Dexmedetomidine vs remifentanil intravenous anaesthesia and spontaneous ventilation for airway foreign body removal in children

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Background. To compare the safety and efficacy of dexmedetomidine/propofol (DP)-total i.v. anaesthesia (TIVA) vs remifentanil/propofol (RP)-TIVA, both with spontaneous breathing, during airway foreign body (FB) removal in children.

Methods. Seventy-seven children undergoing rigid bronchoscopy for FB removal were randomly allocated to receive either RP-TIVA and spontaneous ventilation (Group RP, n=38) or DP-TIVA and spontaneous ventilation (Group DP, n=39). Heart rate, arterial pressure, pulse oxygen saturation ($S_{PO_2}$), respiratory rate, end-tidal CO$_2$ ($E_{CO_2}$), and induction time were recorded. Adverse events, the intervention for these events, and postoperative care duration were also assessed.

Results. The mean induction times were comparable between the two groups (Group RP 12.2 min vs Group DP 13.1 min, $P>0.05$). At the end of the procedure, the mean $E_{CO_2}$ was higher in Group RP (Group RP 6.8 kPa vs Group DP 5.8 kPa, $P<0.001$), and respiratory rate was lower in Group RP (Group RP 20.4 vs Group DP 35.8, $P<0.001$). Additionally, the perioperative haemodynamic profile was more stable in Group DP than that in Group RP. The incidence rate of breath-holding and intervention were comparable between the two groups. In the post-anaesthesia care unit (PACU), no hypoxaemia was observed, and emergence time increased in Group DP (Group DP 65.1 min vs Group RP 23.8 min, $P<0.0001$). The incidence of cough in PACU was higher in Group RP (Group RP 55.3% vs Group DP 10.3%, $P<0.0001$).

Conclusions. Compared with RP-TIVA, DP-TIVA provided more stable respiratory and haemodynamic profiles, but required a longer recovery time.


Keywords: anaesthesia, paediatric; anaesthetic techniques, bronchoscopy; analgesics opioid, remifentanil; complications, hypoxaemia; pharmacology, dexmedetomidine

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Children younger than 3 yr old are at high risk of airway foreign body (FB) aspiration. A large proportion of patients in this population are referred to teaching hospitals. Prompt and early FB removal with a rigid bronchoscope is essential for reducing complications and mortality rates. The procedure is performed under general anaesthesia with spontaneous or controlled ventilation, based mostly on anaesthetists’ preference. Besides hypoxaemia, the most commonly observed adverse event (AE) for rigid bronchoscopy is barotrauma, a severe AE associated with ventilation control. However, Zhang and colleagues reported that the rate of occurrence of a pneumothorax is 2.31% in children with preoperative respiratory impairment. Considering the advantages of spontaneous ventilation (better ventilation/perfusion, V/Q ratio during general anaesthesia, guaranteed adequate anaesthesia depth, and absence of barotrauma), spontaneous ventilation techniques are appropriate for airway FB removal in children with preoperative respiratory impairment.

Because of their pharmacological properties, the combination of propofol and remifentanil confers particular value for airway endoscopy in spontaneously breathing adult and paediatric patients. However, spontaneous breathing may be difficult to maintain with remifentanil, and significant hypercapnia may occur. Previous studies have demonstrated that dexmedetomidine offers an ideal condition for rigid bronchoscopy by producing obtund airway reflexes and stable haemodynamic and respiratory profiles in spontaneously ventilating children. Based on these findings, we hypothesized that dexmedetomidine/propofol (DP)-total i.v. anaesthesia (TIVA) with spontaneous ventilation might provide a better...
perioperative respiratory profile for FB removal in children than remifentanil/propofol (RP)-TIVA with spontaneous ventilation.

Methods
This study was registered with the China Clinical Research Information Service (Registration number, ChiCTR—TRC-13003015), and conformed with the tenets of the Declaration of Helsinki. After obtaining approval from the Hospital Ethics Committee (Shanghai Eye, Ear, Nose and Throat Hospital, No. KY 2012–036) and written informed consent from parents or legal guardians of the children, we enrolled 77 children with American Society of Anesthesiologist physical status I or II, aged 6–60 months, undergoing FB removal under rigid bronchoscopy (between September 2012 and March 2013). Patients with congenital disease, asthma, pre-existing pneumothorax, severe preoperative respiratory impairment (i.e. single-lung emphysema and the other atelectasic), and allergy to local anaesthesia were excluded from the study.

An experienced surgeon and anaesthetist who had performed at least 50 previous FB removal cases participated in this study. Patients fasted for 6 h and no premedication was given. On arrival in the operating theatre, patients were randomly (computer-generated) assigned to receive either DP-TIVA (n=39) or RP-TIVA (n=38). Volatile induction with sevoflurane was performed and anaesthetic maintenance was switched to TIVA as soon as i.v. access was obtained. Propofol infusion was set at a constant rate of 200 μg kg⁻¹ min⁻¹. In Group DP, dexmedetomidine was administered i.v. as a bolus of 4 μg kg⁻¹ followed by infusion of 1–2 μg kg⁻¹ h⁻¹; the bolus was given over 10 min to prevent haemodynamic depression. In Group RP, remifentanil was started at 0.05 μg kg⁻¹ min⁻¹ and was adjusted in 0.05 μg kg⁻¹ min⁻¹ increments to titrate a 50% reduction in the baseline respiratory rate. Lidocaine (1%; 2 mg kg⁻¹) was sprayed on the oropharynx, supraglottic, and glottic structures, and into the trachea via a direct laryngoscope. If there was no reflex response from the patient within 2 min after lidocaine application, airway instrumentation was begun, and 100% oxygen was administered via a side arm of the rigid bronchoscope (Karl-Storz, Tuttlingen, Germany).

Baseline heart rate (HR), mean arterial pressure (MAP), respiratory rates, and pulse oxygen saturation (SpO₂) were recorded before induction (T₀), HR, MAP, and respiratory rate were monitored at the following time points: during laryngoscopy when lidocaine was sprayed (Tlaryn), during insertion of the rigid bronchoscope (Trbron), 5 min after the start of the procedure (Ts), during extubation of the rigid bronchoscope at the end of the procedure (Tenld), 5 min after the discontinuation of anaesthetics (T₁₅), and at the time of discharge from the post-anesthesia care unit (PACU) (Tdis). Because it was difficult to record the end-tidal CO₂ (ECO₂) in children before the procedure, 40 mm Hg was estimated as the baseline value. We recorded ECO₂ values at Tenld, T₁₅, and 10 min (T₁₅+10) after the procedure. The incidence of AEs, including bucking, breath-holding (light, <10 s; severe, >30 s), body movement, hypoxaemia (SpO₂ <90% lasting >15 s), laryngospasm, and pneumothorax, was recorded. Interventions for these AEs were also recorded. Additional propofol 0.5–1 mg kg⁻¹ was given to deepen anaesthesia and assisted ventilation was provided if necessary. After the procedure, a laryngeal mask airway was inserted to detect the ECO₂. Patients were transferred on their lateral side to the PACU for recovery. Once children reached a modified Aldrete score >10, they were transferred back to the ward. Induction time was defined as the time from volatile induction to the insertion of the rigid bronchoscope. Recovery time was defined as the time from anaesthesia discontinuation to PACU discharge.

Patients were monitored for an additional 6 h after returning to the ward. Only those who developed desaturation and dyspnoea received an emergency X-ray. All patients with successful FB removal routinely received a postoperative X-ray on the following day. If the X-ray was negative, the patient was discharged. Patients with failed FB-removal due to non-organic FB stuck in the bronchioles were transferred to a nearby hospital for thoracotomy. In patients who failed FB removal with an organic FB located in a further lobe, antibiotics were administered for 2–3 days and another rigid bronchoscopy was attempted.

Ryu and colleagues reported 29% desaturation in patients with RP anaesthesia and 3% desaturation in patients with DP during flexible bronchoscopy. We used previously detailed power analyses, taking into account expected standard deviations, to estimate that a sample of at least 38 patients would be required to detect a significant difference between the two groups at the level of 0.05 with a power of 0.8. Desaturation rates were our primary outcome parameter, and all other measured parameters were considered secondary outcome parameters.

Data are reported as mean (SD), unless otherwise noted. Parametric data were analysed with an unpaired Student’s t-test. Ordinal data were analysed using the Mann–Whitney ranked-sum test. Nominal data were analysed using either χ² or Fisher’s exact test. Interaction between time and group factors in a two-way analysis of variance (ANOVA) with repeated measurements was used to analyse differences of respiratory and haemodynamic profiles (i.e. HR, MAP, respiratory rate, and ECO₂) between patients in Group DP and in Group RP. The post hoc Bonferroni test was used to compare differences in respiratory and haemodynamic variables between the two groups at different time points. P-values of <0.05 were considered significant.

Results
Seventy-seven paediatric patients were enrolled (Group DP (n=39), Group RP (n=38)) and completed the study (Fig. 1). One child in Group DP and two children in Group RP were excluded from the study because of neuromuscular blocking agent use. Clinical characteristics of the two groups of children are shown in Table 1. Distribution of age, gender, weight, duration of FB, and type of FB were not significantly different between the two groups.

During the procedure, none of the patients presented with severe breath-holding, body movement, or progressive
hypoxaemia. Induction times, anaesthesia durations, maximal remifentanil administration rate, AEs, and recovery times are listed in Table 2.

Regarding haemodynamic variables, DP and RP both slowed HR and decreased MAP. Repeated-measurement ANOVA with a post hoc Bonferroni test showed a difference in HR over times between the two groups, with HR at $T_5$, $T_{end}$, $T_{+5}$, $T_{+10}$, and $T_{dis}$ being significantly lower in Group DP than in Group RP (Fig. 2A, $P=0.0002$). Bradycardia (HR < 60 beats min$^{-1}$) was seen in two children during DP induction and atropine 0.01 mg kg$^{-1}$ was given. There was a significantly increased MAP in the DP vs RP group over time (Fig. 2B, $P=0.0025$, two-way ANOVA with repeated measurement). The post hoc Bonferroni test showed that children who received DP had a higher MAP at $T_{lary}$, $T_{bron}$, $T_5$, $T_{end}$, $T_{+5}$, and $T_{+10}$ than those who received RP.

The respiratory rate and $E’_{CO_2}$ at different time points in the two groups are shown in Figure 3. In Group RP, the respiratory rate was maintained at 50% reduction in the baseline value during the procedure (Fig. 3A) and resulted in a high mean

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**Table 1** Patient characteristics. Data are expressed as mean (SD) or as the number of patients. *Median (min – max). DP, dexmedetomidine/propofol group; RP, remifentanil/propofol group; FB, foreign body

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group DP (n=39)</th>
<th>Group RP (n=38)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (months)*</td>
<td>20 (6–60)</td>
<td>19 (12–57)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>13.0 (3.1)</td>
<td>12.6 (2.4)</td>
</tr>
<tr>
<td>Sex (n, male/female)</td>
<td>27/12</td>
<td>24/14</td>
</tr>
<tr>
<td>Period of FB aspiration (days)*</td>
<td>4 (1–30)</td>
<td>3.5 (1–180)</td>
</tr>
<tr>
<td>Type of FB (organic/inorganic/ others)</td>
<td>29/6/4</td>
<td>31/5/2</td>
</tr>
<tr>
<td>Location of FB (right:left:both)</td>
<td>19:11:3</td>
<td>21:14:2</td>
</tr>
<tr>
<td>Preoperative respiratory impairment [n (%)]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obstructive emphysema</td>
<td>17 (43.6)</td>
<td>10 (26.3)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>16 (41.0)</td>
<td>18 (47.4)</td>
</tr>
<tr>
<td>Atelectasis</td>
<td>4 (10.3)</td>
<td>7 (18.4)</td>
</tr>
</tbody>
</table>

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Fig 1 CONSORT flow diagram. Seventy-seven children were randomized; three children (one from Group DP, two from Group RP) were excluded due to neuromuscular blocking agent use. DP, dexmedetomidine/propofol group; RP, remifentanil/propofol group.
Dexmedetomidine vs remifentanil in airway clearing

Fig 2 Changes in HR (A) and MAP (B) at different perioperative time points. Repeated-measurement ANOVA showed significant difference in HR over times between the DP group and the RP group, with HR at T0, Tend, T-10, and Tdis lower in Group DP than in Group RP. There was a significantly increased MAP in the DP vs RP groups over time. T0, baseline value before anaesthesia; Tlaryn, at insertion of a laryngoscope; Tbron, at insertion of a rigid bronchoscope; T5, 5 min after the start of the procedure; Tend, at the end of the procedure; T-5 and T+5, 5 and 10 min after the procedure, respectively; Tdis, at discharge from the PACU. *P<0.05, **P<0.01, ***P<0.001.

![Graph A](https://academic.oup.com/bja/article-abstract/112/5/892/272764)

Fig 3 Changes in respiratory rate (A) and E\textsubscript{CO2} (B) at different perioperative time points. Repeated-measurement ANOVA showed significant difference in respiratory rate and E\textsubscript{CO2} over times between the DP group and the RP group. Respiratory rate was significantly lower at Tlaryn, Tbron, T5, Tend, and T+5 in Group RP than in Group DP. End-tidal CO\textsubscript{2} was higher at Tend in Group RP. T0, baseline value before anaesthesia; Tlaryn, at insertion of a laryngoscope; Tbron, at insertion of a rigid bronchoscope; T5, 5 min after the start of the procedure; Tend, at the end of the procedure; T-5 and T+5, 5 and 10 min after the procedure, respectively; Tdis, at discharge from the PACU. *P<0.05, **P<0.01, ***P<0.001.

![Graph B](https://academic.oup.com/bja/article-abstract/112/5/892/272764)

Table 2 Time quantum, highest remifentanil rate, and AEs. Data are expressed as mean (so) or as the number of patients (%). DP, dexmedetomidine/propofol group; RP, remifentanil/propofol group; PACU, post-anaesthesia care unit. ***P<0.0001, Group DP vs Group RP

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group DP (n = 39)</th>
<th>Group RP (n = 38)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Induction time (min)</td>
<td>13.1 (1.8)</td>
<td>12.3 (2.0)</td>
</tr>
<tr>
<td>Duration of anaesthesia (min)</td>
<td>21.1 (5.6)</td>
<td>21.7 (6.8)</td>
</tr>
<tr>
<td>Adverse events</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bucking [n (%)]</td>
<td>10 (25.6)</td>
<td>12 (31.6)</td>
</tr>
<tr>
<td>Breath-holding &lt; 10 s [n (%)]</td>
<td>5 (12.8)</td>
<td>6 (15.8)</td>
</tr>
<tr>
<td>Hypoxaemia &lt; 90% [n (%)]</td>
<td>7 (17.9)</td>
<td>10 (26.3)</td>
</tr>
<tr>
<td>Bradycardia (&lt; 60 beats min\textsuperscript{-1}) [n (%)]</td>
<td>2 (5.1)</td>
<td>0</td>
</tr>
<tr>
<td>Highest remifentanil rate (\mu g kg\textsuperscript{-1} min\textsuperscript{-1})</td>
<td>0.12 (0.11)</td>
<td></td>
</tr>
<tr>
<td>Recovery time (min)</td>
<td>65.1 (13.9)***</td>
<td>23.8 (4.4)</td>
</tr>
<tr>
<td>Cough in PACU [n (%)]</td>
<td>4 (10.3)***</td>
<td>21 (55.3)</td>
</tr>
</tbody>
</table>

\(E_{\text{CO}_2}\) (6.8 kPa) at the end of the procedure (Fig. 3a). In Group DP, the respiratory rate was approximately maintained at the baseline level during the procedure and correlated with a normal mean \(E_{\text{CO}_2}\) (5.8 kPa) at the end of the procedure. Once anaesthetics were discontinued, respiratory rate increased and \(E_{\text{CO}_2}\) decreased rapidly, with both parameters returning to normal levels, in both patient groups, within 5 min.

In the PACU, 21 RP group patients (55.3%) coughed without treatment, and only four DP group children (10.3%) experienced coughing (P<0.0001). No desaturation was observed in any patient while recovering on 40% oxygen. No laryngospasm, pneumothorax, or arrhythmias were observed in any patient. Time to emergence (Table 2) was significantly longer in Group DP (65.1 min) than in Group RP (23.8 min; P<0.0001).
Discussion

We compared DP-TIVA with RP-TIVA in terms of haemodynamic and respiratory profiles, AEs, and recovery time for airway FB removal in spontaneously breathing children. DP-TIVA provided more stable respiratory and haemodynamic profiles that RP-TIVA, but significantly prolonged recovery time.

Rigid bronchoscopy for airway FB removal is a brief but intense procedure that demands special anaesthesia management, including unhindered airway access for the surgeons, adequate oxygenation and gas exchange to avoid hypoxaemia, and stabilized haemodynamics. Spontaneous ventilation provides better V/Q matching, effective alveolar ventilation, and no barotrauma. Volatile induction/maintenance anaesthesia for airway FB removal reportedly stabilizes respiration, HR, and MAP, but causes significant environmental pollution. Combination of RP-TIVA in spontaneously breathing children is an alternative approach, but may cause respiratory depression leading to hypercarbia or apnoea. Because of these limitations, another option that provides FB surgery-specific airway access while preserving optimal respiration is beneficial.

Dexmedetomidine uniquely provides analgesia without causing respiratory depression. We observed similar desaturation, bucking, and light breath-holding rates in the DP and RP groups, suggesting that DP-TIVA relieves intratracheal procedure stimuli as effectively as RP-TIVA. The DP group respiratory profile was stable, respiratory rate was maintained at baseline levels during the procedure, and the $\text{CO}_2$ was normal at $T_{\text{end}}$, indicating that dexmedetomidine did not impair respiratory drive. The RP group respiratory rate decreased to half of the baseline value throughout anaesthetic maintenance, resulting in hypercarbia at $T_{\text{end}}$. Although respiratory rate and $\text{CO}_2$ returned to the baseline level quickly after anaesthesia discontinuation, caution is required when administering RP-TIVA to patients with a before operation-compromised respiratory drive, to prevent excessive respiratory depression.

Consistent with our previous study, HR and MAP decreased but MAP maintained a mean value >50 mm Hg in Group RP during the procedure. Two DP group children aged >40 months received atropine 0.01mg kg$^{-1}$ to treat bradycardia during induction. Our findings are consistent with reported tolerance of dexmedetomidine in children, suggesting that DP is effective and without clinically significant AEs when used for paediatric airway FB removal. High-dose dexmedetomidine causes peripheral vasoconstriction and increased systolic arterial pressure in adults. In our study, DP lowered HR, but increased MAP, vs RP-TIVA.

In the PACU, 55.3% of RP patients coughed, a sign of airway reflex return, while only 10.3% of DP children coughed. Recovery time was also significantly shorter in Groups RP vs DP (23.8 vs 65.1 min, respectively). Prolonged emergence and decreased coughing with DP may reflect the longer elimination $t_{1/2}$ of dexmedetomidine (2 h) vs remifentanil (5 min).

Our study has limitations. First, the anaesthetist was not blinded to drug assignment. Secondly, because of large interindividual variation in respiratory depressant responses, individualized dose titration was necessary. Therefore, remifentanil started at 0.05 $\mu$g kg$^{-1}$ min$^{-1}$ with the incremental addition of 0.05 $\mu$g kg$^{-1}$ min$^{-1}$ until the respiratory rate was 50% of baseline. Recommended dexmedetomidine dosing involves a loading infusion of 1.0 $\mu$g kg$^{-1}$ over 10 min, followed by a continuous infusion of 0.2–0.7 $\mu$g kg h$^{-1}$. We used a dexmedetomidine dose 4 $\mu$g kg$^{-1}$ bolus followed by 1–2 $\mu$g kg h$^{-1}$ for airway FB removal in paediatric patients. Although the altered haemodynamic profile was not significant in children, this high dexmedetomidine dosage may cause dramatic haemodynamic changes in elderly patients. Thirdly, our sample size was limited. Lastly, paediatric patients with severe preoperative respiratory impairment secondary to FB aspiration were not included. In clinical practice, we find it difficult to maintain spontaneous ventilation with RP-TIVA in those patients because of a pre-existing comprised respiratory drive.

In summary, DP-TIVA with spontaneous ventilation provides adequate anaesthesia depth at 4 $\mu$g kg$^{-1}$ loading and 1–2 $\mu$g kg h$^{-1}$ infusion in children for airway FB removal by rigid bronchoscopy. Compared with RP-TIVA with spontaneous ventilation, DP-TIVA caused less haemodynamic and respiratory changes. However, recovery of consciousness and cough reflex were delayed in DP vs RP patients, likely due to different elimination half-lives. Nonetheless, particularly in children with severe preoperative airway impairment, the beneficial respiratory profile obtained with dexmedetomidine may make it a suitable agent for rigid laryngoscopic airway FB removal.

Authors’ contributions

K.C. is the first author for this article and contributed to all aspects of this study. M.Y. and C.-B.H. made substantial contributions to the conception and design of the study, data collection and explanation, and manuscript writing. X.S. is the corresponding author for this study, designed the study, and performed draft revisions. All authors have approved the current manuscript to be released for publication.

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Declaration of interest

None declared.

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