

DG: CONSORT 2010 explanation and elaboration: Updated guidelines for reporting parallel group randomised trials. *BMJ* 2010; 340:c869

3. Brookes ST, Whitely E, Egger M, Smith GD, Mulheran PA, Peters TJ: Subgroup analyses in randomized trials: Risks of subgroup-specific analyses; Power and sample size for the interaction test. *J Clin Epidemiol* 2004; 57:229–36
4. Kumakura S, Yamaguchi K, Sugawara Y, Murakami T, Kikuchi T, Inada E, Nagaoka I: Effects of nitrous oxide on the production of cytokines and chemokines by the airway epithelium during anesthesia with sevoflurane and propofol. *Mol Med Rep* 2013; 8:1643–8

(Accepted for publication November 19, 2018.)

Is a Single Dose of Propofol Good Enough to Prevent Respiratory Complications beyond the Induction Phase?

To the Editor:

Ramgolam *et al.* reported that IV propofol, compared to sevoflurane induction, had protective effect against perioperative respiratory adverse events in high-risk children.¹ The investigators also calculated the relative risk for perioperative respiratory adverse events adjusted for age, sex, American Society of Anesthesiologists Physical Status, and weight. However, we feel that other identified risk factors for perioperative respiratory adverse events, which include history of prematurity,² obstructive sleep apnea,³ attempts at laryngeal mask airway insertion,⁴ and awake *versus* deep removal of laryngeal mask airway,⁴ were not mentioned.

Regarding the nonopioid analgesia, the children had received either regional or local analgesia. However, it is not clear whether the term “regional analgesia” means caudal analgesia or peripheral nerve blocks. The reason for highlighting this issue is that caudal analgesia has been reported to reduce the incidence of laryngospasm, although the mechanism is not clearly elucidated.⁵ Likewise, the authors have emphasized that the choice of opioid will have no impact on perioperative respiratory adverse events. However, it is evident

that IV fentanyl is associated with coughing, the reported incidence of which is 46 to 60% in children.⁶ Compared to other opioids, morphine releases significant amounts of histamine, enough to trigger bronchospasm. Therefore, it might not be wise to use morphine in a child with hyperreactive airways when better options are available. It would be interesting to see the results if the analgesia is also considered as one of the independent variables in their analysis.

The maintenance of anesthesia was done with sevoflurane in both groups. The investigators stated that the induction dose of propofol also protected against postoperative unwanted respiratory complications, even when sevoflurane was used in the maintenance phase. Does the protective effect of a single dose of propofol last beyond the induction period? If so, we would be interested to know whether there is an interaction effect between these two agents. From a previous large observational study, it is clear that propofol is superior in preventing perioperative respiratory adverse events to sevoflurane when used for maintenance.⁴ Future randomized clinical trials are needed to investigate the beneficial effect of propofol when used for both induction and maintenance of anesthesia in children with high risk for perioperative respiratory adverse events.

The investigators are to be applauded for conducting this pragmatic randomized clinical trial, which has a genuine external validity and is applicable in clinical practice.

Competing Interests

The authors declare no competing interests.

Asish Subedi, M.D., Krishna Pokharel, M.D. BP Koirala
Institute of Health Sciences, Dharan, Nepal (A.S.).
ashish.subedi@bpkihs.edu

References

1. Ramgolam A, Hall GL, Zhang G, Hegarty M, von Ungern-Sternberg BS: Inhalational versus intravenous induction of anesthesia in children with a high risk of perioperative respiratory adverse events: A randomized controlled trial. *ANESTHESIOLOGY* 2018; 128:1065–74
2. Tait AR, Malviya S, Voepel-Lewis T, Munro HM, Seiwert M, Pandit UA: Risk factors for perioperative adverse respiratory events in children with upper respiratory tract infections. *ANESTHESIOLOGY* 2001; 95:299–306
3. Brown KA, Laferrière A, Moss IR: Recurrent hypoxemia in young children with obstructive sleep apnea is associated with reduced opioid requirement for analgesia. *ANESTHESIOLOGY* 2004; 100:806–10
4. von Ungern-Sternberg BS, Boda K, Chambers NA, Rebmann C, Johnson C, Sly PD, Habre W: Risk assessment for respiratory complications in paediatric

anaesthesia: A prospective cohort study. *Lancet* 2010; 376:773–83

5. Khalil SN, Matuszczak ME, Maposa D, Bolos ME, Lingadevaru HS, Chuang AZ: Presurgical fentanyl vs caudal block and the incidence of adverse respiratory events in children after orchidopexy. *Paediatr Anaesth* 2009; 19:1220–5
6. Han JI, Lee H, Kim CH, Lee GY: The frequency of fentanyl-induced cough in children and its effects on tracheal intubation. *J Clin Anesth* 2010; 22:3–6

(Accepted for publication November 19, 2018.)

Does Intravenous *versus* Inhalational Induction of Anesthesia Only Decrease Perioperative Respiratory Events during the Induction Period?

To the Editor:

We read with interest the study by Ramgolam *et al.*,¹ in which they demonstrated that IV induction in children 8 yr and under was associated with fewer perioperative airway complications compared with inhalational induction with sevoflurane and nitrous oxide. We commend the authors for setting up a randomized trial to improve the delivery of anesthetic care for children with higher risk of airway complications. Upon analysis of the complications data, it seems that the majority of the complications occurred during the induction process for the inhalational group (47 events out of a total of 64), while the IV induction group had fewer complications during the induction period. In contrast, the IV induction group had relatively more respiratory complications during the rest of the intraoperative and postoperative periods (26 events out of a total of 39). However, given the manner in which the data are presented (*any* [1 or more] respiratory event), it is impossible to truly decipher the incidence of *any* postinduction perioperative respiratory events from the manuscript. When minimized (difference between *any* unadjusted perioperative and *any* unadjusted induction respiratory events), it appears that there was no statistical difference

in postinduction events between the two groups (23/149 [15.4%] *vs.* 17/149 [11.4%], relative risk [RR]: 0.7, 95% CI: 0.4 to 1.3, $P = 0.4$). This calculation is limited, however, by the fact that each patient may have had more than one event over the perioperative course, and the study did not specifically note the rates of *any* postinduction respiratory events. It would have been beneficial to include this analysis in order to discern whether the difference in respiratory events was limited to the induction period.

We agree with the accompanying editorial² in that intravenous inductions tend to be much faster than inhalational inductions are, especially when large doses of propofol are used. The rapidity of progression through the excitatory stages to a deep stage of anesthesia during induction may have been the mediating factor in this study (with the actual agents being less important). With this in mind, a possible limitation of this investigation is the particular anesthesia workstation (Primus, Drägerwerk, AG, Germany) that was used for the inhalation inductions. This machine has been shown to have 300% longer wash-in times in simulated test conditions when compared to GE Datex (Germany) machines.³ The prolonged wash-in time associated with this machine and perhaps a longer excitatory phase of anesthesia may have led to a higher incidence of respiratory complications during induction. These results, therefore, may not be generalizable to institutions that use machines with faster anesthetic wash-in times.

Competing Interests

The authors declare no competing interests.

Thanh T. Nguyen, M.D., Humphrey V. Lam, M.D., Thomas M. Austin, M.D., M.S. University of Colorado School of Medicine, Aurora, Colorado (T.T.N.). thanh.nguyen4@childrenscolorado.org

References

1. Ramgolam A, Hall GL, Zhang G, Hegarty M, von Ungern-Sternberg BS: Inhalational *versus* intravenous induction of anesthesia in children with a high risk of perioperative respiratory adverse events: A randomized controlled trial. *ANESTHESIOLOGY* 2018; 128:1065–74
2. Davidson AJ: Induction of anesthesia for children: Should we recommend the needle or the mask? *ANESTHESIOLOGY* 2018; 128:1051–2
3. Kern D, Larcher C, Basset B, Alacoque X, Fesseau R, Samii K, Minville V, Fourcade O: Inside anesthesia breathing circuits: Time to reach a set sevoflurane concentration in toddlers and newborns: Simulation using a test lung. *Anesth Analg* 2012; 115:310–4

(Accepted for publication November 19, 2018.)