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Respiration and the Airway

Premedication with salbutamol prior to surgery does not decrease the risk of perioperative respiratory adverse events in school-aged children

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Abstract

Background: Perioperative respiratory adverse events (PRAE) remain the leading cause of morbidity and mortality in the paediatric population. This double-blinded randomized control trial investigated whether inhaled salbutamol premedication decreased the occurrence of PRAE in children identified as being at high risk of PRAE.
Methods: Children with at least two parentally reported risk factors for PRAE undergoing elective surgery were eligible for recruitment. They were randomized to receive either salbutamol (200 μg) or placebo prior to their surgery and PRAE (bronchospasm, laryngospasm, airway obstruction, desaturation, coughing and stridor) were recorded.
Results: Out of 470 children (6–16 yr, 277 males, 59%) recruited, 462 were available for an intention-to-treat analysis. Thirty-two (14%) and 27 (12%) children from the placebo and salbutamol groups experienced PRAE. This difference was not significant [odds ratio (OR): 0.83, 95% confidence interval (CI): 0.48–1.44, *P*: 0.51]. Oxygen desaturation [14/232 (6%) *vs* 14/230 (6%), OR: 1.01, 95% CI: 0.47–2.17, *P*: 0.98] and severe coughing [12/232 (5%) *vs* 10/230 (4%), OR: 0.83, 95% CI: 0.35–1.97, *P*: 0.68] were the most common PRAE, but did not significantly differ between the groups. The occurrence of PRAE was slightly lower in children with respiratory symptoms who received salbutamol compared with placebo [16/134 (12%) *vs* 21/142 (15%), OR: 0.93, 95% CI: 0.38–2.26, *P*: 0.87], but was not significantly different.
Conclusions: Premedication with salbutamol to children aged between 6 and 16 years and at high risk of PRAE prior to their surgery did not reduce their risk of PRAE.
Trial registration number: ACTRN12612000626864 (www.anzctr.org.au).

Key words: β-2 agonist, salbutamol; perioperative respiratory adverse events; prevention; paediatric population

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Editor's key points

- It is not known if inhalation of salbutamol before anaesthesia decreases the incidence of perioperative respiratory complications in children at increased risk of complications.
- Preoperative inhalation of salbutamol did not significantly reduce the incidence of respiratory complications in children aged 6-16 years undergoing elective surgery.

Perioperative respiratory adverse events (PRAE) are the most common complications in paediatric anaesthesia. They can potentially lead to significant neurological harm due to hypoxia.[1] Children with respiratory symptoms linked to airway inflammation and bronchial hyper-reactivity [e.g. respiratory tract infections (RTI) or asthma] are at higher risk of PRAE.[1–5] These symptoms are present in >25% of children presenting for surgery.[5–10] Paediatric anaesthetists thus face the complex task of identifying at-risk children and deciding whether to proceed with anaesthesia or postpone the procedure.[5]

β-2-Adrenergic agonists (e.g. salbutamol) act as bronchodilators in individuals with asthma.[11] While salbutamol effectively prevents an increase in respiratory resistance during intubation, its role in decreasing the incidence of PRAE is controversial.[12–14] Preoperative salbutamol is commonly used, especially in children with RTI,[15] and an observational study from our group showed that preoperative salbutamol in children with a recent moist cough significantly reduced the incidence of perioperative bronchospasm.[10]

The primary objective of this double-blinded randomized control trial was to investigate whether inhaled salbutamol premedication decreased the occurrence of PRAE. We hypothesized that children receiving salbutamol would experience significantly less PRAE compared with children receiving placebo. The secondary outcomes of this study assessed whether the risk of PRAE was reduced in children with at least one respiratory symptom receiving salbutamol compared with placebo and also whether the occurrence of PRAE varied during the different phases of anaesthesia between the placebo and treatment groups.

Methods

Study design

This trial was conducted as a single centre, double-blind, placebo-controlled and parallel-group study at Princess Margaret Hospital for Children in Perth, Western Australia between December, 2012 and February, 2015. Princess Margaret Hospital for Children is the only tertiary paediatric centre in Western Australia and caters for a large heterogeneous population with approximately 15 000 anaesthetics administered every year. Approval for this study was obtained from the Princess Margaret Hospital for Children Ethics Committee (2009/EP) and the University of Western Australia Committee (RA/4/1/5892). The trial was registered with the Australian and New Zealand Clinical Trial Registry (www.anzctr.org.au, ACTRN12612000626864).

Potential participants to the study were first identified from the elective surgery list by a research team member based on their age and type of surgery. The research team member then approached the anaesthetist in charge of the identified patients to determine their suitability for participation to the study. Following the latter's approval, the researcher approached the family to determine final eligibility for the study. This was based on the presence of at least two risk factors for PRAE and the absence of any exclusion criteria (Fig. 1). Written informed voluntary consent was obtained from parents and assent from child, prior to enrolment of the participants in the study. Recruited children were block randomized and assigned to one of the two groups, in a 1:1 ratio to receive either salbutamol or placebo. Any PRAE listed in Table 1 that met the definitions given was recorded by the anaesthetist during the perioperative period and by the post-anaesthesia care unit (PACU) nurse during the recovery period of anaesthesia.

No interim analyses for efficacy or futility were performed and an independent data monitoring committee was in place in case any unexpected reviews of un-blinded data needed to be performed. No changes were made to the initial protocol design between the start and end of the study.

Study population

Children aged between 6 and 16 yr (until end of 16th birthday) with at least two parentally reported risk factors for PRAE, and without any contraindication for salbutamol, undergoing elective surgery were eligible for recruitment into the study. The risk factors for PRAE were previously defined by our group in a large observational trial and detailed in Fig. 1.[1] The exclusion criteria are also summarized in the same figure. Participants were able to voluntarily withdraw consent at any point in time during the study.

Drug administration

Children were randomized to two actuations of either salbutamol (100 μg Ventolin® per actuation, GlaxoSmithKline, UK) or placebo (hydrofluoroalkane propellant, HFA-134a, GlaxoSmithKline, UK) delivered via a disposable spacer (Lite Aire®, Thayer Medical, Tucson, USA) using slow inhalations to near total lung capacity with a 5 s breath hold.

Treatment was administered at least 20 minutes preoperatively to ensure maximal bronchodilation.[16] In cases of unanticipated theatre delays, impacted participants were monitored and readministered the treatment 20 minutes prior to their rescheduled surgery if their waiting time since the initial administration of the drug had exceeded 1 h (half-life of salbutamol: ~2.5 h). The same inhaler attributed through the randomization process was used and the same dose was administered. This ensured that treatment was fully active in all patients over the perioperative period, irrespective of alterations in the timing of surgery.

Anaesthesia management

All children were anaesthetized in accordance with the safety standards of the Australian and New Zealand College of Anaesthetists (ANZCA) and the Department of Anaesthesia and Pain Management of Princess Margaret Hospital for Children using the institutional anaesthesia workstations (Draeger Primus, Luebeck, Germany).[17] Minimal and standardized routine anaesthesia monitoring always included ECG, non-invasive blood pressure measurements, capnography and pulse oximetry.

Anaesthesia induction was performed as deemed appropriate by the attending anaesthetist with either incremental inhalation of sevoflurane (up to 8 vol%) or i.v. propofol (>3 mg kg^{-1}). The method of sevoflurane inhalation and i.v. propofol