Salbutamol premedication in children with a recent respiratory tract infection

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Summary

Background: Premedication with β-2 agonists (e.g., salbutamol) is effective in preventing increases in total respiratory resistance and in decreasing the incidence of perioperative bronchospasm in asthmatic children. Because children with recent respiratory tract infection (RTI) exhibit bronchial hyperreactivity similar to that observed in asthmatic children, the use of salbutamol in children with RTI has become popular among pediatric anesthetists for the prevention of perioperative respiratory adverse events (PRAE). In a prospective observational study, we therefore assessed the usefulness of salbutamol premedication on the occurrence of PRAE.

Methods: Results from 600 children (0–16 years) undergoing general anesthesia were analyzed: 200 children with a recent RTI who received preoperative salbutamol 10–30 min prior to surgery, 200 children with a recent RTI without salbutamol premedication, and 200 children without a RTI during the last 4 weeks. All PRAE (laryngospasm, bronchospasm, oxygen desaturation [<95%], severe coughing) were recorded.

Results: Children with a recent RTI who received salbutamol demonstrated a significantly reduced incidence of perioperative bronchospasm (5.5% vs 11%, P = 0.0270) and severe coughing (5.5% vs 11.5%, P = 0.0314) compared with children who had an RTI but did not receive salbutamol. However, healthy children presented with the lowest rate (bronchospasm 1.5%, severe coughing 4.5%) of respiratory complications compared with children with a recent RTI independent whether or not they received salbutamol preoperatively.

Conclusions: The results from this audit suggest that children with a history of a recent RTI have significantly less PRAE following a premedication with salbutamol compared with no premedication. Therefore, premedication with salbutamol might be considered in children with recent RTI.

Keywords: paediatric anaesthesia; bronchodilator; salbutamol; respiratory complications; respiratory tract infection; premedication

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Perioperative respiratory adverse events (PRAE) remain a major cause of morbidity and mortality in pediatric anesthesia (1–5). These PRAE (especially bronchospasm and laryngospasm) can precipitate hypoxemia and lead to life-threatening events, particularly in children because they have lower oxygen reserves (6). The presence of bronchial hyperreactivity (BHR) such as that observed in asthma, following respiratory tract infection (RTI) (7–10), and in the presence of passive smoking are significant risk factors for the occurrence of PRAE. These underlying diseases lead to airway inflammation with subsequent alteration of the autonomic nervous system and enhancement of airway responsiveness to different stimuli encountered during anesthesia.

In routine clinical practice, anesthetists are challenged everyday by a large number of children with recent RTI presenting for anesthesia (11). Although there is an increased risk of respiratory complications in the presence of recent respiratory infections, particularly in the first 2 weeks following an RTI (9,10,12–15), anesthetists still proceed and perform anesthesia in these children for several reasons: first, RTI occurs frequently, especially in young children and children undergoing ear, nose, and throat procedures (5,10,16) added to this the clinical uncertainty for how long to postpone the procedure following an RTI. Second, there are adverse economic and emotional impacts because of cancelation of surgery. Therefore, it is of paramount importance for the anesthetist in charge of these patients to choose an anesthetic strategy that minimizes the occurrence of PRAE.

Premedication of the child with a β-2 agonist such as salbutamol has been demonstrated to be effective in preventing increases in total respiratory resistance (17) and in decreasing the incidence of perioperative bronchospasm in asthmatic children (18). Because children with recent RTI exhibit bronchial hyperreactivity similar to that observed in asthmatic children (19), the use of salbutamol in children with RTI has become popular among pediatric anesthetists for the prevention of PRAE. However, to our knowledge, there have been no studies assessing the usefulness of salbutamol premedication in children with recent RTI anesthetized with sevoflurane and invasive airway management (laryngeal mask or tracheal tube). Therefore, to design a prospective randomized controlled study, we performed an observational study to investigate the impact of salbutamol premedication on the incidence of perioperative laryngospasm, bronchospasm, desaturation (<95%), and severe coughing in children with a recent RTI.

Methods
This prospective quality assurance study was approved by the Local Research Ethics Committee and written parental consent was waived. In this prospective study, 600 children aged 0–16 years undergoing general anesthesia with a laryngeal mask airway or a tracheal tube were included. Because this study served also as a pilot study to allow for the design of a randomized controlled trial, 200 consecutive children were included for each of the three groups. As soon as the planned group size was reached, enrollment was then discontinued. Four hundred children had a recent upper respiratory tract infection (RTI) (moist cough within the last 2 weeks prior to surgery as reported by the parents but no symptoms of a current infection), while 200 children had not suffered from a RTI within the last 4 weeks. Two hundred children with an RTI received preoperative salbutamol (2.5 mg if weight <20 kg, 5 mg if weight >20 kg) through a nebulizer 10–30 min prior to surgery and 200 children with an RTI did not receive salbutamol. Whether or not the children received salbutamol preoperatively was left to the attending anesthetist who was unaware of the study taking place until all children were included. Exclusion criteria were airway malformations, major airway reconstructive or cardiothoracic surgery, or a current RTI. Anesthesia was induced with either inhalational sevoflurane or i.v. propofol, while anesthesia was maintained with sevoflurane in all cases. The choice of airway management was not standardized but left to the discretion of the anesthetist in charge. Only children undergoing anesthesia with an invasive airway device (LMA or tracheal tube) were included in the audit, while children receiving only a face mask or nasal prongs were excluded.

All respiratory adverse events in the perioperative period (laryngospasm, bronchospasm, oxygen desaturation (<95%), severe coughing) were recorded. Laryngospasm was defined as a complete airway obstruction associated with muscle rigidity of the abdominal and chest walls. Bronchospasm was
defined as the occurrence of an increased respiratory effort, especially during expiration, and wheeze on auscultation.

Statistics
Statistical analyzes were performed using SAS software version 9.1 (SAS Institute, Cary, NC, USA). The differences between the groups with a recent URTI (Salbutamol vs no salbutamol) were determined using a chi-square test. A \( P \) value <0.05 was considered statistically significant.

Results
The patient characteristics are given in Table 1 demonstrating no differences between the three groups. Children with moist cough in the last 2 weeks prior to surgery who received a premedication with salbutamol demonstrated a significantly reduced incidence of perioperative bronchospasm (5.5% vs 11%, \( P = 0.0270 \)) and severe coughing (5.5% vs 11.5%, \( P = 0.0314 \)) compared with children who had an RTI but did not receive salbutamol (Table 2). However, healthy children presented with the lowest rate of respiratory complications compared with children with a recent RTI, independent of whether or not they received salbutamol preoperatively.

### Table 1
Characteristics of patients with a recent moist cough (≤2 weeks) receiving or not receiving salbutamol per inhalation preoperatively and healthy children (no cold in the last 2 weeks)

<table>
<thead>
<tr>
<th></th>
<th>Salbutamol</th>
<th>No Salbutamol</th>
<th>Healthy children</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>200</td>
<td>200</td>
<td>200</td>
</tr>
<tr>
<td>Male : female</td>
<td>113 : 87</td>
<td>116 : 84</td>
<td>114 : 86</td>
</tr>
<tr>
<td>Age, years</td>
<td>7 (0–16)</td>
<td>7 (0–16)</td>
<td>7 (0–16)</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>29.15 (4.3–85)</td>
<td>28.45 (4.3–116)</td>
<td>29.3 (4.5–105)</td>
</tr>
<tr>
<td>Asthma</td>
<td>42 (21.0%)</td>
<td>38 (19.0%)</td>
<td>41 (20.5)</td>
</tr>
<tr>
<td>Hay fever</td>
<td>22 (11.0%)</td>
<td>23 (11.5%)</td>
<td>23 (11.5%)</td>
</tr>
<tr>
<td>Eczema</td>
<td>31 (15.5%)</td>
<td>32 (16.0%)</td>
<td>34 (17.0%)</td>
</tr>
<tr>
<td>Passive smoking</td>
<td>63 (31.5%)</td>
<td>59 (29.5%)</td>
<td>62 (31.0%)</td>
</tr>
<tr>
<td>Bronchial hyperreactivity at exercise</td>
<td>24 (12.0%)</td>
<td>23 (11.5%)</td>
<td>25 (12.5%)</td>
</tr>
<tr>
<td>Dry cough at night</td>
<td>29 (14.5%)</td>
<td>28 (14.0%)</td>
<td>29 (14.5%)</td>
</tr>
<tr>
<td>Airway management, consultant : trainee</td>
<td>72 (36.0%) : 128 (64.0%)</td>
<td>75 (37.5%) : 125 (62.5%)</td>
<td>71 (35.5%) : 129 (64.5%)</td>
</tr>
<tr>
<td>Laryngeal mask airway</td>
<td>141 (70.5%) : 59 (29.5%)</td>
<td>154 (77.0%) : 46 (23.0%)</td>
<td>142 (71.0%) : 58 (29.0%)</td>
</tr>
<tr>
<td>LMA : tracheal tube (TT)</td>
<td>141 (70.5%) : 59 (29.5%)</td>
<td>154 (77.0%) : 46 (23.0%)</td>
<td>142 (71.0%) : 58 (29.0%)</td>
</tr>
<tr>
<td>TT cuffed : TT uncuffed</td>
<td>91 (45.5%) : 109 (54.5%)</td>
<td>94 (47.0%) : 106 (53.0%)</td>
<td>95 (47.5%) : 105 (52.5%)</td>
</tr>
<tr>
<td>Duration of anesthesia, min</td>
<td>54 (15–169)</td>
<td>50 (15–182)</td>
<td>53 (20–176)</td>
</tr>
<tr>
<td>ENT surgery</td>
<td>75 (37.5%)</td>
<td>72 (36.0%)</td>
<td>74 (37.0%)</td>
</tr>
<tr>
<td>General surgery</td>
<td>45 (22.5%)</td>
<td>46 (23.0%)</td>
<td>41 (20.5%)</td>
</tr>
<tr>
<td>Dental surgery</td>
<td>13 (6.5%)</td>
<td>10 (5.0%)</td>
<td>15 (7.5%)</td>
</tr>
<tr>
<td>Orthopedic surgery</td>
<td>11 (5.5%)</td>
<td>14 (7.0%)</td>
<td>9 (4.5%)</td>
</tr>
<tr>
<td>Plastic surgery</td>
<td>35 (17.5%)</td>
<td>39 (19.5%)</td>
<td>37 (18.5%)</td>
</tr>
<tr>
<td>Other surgery</td>
<td>21 (10.5%)</td>
<td>19 (9.5%)</td>
<td>24 (12.0%)</td>
</tr>
</tbody>
</table>

Discussion
This prospective audit confirms that children with recent RTI are more likely to have respiratory complications during the perioperative period. Nevertheless, premedication with salbutamol in children with a recent RTI presenting to anesthesia with moist cough led to a significant reduction in perioperative bronchospasm and severe coughing.

There have been many studies highlighting the association between RTI and PRAE (8,9,14,15,20–22). In agreement with the literature (10,15,21), we found that a child’s history of a current or recent RTI (<2 weeks) increased the risk for respiratory adverse events compared with healthy children, whether or not salbutamol was administered. The significantly higher incidence of PRAE in children with a recent RTI might be attributed to airway...
Coughing 11 (5.5%)  
Desaturation 13 (6.5%)  
Bronchospasm 10 (5.0%)  
Laryngospasm 19 (9.5%)  

bronchial hyperreactivity caused by a recent RTI (17,30), the use of salbutamol in children with sevoflurane anesthesia in asthmatic children resistance caused by tracheal intubation during administration (27–29). Because salbutamol has been shown to prevent the increase in respiratory resistance following tracheal intubation during sevoflurane anesthesia in asthmatic children (17,30), the use of salbutamol in children with bronchial hyperreactivity caused by a recent RTI does most probably have the same underlying mechanism leading to a decrease in the incidence of respiratory adverse events as highlighted by this audit. It is noteworthy that salbutamol exerts its bronchodilatory effects by acting only on the airway compartment of the lung, thus protecting from the cholinergic-induced bronchoconstriction encountered under anesthesia (31,32).

The results of the present study are, however, in disagreement with early results given by Elwood et al. (33), who failed to demonstrate the usefulness of a bronchodilator premedication (either ipratropium or albuterol) in reducing the incidence of PRAE. However, they studied a small number of children and included those with rather minor RTI (e.g. sore throat). In addition, there was a lack of uniformity in the choice of the premedication (anti-cholinergic and β-2 agonist) and half of the children were anesthetized via a face mask that may have masked potential effects of the β-2 agonist administration. Airway maintenance with a face mask reduces the occurrence of PRAE because stimulation of the upper airways and consequently the parasympathetic system is abolished, thus reducing the risk for PRAE when compared with airway instrumentation with an endotracheal tube or a laryngeal mask airway (15). Furthermore, anesthesia was maintained with halothane, a potent bronchodilator. In the present study, we excluded all children having airway maintenance with a face mask during anesthesia and considered only those children with a severe RTI (moist cough) within the preceding 2 weeks. We believe this strengthens our findings and highlights the usefulness of salbutamol as a premedication in this regard. There is no doubt that the observational nature of this study represents limitations and a cause–effect study needs to be performed to ascertain our findings. Nevertheless, several factors were controlled in order to minimize bias in collecting the data. For instance, none of the anesthetists responsible for the patients were aware of the study taking place until the end of the data collection. It is therefore reasonable to assume that children who were judged to be at a particularly high risk for respiratory complications were more likely to be given salbutamol than not. This could have decreased the impact of salbutamol administration on the occurrence of respiratory adverse events given that some of the children with moist inflation, interaction with the autonomic nervous system and consecutively to airway sensitivity induced by the RTI (23,24). While the timing for the peak occurrence of perioperative respiratory adverse events is still under debate, growing evidence suggests that children are at the highest risk for respiratory adverse events in the first 2 weeks following an RTI (10,15,16). Among the symptoms of RTI reported by the parents, moist cough, green runny nose, and fever were associated with higher rates of respiratory adverse events compared with dry cough and clear runny nose. These symptoms are most often encountered when there is a systemic reaction to the RTI or a superimposed bacterial infection. Therefore, these symptoms should be regarded in the context with the timing of RTI in the decision-making process whether or not to postpone the procedure. RTI with moist cough generally involves both the upper and the lower airways leading to BHR, which can last for up to 6–8 weeks (25,26), but which is generally reversible with bronchodilator administration (25). Consequently, to assess the impact of salbutamol on high risk children, we only included children with a recent (<2 weeks) moist cough into this quality assurance project.

Pretreatment with beta 2-adrenergic agonists, e.g. albuterol or fenoterol, has been shown to reduce total respiratory resistance following tracheal intubation in adults (27–29). Because salbutamol has been shown to prevent the increase in respiratory resistance caused by tracheal intubation during sevoflurane anesthesia in asthmatic children (17,30), the use of salbutamol in children with bronchial hyperreactivity caused by a recent RTI

<table>
<thead>
<tr>
<th></th>
<th>Salbutamol</th>
<th>No salbutamol</th>
<th>P value</th>
<th>Healthy children</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laryngospasm</td>
<td>19 (9.5%)</td>
<td>32 (16.0%)</td>
<td>0.0513</td>
<td>5 (2.5%)</td>
</tr>
<tr>
<td>Bronchospasm</td>
<td>10 (5.0%)</td>
<td>22 (11.0%)</td>
<td>0.0270</td>
<td>3 (1.5%)</td>
</tr>
<tr>
<td>Desaturation</td>
<td>13 (6.5%)</td>
<td>21 (10.5%)</td>
<td>0.1515</td>
<td>12 (6.0%)</td>
</tr>
<tr>
<td>Coughing</td>
<td>11 (5.5%)</td>
<td>23 (11.5%)</td>
<td>0.0314</td>
<td>9 (4.5%)</td>
</tr>
</tbody>
</table>
cough did not receive salbutamol. Although this has the potential to mask the positive effects of salbutamol, the present audit demonstrates significant differences between the groups emphasizing the usefulness of salbutamol pretreatment in clinical practice. Moreover, these results are of high importance because they provide valuable information on the variables that should be taken into account when designing a prospective randomized controlled study to assess the protective effect of salbutamol given as premedication in children with a recent RTI.

In fact, the preoperative administration of salbutamol led to risk reductions of at least 35% of all PRAE’s examined in this study. However, given the actual sample size (n = 200 per group) only bronchospasm and severe coughing showed significant group differences.

In conclusion, the results of the present audit demonstrate that children undergoing anesthesia with a history of a recent RTI and moist cough have significantly less respiratory adverse events following a premedication with salbutamol compared with no premedication. Moreover, healthy children without a recent RTI had the lowest incidence of respiratory complications compared with children with an RTI with or without salbutamol pretreatment. Therefore, we suggest that premedication with salbutamol should be considered in children with recent RTI because it might significantly reduce the incidence of respiratory adverse events.

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