanical ventilation post-operation. The primary outcome was successful rate of first weaning trial. The minor outcomes included time for extubation, vital parameters, weaning time, emergency agitation, coughing score and the incidence of respiratory adverse complications on emergency.

Patients and methods

Eligibility criteria

After obtaining approval from the Hospital Ethics Committee and written informed consent from patients, this retrospective, observational study was conducted between January 2011 and December 2015, in the anesthesiology department of the Eye and ENT Hospital of Fudan University (Shanghai, China), which is a tertiary-care university referral hospital. A total of 1255 cases of foreign body aspiration, aged 3–48 months, underwent rigid bronchoscopy. Exclusion criteria were: incomplete information, intubation or tracheotomy pre-operation, need for further invasive manipulation such as tracheotomy or thoracentesis, and emergency with non-invasive mechanical ventilation. All data were collected retrospectively based on patient charts.

In all cases, anesthesia was induced with 8% sevoflurane in oxygen (6–8 l/min), followed by intravenous fentanyl (0.5 μg/kg), propofol (2–4 mg/kg) and succinylcholine (1 mg/kg), and maintained with total intravenous anesthesia (TIVA) with remifentanil–propofol (12–20 μg/kg/h and 6–12 mg/kg/h, respectively). For topical anesthesia, 2% lidocaine (maximum dose 4 mg/kg) was sprayed onto the epiglottis, larynx, and between the vocal cords. Manual jet ventilation (MJV, Manujet III, VBM, Germany) was used throughout the surgery. MJV was performed before insertion of the bronchoscopy by placing a special slim tube (inner diameter = 0.5 mm) transnasally into the trachea. MJV guarantees a quick and efficient oxygenation during the procedure and has a high-pressure oxygen/air outlet, which is adjustable between 0.35 and 0.7 bar (5–10 psi). The surgeons were all experts of pediatric airway surgery who had relevant experience for more than 5 years.

Postoperative management

After airway foreign body retrieval, laryngeal mask airway is the most commonly used supraglottic airway (SGA) for airway support, followed by mask and nasopharyngeal airway. If severe hypoxemia occurred, which was defined as an episode of progressive decrease of desaturation < 80% for > 60 s, tracheal intubation was needed for ventilation support therapy after extraction of foreign body and rigid bronchoscopy. Prior to intubation, succinylcholine (1 mg/kg) and propofol (2 mg/kg) were bolused to facilitate tracheal intubation. The ventilator settings included: mode (pressure support ventilation, PSV), peak inspiratory pressure (PIP) 10 cmH_2O, rate: 15–20/min, positive end expiratory pressure (PEEP): 4 cmH_2O (or 5–6 cm if $FiO_2 > 0.90$), inspiratory time: 0.3–0.5 s, and FiO_2: 0.4–1.0, depending on the clinical situation.

A total of 57 cases with short-term (within hours) supportive mechanical ventilation after airway foreign body retrieval were included in this study. Extubation was accomplished in post-anesthesia care unit (PACU) by anesthesiologists.

Anesthetics for sedative choice

The primary sedative choice for mechanical ventilation, either with dexmedetomidine ($n = 30$, 0.8 μg/kg bolus over 10 min followed by an infusion of 0.4 μg/kg/h) or remifentanil–propofol ($n = 27$, 0.05–0.2 μg/kg/min and 4–6 mg/kg/h, respectively), was based on a longitudinal practice alter (remifentanil as the first choice prior to 2012, whereas after 2012, after added to our hospital formulary, most patient with airway compromise received dexmedetomidine to maintain spontaneous respiration.)

Weaning trial

The sedative infusion was terminated if the patient met the following criteria: $SPO_2 > 90\%$ (with $FiO_2 < 0.50$), $ETCO_2 < 55$ mmHg, minimal secretions and stable cardiopulmonary status. Weaning trial of spontaneous breathing trials (SBTs) with low-level pressure support [9] was attempted. Extubation was performed if three of the following four conditions were met: (1) regular respiratory pattern (within 15–30 bpm); (2) effective protective airway reflex without persisting coughing; (3) eye open or facial grimace with face touching; (4) $SPO_2 > 90\%$ ($FiO_2 < 0.50$).

For patients suffered from the failed first weaning failure, an alternative infusion of dexmedetomidine (1 μg/kg bolus over 10 min followed by an infusion of 0.8 μg/kg/h) was used for sustained mechanical ventilation.

The weaning time referred to the time from termination of dexmedetomidine (or remifentanil–propofol) infusion to the time that meet the criteria of extubation. Extubation time was defined as the time from termination of infusion to successful extubation. Extubation failure is defined as inability to tolerate removal of tracheal tube, usually with severe hypoxemia episode, with the rescue method of reintubation or supraglottic airway. Patients were kept in the PACU until the Aldrete score was ≥ 9 [10].

Observed demographic characteristics

Data of each patient was obtained by two observers who were blinded to the patient grouping. The medical records included age, gender, weight, the type and location of foreign body, duration of foreign body retention, duration of the procedure, occurrence of adverse respiratory events, sedative choice, vital signs after extubation and outcome.

Adverse outcomes

Coughing score after extubation was defined as: Grade 0 = no cough; Grade 1 = occasional cough of mild severity; Grade 2 = cough persistence < 5 s of moderate severity; Grade 3 = severe, persistent cough for > 5 s (bucking) [11]. In our study, persistent coughing was defined as coughing score ≥ 3. Emergence delirium (ED) was defined using the Pediatric Anesthesia Emergence Delirium (PAED) score ≥ 12 [12].

In our previous study, the incidence of successful extubation was 85% in pediatric patients with mechanical ventilation after foreign body retrieval.

Statistical analysis

All data were analyzed using SPSS 16.0 software (SPSS Inc, Chicago, IL, USA). Quantitative variables (with abnormal distribution) are presented as median (min–max) and analyzed by Student's *t* test. Data with non-parametric distribution were compared using Mann–Whitney *U* test. Qualitative data are expressed as frequencies and compared using Chi-squared test or Fisher's exact test. Risk ratios are reported for success rate of weaning trial. Differences were considered significant when $p < 0.05$.

Results

A total of 57 patients with therapeutic mechanical ventilation after rigid bronchoscopy were enrolled in the study (Fig. 1). The patient demographic data were compared between the two groups (Table 1). The median (IQR, [range]) age was 17 (15–36 [2–48]) months. There were no differences in age, weight, gender, type and retention time of foreign body, anesthesia and surgery time, and reason for mechanical ventilation post-operation between the two groups (Table 1). There were no significant differences in the end-tidal carbon dioxide ($ETCO_2$) concentration on initiation of intubation, time for $ETCO_2$ to reach < 55 mmHg and weaning time between the two groups. The mean blood pressure, heart rate and respiratory rate were lower at extubation in the RP group without significant difference, and also at 1 and 5 min after extubation. There were no significant differences in the incidence of persistent coughing and emergence agitation (shown in Table 2). As compared to the D group, time to resume spontaneous breathing was significantly longer (8 [5–42] min vs 12 [6–83] min) and first extubation failure was higher in the RP group (adjusted OR 3.2, 95% CI 1.35–5.6, $p = 0.002$). There were six episodes during the weaning phase including: breath holding ($n = 1$), persistent coughing ($n = 2$) and laryngospasm ($n = 2$) in the RP group, and tracheorrhagia ($n = 1$) in the D group. Among the six patients with failed weaning trial and extubation, three patients accepted mask ventilation with an uneventful recovery, while the other three cases (50%) required re-intubation within half hour after extubation, sedative agents were switched to dexmedetomidine-based mechanical

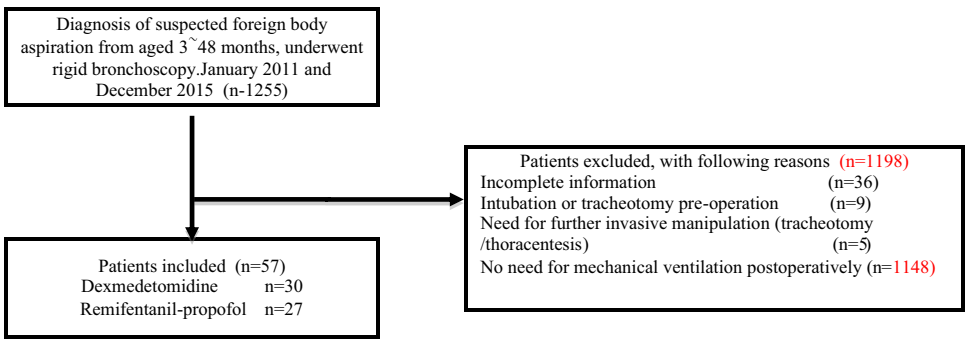

Fig. 1 Patient inclusion

Table 1 Demographic and recovery data in the two study groups

Characteristics	D Group ($n=30$)	RP Group ($n=27$)	p
Age [months] (range)	15 (7–48)	16 (9–46)	0.74
1–3 months	1	0	
3–6 months	2	2	
6–12 months	1	3	
12–24 months	7	9	
24–48 months	4	2	
Weight [kg] (range)	12 (8.5–15)	11 (5.5–16)	0.61
Gender (male/female)	18/12	14/13	0.58
Interval between removal and aspiration episode [days] (range)	19.5 (1–64)	21 (1–90)	0.81
Type of FB			
Organic/inorganic	21/7	19/8	0.36
Location of FB			0.27
Right main bronchus (n, %)	13 (43.3)	9 (33.3)	
Left main bronchus (n, %)	11 (36.7)	10 (37)	
Main stem (n, %)	4 (13.3)	5 (18.5)	
Subglottic region (n, %)	2 (6.7)	3 (11.1)	
Duration of anesthesia [min] (range)	27 (13–76)	22 (11–70)	0.95
Surgery time [min] (range)	14 (6–50)	12 (11–68)	0.48
Reason for MV post-operation (n, %)			
Tracheorrhagia	1 (3.3)	1 (3.7)	0.63
Segmental atelectasis	3 (10)	2 (7.4)	0.51
Breath holding	6 (20)	6 (22.2)	1.0
Laryngospasm/bronchospasm	19 (63.3)	15 (55.6)	0.49
Pneumothorax	1 (3.3)	2 (7.4)	1.0
Cardiac shock	0 (0)	1 (3.7)	0.92

Data are expressed as median (min–max) and the number (percentage) of patients

FB foreign body, *MV* mechanical ventilation

ventilation, and successful extubation was achieved on the very next attempt.

Discussion

As compared to remifentanil–propofol, dexmedetomidine was more advantageous in facilitating extubation in children requiring mechanical ventilation after foreign body retrieval.

In patients with inhaled foreign body, a non-invasive ventilation (such as laryngeal mask airway) is usually used after the rigid bronchoscopy until spontaneous respiration is achieved. A minority of pediatric patients met the criteria for supportive mechanical ventilation, due to respiratory adverse events, such as hypoxemia (usually caused by consistent coughing), tracheorrhagia, segmental atelectasis (by X-ray), pneumonia, pneumothorax and laryngospasm/bronchospasm. Prompt intubation and short-term mechanical ventilation lead to better oxygenation and outcome. In our previous study, the incidence of successful extubation was 85% in pediatric patients with mechanical ventilation after foreign body retrieval. The option of sedatives and anesthesia for ventilation support in patients remains an intractable issue for both anesthetists and intensive care physicians. Due to its superior characteristics in airway surgery, we hypothesize that dexmedetomidine can facilitate extubation and decrease adverse events.

Short-acting sedative is the major adjuvant drug for pressure support ventilation, with the improvement of ventilation–perfusion ratio (V/Q).

Weaning failure is associated with worse outcome, and is usually caused by the following two conditions: persistent airway inflammation (leads to segmental emphysema, atelectasis and bronchospasm) [13] and hyperactive airway (caused by abundant secretions) [14, 15]. Ideal drugs for sedation could improve the pathophysiological changes, maintain adequate oxygenation, facilitate uneventful extubation and decrease the reintubation in emergency.

In our study, relative to the original 1255 cases enrolled data, only 57 cases finally met the conditions of entry into two groups who need mechanical ventilation, most cases were supported by mask or laryngeal mask airway without

Table 2 Extubation-related events

Characteristics	D Group ($n=30$)	RP Group ($n=27$)	P value [95% CI]	RR [95% CI]
Emergence agitation (n, %)	0 (0)	1 (3.7)	1.17 [0.07–12.54]	0.97 [0.26–3.47]
$ETCO_2$ while intubation (mmHg)				
Mean	61	58	0.09 [0.32–6.43]	1.14 [0.89–4.32]
Median	57	53		
IQR	10	14		
Range	48–72	43–69		
TCO_2 (min)				
Mean	55	65	0.06 [0.01–3.21]	0.65 [0.25–2.69]
Median	52	63		
IQR	21	18		
Range	39–64	28–96		
Ts (min)				
Mean	14*	18	0.02 [0.00–3.45]	0.56 [0.14–6.57]
Median	8	12		
IQR	15	19		
Range	5–42	6–83		
Weaning time (min)				
Mean	60	52	0.87 [0.23–7.54]	0.96 [0.12–6.56]
Median	54	61		
IQR	31	38		
Range	21–95	26–102		
Time to extubation (min)				
Mean	68	58	0.56 [0.13–12.32]	1.27 [0.92–3.93]
Median	65	52		
IQR	15	27		
Range	39–82	29–92		
Time to awake (min)				
Mean	104	89	0.07 [0.13–12.32]	1.62 [0.56–10.5]
Median	98	65		
IQR	43	35		
Range	45–112	46–108		
Weaning success (n, %)	29 (96.7)*	22 (81.4)	0.04 [0.07–11.67]	1.09 [0.06–5.32]
Breath holding (n, %)	0	1 (3.7)	0.12 [0.01–9.42]	0.98 [0.23–3.46]
Persistent coughing (n, %)	0	2 (7.4)	0.12 [0.07–12.54]	0.98 [0.23–3.46]
Laryngospasm (n, %)	0	2 (7.4)	0.12 [0.07–12.54]	0.98 [0.26–3.46]
Tracheorrhagia (n, %)	1 (100)	0 (0)	0.32 [0.02–9.63]	1.01 [0.02–4.32]
Reintubation rate (n, %)	0*	3 (11.1)	0.08 [0.07–16.58]	0.47 [0.12–7.38]

Persistent coughing: coughing score ≥ 3

Emergence agitation was defined as Pediatric Anesthesia Emergence Delirium score ≥ 12

Data are expressed as number of patients (%) (Chi-square test) $*p<0.05$

T_{CO2} time taken for $ETCO_2$ to decrease to <55 mmHg, *Ts* time taken to resume spontaneous breathing after termination of infusion

further deteriorate oxygenation postoperatively. A failure of planned extubation usually includes post-extubation laryngeal edema [16] and weaker cough [17]. Severe hypoxemia caused by persistent coughing and apnea was the main reason for extubation failure.

This study confirmed the beneficial effect of dexmedetomidine for sedative patients who need postoperative mechanical ventilation. There were no differences in the fundamental complications between the two groups. The time for patients to resume spontaneous breathing and decrease of $ETCO_2$ was quicker in the D group. In our study, dexmedetomidine (bolus 1 μg/kg followed by 0.8 μg/kg/h) did not significantly increase the weaning time as compared to remifentanil–propofol infusion. However, after termination

of the infusion, the time to resumption of spontaneous respiration was significantly shorter.

Remifentanil is an ultra short-acting opioid analgesic. In combination with propofol, remifentanil could facilitate weaning from mechanical ventilation in pediatric intensive care [18]. In the current study, weaning failure in the first attempt was found in 6 out of 57 patients, due to breath holding, laryngospasm, persistent coughing and tracheorrhagia. In our study, three patients required reintubation following successful weaning trial in the remifentanil group, due to episodes of breath holding and laryngospasm. Remifentanil has well known analgesic and anesthetic properties. After remifentanil withdrawal, airway reflex and spontaneous respiration recovers rapidly [19] and pronociceptive system sensitization related hyperalgesia also resumes [20], combined with the development of agitation [21]. Aggressive airway reflex irritated by inflammation and secretion will cause persistent cough and laryngospasm, and deteriorate gas exchange leading to compromised airway.

The α_2 agonist dexmedetomidine could attenuate airway–circulatory reflexes [22], maintain adequate sedation without hemodynamic instability or respiratory-drive depression [23–25], thereby attenuating hemodynamic stress secondary to hyperadrenergic over-reactivity [26]. It is also more effective than midazolam for sedation during prolonged mechanical ventilation [27]. As compared to mechanical ventilation, spontaneous respiration can attain better oxygenation and lower pulmonary shunt [28, 29]. Dexmedetomidine may help eliminate emergence agitation [30, 31], decrease the time from full to partial ventilatory support, and thereby facilitate earlier extubation [32].

In our study, 29 out of 30 patients in the dexmedetomidine group were successfully extubated without any weaning failure, only 1 patient suffered with tracheorrhagia followed by mask ventilation. We all use “no touch” technique [33] during emergence. As dexmedetomidine does not depress respiratory drive, the time to resume spontaneous breathing is significantly shorter in D group. Time to awake and extubate was longer in Group D than in Group RP, although there are no significant difference. Besides the sedative property of dexmedetomidine, it can also decrease secretion, led to less emergence agitation and upper airway reaction, and prolong the time of smooth emergency. While in remifentanil group, the hyperalgesia effect may play a major part in airway sensitivity, result in higher incidence of persistent coughing and breath holding, with the result of faster emergence. In pediatric patients with mechanical ventilation support following compromised airway, dexmedetomidine increased endotracheal tube tolerance, facilitated resumption of spontaneous respiration, and optimized ventilation and oxygen. During emergency, dexmedetomidine effectively suppresses cough [34] and agitation, facilitate successful extubation.

There were several limitations in our study. First, the small sample size of our patients exhibited various pathophysiological characteristics, from airway inflation to manipulation irritation, which could lead to patient bias. Second, the data were collected at different time periods with various strategies, which may lead to selection bias. We studied a relatively intensive patient population who needed mechanical ventilation after rigid bronchoscopy, and excluded children who needed sustained invasive manipulation, which may subject these children to unacceptable greater risks for postoperative respiratory complications. Hence, the results of our study may not be representative of the normal general population, and the beneficial effect of dexmedetomidine must be interpreted with caution. We plan to undertake more well-designed prospective clinical studies in the future to further confirm the advantages of dexmedetomidine in weaning.

In summary, dexmedetomidine sedation may be a more beneficial strategy, as compared to traditional analgesic and sedative combined regimens, in pediatric patients who need supportive ventilation after foreign body removal. Further studies would be needed to evaluate the usefulness of sedatives in such circumstances.

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Compliance with ethical standards

Ethical approval The institutional review board (EENT) waived the need for informed consent. Reference number: KY 2012-002.

Conflict of interest The authors declare that they have no conflict of Interest.

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