Original Article

# Using fentanyl and propofol for tracheal intubation during sevoflurane induction without muscle relaxants in children: A randomized prospective study


**ABSTRACT**

**Context:** Tracheal intubation is frequently facilitated with sevoflurane induction without the use of muscle relaxants in children.

**Aim:** The aim of this study was to compare the effects of two different doses of propofol preceded by a fixed dose of fentanyl during sevoflurane induction on quality of tracheal intubation in children.

**Settings and Design:** This was a prospective randomized study.

**Subjects and Methods:** Ninety American Society of Anesthesiologists I-II children aged 2–6 years were randomly assigned to one of two equal groups to receive 2 μg/kg of fentanyl with 2 mg/kg of propofol (Group I) or 2 μg/kg of fentanyl with 3 mg/kg of propofol (Group II) during sevoflurane induction. The intubating conditions and hemodynamic responses were evaluated. The time from sevoflurane induction to loss of consciousness, to intravenous line insertion, and to intubation was measured. The occurrence of any adverse effect was recorded.

**Statistical Analysis Used:** Results were analyzed using Student's *t*-test, paired *t*-test, and Chi-square test. $P < 0.05$ was considered statistically significant.

**Results:** The incidence of excellent intubating conditions was achieved more significantly in Group II (41/45 patients, 91%) than that in Group I (31/45 patients, 69%) ($P = 0.008$) (95% confidence interval [CI] =0.39–0.8). Whereas, there were no significant differences between the two groups in terms of the overall acceptable intubating conditions in Group I (40/45 patients, 89%) and Group II (43/45 patients, 96%) ($P = 0.81$) (95% CI = 0.71–1.31). No patient developed any adverse effect.

**Conclusion:** The administration of 3 mg/kg propofol preceded by 2 μg/kg fentanyl provided a higher proportion of excellent intubating conditions compared with 2 mg/kg propofol preceded by 2 μg/kg fentanyl during sevoflurane induction in children without muscle relaxants.


**Key words:** Children; fentanyl; intubation; propofol; sevoflurane


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## Introduction

Tracheal intubation without prior administration of muscle relaxants is well-established practice among anesthesiologists in pediatric anesthesia.[1,2] Such technique may be one of the choices for the anesthetist when the use of muscle relaxants is precluded, where the use of a nerve stimulator to identify the nerves integrity is required as in ENT procedures such as cochlear implants. It is also useful if the use of depolarizing or nondepolarizing neuromuscular blocking drugs is contraindicated such as myopathy.[2,3] Usage of sevoflurane alone without a muscle relaxant for inhalation induction of anesthesia and tracheal intubation has been widely investigated in pediatric patients.[4-6] However, the incidence of acceptable intubating conditions is not satisfactory (ranges between 35% and 87%).[7,8]

The drawback of this technique is the occurrence of laryngospasm during tracheal intubation, and in addition, a relatively long time is required to achieve adequate depth of anesthesia and sufficient relaxation of oropharyngeal muscles to enhance the quality of intubating conditions.[4,9] Moreover, the use of high sevoflurane concentration for intubation has the potential to produce epileptiform electroencephalographic activity and hemodynamic instability, especially in children.[10,11]

Several strategies have been developed to speed the induction time and improve the quality of tracheal intubation during sevoflurane induction in children, such as extended exposure to sevoflurane,[4] high inspired fraction of sevoflurane,[5] clonidine premedication,[12] and addition of nitrous oxide,[13] opioids,[14-17] or propofol.[18]

The objectives of this study were to compare the effects of two different doses of propofol preceded by a fixed dose of fentanyl as a supplement for sevoflurane induction on quality of tracheal intubation and the hemodynamic response to induction and intubation without muscle relaxants in children undergoing elective surgery. The incidence of excellent intubating conditions was considered the primary outcome. The secondary outcomes included hemodynamic response and occurrence of complication during the study.

## Subjects and Methods

After obtaining the Institutional Review Board approval (No. E-14-1071) and informed written consent for each child from at least one of the parents or a legal guardian, we studied ninety children of American Society of Anesthesiologists (ASA) Physical Status I and II, of both sex, aged between 2 and 6 years, and scheduled for elective ENT surgery that required general anesthesia with tracheal intubation.

This randomized clinical trial was conducted at King Abdul-Aziz University Hospital, College of Medicine, King Saud University, Riyadh, Kingdom of Saudi Arabia, between June 2015 and September 2016. The trial has been performed according to the World Medical Association Declaration of Helsinki Ethical Principles for medical research in pediatrics, and it was registered at the ClinicalTrials.gov (NCT02442128).

Children with a history of malignant hyperthermia, gastroesophageal reflux, anticipated difficult intubation, cardiorespiratory disease, respiratory tract infection in the previous 2 weeks, neurological or neuromuscular disease, known sensitivity to the drugs used, and children who refused to undergo an inhalational induction or in whom intravenous (IV) access had already been inserted were excluded from the study. All patients fasted 6 h for solid food and 4 h for clear liquids preoperatively and underwent a detailed preoperative preparation. EMLA cream was applied to the skin over a visible vein on the dorsum of both hands of all patients 1 h before surgery, and all patients were premedicated with 0.3 mg/kg oral midazolam (maximum dose of 12 mg) 30 min before induction. Children who refused to take oral midazolam were excluded from the study. No IV line was inserted and children were allowed to watch cartoon movies during their stay in the holding area.

Upon arrival at the operating theater, standard monitoring was used throughout the study, including noninvasive blood pressure, temperature, electrocardiogram, and pulse oximetry. Expired concentrations of sevoflurane, carbon dioxide ($CO_2$), and oxygen during the study were continuously monitored using gas analyzer of the anesthesia workstation (a Datex Capnomac airway gas monitor, Datex-Ohmeda, Helsinki, Finland).

After preoxygenation for 3 min with 100% oxygen, anesthesia was induced by a circle system with sevoflurane (Aesica Queenborough Ltd., for Abbott Laboratories Ltd., UK) in 100% oxygen (6 L/min) through a facemask, with a gradual increase of sevoflurane concentration with every single breath to a maximum of 6 vol%. Initially, patients breathed spontaneously and the facemask ventilation was then gently manually assisted when they became apneic using a 10 $cmH_2O$ inspiratory pressure to maintain oxygen saturation above 95% and an end-tidal $CO_2$ between 35 and 40 mmHg.

After loss of consciousness and the eyelash reflex, the inspired concentration of sevoflurane concentration was reduced to 3% and IV access was secured in all children using a 22-G cannula sited on the dorsum of a hand.

The allocated children were randomly assigned using a computer-generated random number table technique to one

of two groups: Group I (administered with 2 mg/kg propofol preceded by 2 μg/kg fentanyl, $n = 45$) and Group II (administered with 3 mg/kg propofol preceded by 2 μg/kg fentanyl, $n = 45$). All syringes with study drugs were prepared and diluted with saline to the total volume 10 ml by an independent investigator who was not participated in any other part of the study.

In both groups, fentanyl was first administered IV over 30 s followed by propofol over 20 s. Ninety seconds after administration of propofol, laryngoscopy and oral tracheal intubation with an appropriate-sized noncuffed tracheal tube was performed using a suitable-sized Macintosh laryngoscope by a second, an experienced unbiased anesthetist (one of the authors) who enters the anesthetic room when the child was asleep and unaware of the patient's randomization group. Caution was taken to avoid touching the carina during intubation process.

Each study drug was administered by an observer who was completely blinded to the study and to the group allocation of the child, and also, the attending anesthesiologist who intubated patients, recorded all parameters, and graded the airway conditions remained blinded to the study drug given and the master codes were held by a person who did not participate in the observation.

The quality of tracheal intubating conditions was evaluated according to the previously described scoring system proposed by Viby-Mogensen *et al*.[19] [Table 1]. Five factors were considered for assessment: jaw relaxation, ease of laryngoscopy, vocal cord position, coughing, and patient movement as excellent (1), good (2), or poor (3). Using the above criteria, the overall intubating conditions were judged as "excellent" if all scored 1, "good" if any scored 2, and "poor" if any scored 3. Good or excellent scores were considered as clinically acceptable intubation conditions and poor scores were considered as unacceptable.

Intubation was not attempted if the vocal cords were judged to be closed to avoid airway complications. A bolus dose of suxamethonium was administered IV in case of failure to intubate the trachea because of closed vocal cords, inadequate jaw relaxation, strong movement, or vigorous coughing on intubation. Once the trachea was intubated, a few breaths were delivered manually to assure tracheal placement of the endotracheal tube. At this point, the study was considered complete, ventilation was gently assisted, and anesthesia was then maintained at the discretion of the anesthesiologist in charge of the case.

The following time intervals were recorded: time from sevoflurane induction to loss of consciousness, to IV line insertion, and to intubation. The number of intubation attempts, end-tidal sevoflurane concentrations, and end-tidal $CO_2$ just before intubation was also recorded. In both groups, heart rate (HR) and mean arterial pressure (MAP) were measured and recorded at the following times: immediately before the inhaled induction as a baseline, immediately after propofol injection, just before laryngoscopy, just after intubation, and at 2 and 5 min after intubation.

**Table 1: Intubating conditions scoring system proposed by Viby-Mogensen *et al*. [19]**

| Variables | Acceptable | | Not acceptable |
|---|---|---|---|
| | Excellent | Good | Poor |
| Ease of laryngoscopy (jaw relaxation) | Easy | Fair | Difficult |
| Vocal cord position | Abducted | Intermediate | Closed |
| Vocal cord movement | None | Moving | Closing |
| Airway reaction (coughing) | None | Slight | Sustained (>10 s) |
| Movement of the limbs | None | Slight | Vigorous |

Overall intubating conditions were defined as Excellent: All variables are excellent, Good: One or more variable good, no quality poor, Poor: The presence of a single variable listed under poor

The primary outcome of this study was the incidence of excellent intubating conditions. The secondary outcomes included hemodynamic response and occurrence of complication during the study. Adverse events such as bradycardia (>30% fall in HR from the baseline), hypotension (>30% fall in MAP from the baseline)), laryngospasm, bronchospasm, hypoxia (oxygen saturation of <90%), and any other significant complication were also recorded.

### Statistical analysis

The average of excellent intubating conditions was estimated to be 41% when using sevoflurane alone for intubation without muscle relaxants,[6] to calculate the required sample size for this study. Accordingly, a sample size of 45 patients per study group was estimated to achieve at least an 80% power ($\alpha = 0.05$) to detect a difference of at least 30%.

Statistical analysis was performed using IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp. We used Student's *t*-test for normally quantitative variables, to compare between two studied groups and paired *t*-test for normally quantitative variables, to compare between two periods in the same group. Categorical data were analyzed using Chi-square ($\chi^2$) test or Fisher's exact test as appropriate. Data are presented as mean ± standard deviation or numbers and percentages. $P < 0.05$ was considered statistically significant.

## Results

One-hundred and three patients on the surgical list were identified as possible participants. Of these, 90 patients

fulfilled all criteria, subsequently consented and were enrolled into two equal groups ($n$ = 45 per group), to participate in the study with no patient dropouts [Figure 1]. Patients were scheduled for elective cochlear implant, tonsillectomy, adenoidectomy, or adenotonsillectomy.

The study groups were similar with respect to number of patients, age, sex, weight, and ASA physical status [$P > 0.05$; Table 2]. The time from sevoflurane induction to loss of consciousness was 67.0 ± 12.1 s in Group I versus 69.9 ± 11.5 s in Group II [$P = 0.122$; Table 2]. The time to IV line insertion was 148.8 ± 28.7 s in Group I versus 152.1 ± 25.6 s in Group II [$P = 0.285$; Table 2]. The time to intubation was 318.4 ± 32.5 s in Group I versus 314.1 ± 25.6 s in Group II [$P = 0.243$; Table 2]. The end-tidal sevoflurane concentration immediately before intubation was 2.7% ±0.2% in Group I versus 2.7% ±0.1% in Group II [$P = 0.105$; Table 2]. The end-tidal $CO_2$ immediately before tracheal intubation was 37.6 ± 1.8 mmHg in Group I versus 36.9 ± 1.8 mmHg in Group II [$P = 0.06$; Tables 2 and 3].

The incidence of excellent intubating conditions (score of 1 in all categories) was achieved more significantly in Group II (41/45 patients, 91%) than that in Group I (31/45 patients, 69%) ($P = 0.008$) (95% confidence interval [CI] =0.39–0.8). Whereas, there were no significant differences between the two groups in terms of the overall incidence of acceptable intubating conditions (good or excellent) in Group I (40/45 patients, 89%) and Group II (43/45 patients, 96%) ($P = 0.81$) (95% CI = 0.71–1.31).

There was no statistically significant difference between groups regarding the ease of laryngoscopy, position of the vocal cords, vocal cord movement, and movement of the limbs ($P$ values of 0.31, 0.55, 0.22, and 0.557, respectively) (95% CI values of 0.40–1.61, 0.65–1.66, 0.72–2.33, and 0.32–1.70, respectively). Comparing the degree of coughing, it was seen that patients in Group I had significantly more coughing episodes than those in Group II ($P = 0.020$) (95% CI = 0.25–0.68).

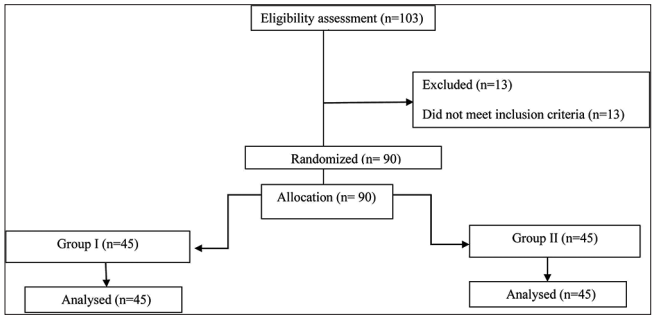


**Figure 1: Flow chart of the study**

Tracheal intubations in all patients were successfully performed at the first attempt, except for one patient with closed vocal cords in Group 1 who received IV bolus dose of suxamethonium to facilitate tracheal intubation.

Before induction, there was no statistically significant difference in HR and MAP between the two groups at baseline values [Figures 2 and 3]. HR showed a significant decrease in both groups, after propofol administration and before laryngoscopy in comparison to baseline values ($P < 0.05$) with no significant difference between the two groups [$P > 0.05$; Figure 2]. However, there was a significant decrease in HR in Group II at all measurements' times following intubation compared to the baseline of the same group and Group I [$P < 0.05$; Figure 2]. Both groups showed a significant decrease in MAP at all measurements' times compared to baseline values ($P < 0.05$) with no significant change between the two groups [$P > 0.05$; Figure 3].

No patient in our study developed bradycardia (defined as >30% fall in HR) or hypotension (defined as >30% fall in MAP), hypoxemia, laryngospasm, bronchospasm, or other complications.

## Discussion

This prospective, randomized study revealed that the administration of 3 mg/kg propofol preceded by 2 μg/kg fentanyl provided a higher proportion of excellent intubating conditions compared with 2 mg/kg propofol preceded by 2 μg/kg fentanyl during sevoflurane induction of anesthesia in healthy premedicated children without muscle relaxants; 91% of excellent intubating conditions were recorded in the

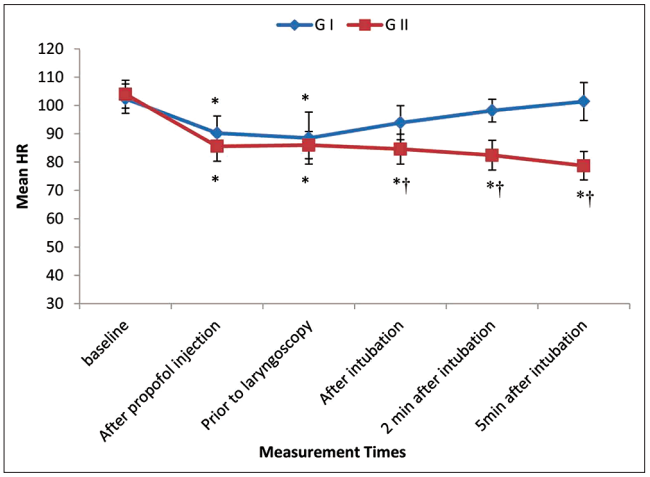


**Figure 2: Comparison of heart rate (HR) among the two groups at predetermined times. Values are presented as mean ±SD. *Significant differences from baseline p < 0.05, †Significant difference between groups $P < 0.05$**

propofol 3 mg/kg - 2 μg/kg fentanyl group compared to 69% in the propofol 3 mg/kg - 2 μg/kg fentanyl group ($P = 0.008$) (95% CI = 0.39–0.8) at similar end-tidal sevoflurane concentrations and similar times to intubation.

Sevoflurane is nonpungent and well tolerated by children, and consequently, it was considered the "near to ideal" agent for induction of anesthesia in children and numerous studies evaluated it as the sole agent for tracheal intubation without the use of muscle relaxants; however, persistence of spontaneous breathing and discontinuation of sevoflurane during tracheal intubation may be associated with the resultant poor intubating conditions in such studies.[4,6,20-22]

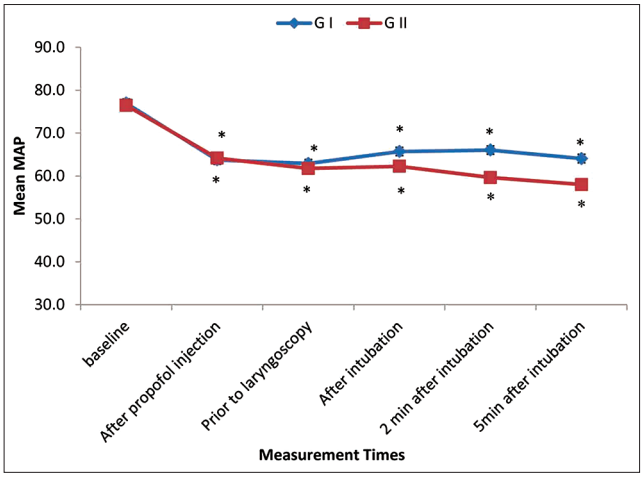


**Figure 3: Comparison of mean arterial pressure (MAP) among the two groups at predetermined times. Values are presented as mean ±SD. *Significant differences from baseline $P < 0.05$**

A drug combination using of single-dose propofol without complementary narcotic during sevoflurane induction has been described by many investigators to achieve rapid depth of anesthesia and improves the conditions for tracheal intubation without muscle relaxants in children. Our results support the findings by Lerman *et al*.[18] who evaluated the intubating conditions after different doses of propofol (0, 0.5, 1, 2, and 3mg/kg) in nonpremedicated children during 8% sevoflurane in 70% nitrous oxide and reported that using 3 mg/kg propofol achieved 90% excellent intubating conditions; however, the authors performed laryngoscopy in approximately 30 s after propofol injection, and this interval may be considered too short to attain the maximum effects of propofol. Contrary to this concept, in our study, laryngoscopy was commenced 90 s after administration of propofol; we believed that drug sequence and timing were crucial contributing factors since intubation should be attempted at or close to the maximum peak effect of combination of fentanyl and propofol to provide adequate depth of anesthesia.

In addition, in the study performed by Siddik-Sayyid *et al*.,[23] they found excellent intubating conditions in 92% of patients using propofol 2 mg/kg compared with 56% of patients using propofol 1 mg/kg after 8% sevoflurane induction without hemodynamic difference between the two groups.

**Table 2: Demographic data and outcome measurements**

| Variables | Group I | Group II | *P* |
|---|---|---|---|
| Number | 45 | 45 | |
| Age (years) | 4.30±1.3 | 4.20±1.50 | 0.288 |
| Weight (kg) | 18.6±3.9 | 19.40±3.30 | 0.170 |
| Sex (M/F) | 25/20 | 24/21 | 0.417 |
| ASA (I/II) | 35/10 | 34/11 | 0.402 |
| Time from sevoflurane to loss of consciousness (s) | 67.0±12.1 | 69.9±11.5 | 0.122 |
| Time from sevoflurane to IV insertion (s) | 148.8±28.7 | 152.1±25.6 | 0.285 |
| Time from sevoflurane to intubation (s) | 318.4±32.5 | 314.1±25.6 | 0.243 |
| End-tidal sevoflurane immediately before intubation (%) | 2.7±0.2 | 2.7±0.1 | 0.105 |
| End-tidal $PCO_2$ immediately before intubation (mmHg) | 37.6±1.8 | 36.9±1.8 | 0.06 |

ASA: American Society of Anesthesiologists. Values are presented as mean±SD and number of patients (*n*)

**Table 3: Assessment of intubating conditions**

| | Group I | | | Group II | | |
|---|---|---|---|---|---|---|
| | Excellent | Good | Poor | Excellent | Good | Poor |
| Ease of laryngoscopy | 44 | 1 | – | 45 | - | - |
| Vocal cord position | 40 | 4 | 1 | 42 | 3 | - |
| Vocal cord movement | 39 | 5 | 1 | 43 | 2 | - |
| Airway reaction (coughing) | 31 | 11 | 3 | 41 | 2 | 2 |
| Movement of the limbs | 43 | 2 | - | 44 | 1 | - |

Another study investigated the IV induction using the combination of propofol and fentanyl without sevoflurane to obtain better intubating conditions without neuromuscular blocking agents. A report by Gupta *et al*.[24] evaluated the use of different doses of propofol preceded by a fixed dose of fentanyl 3 μg/kg during tracheal intubation without muscle relaxants and reported that 3 mg/kg propofol is the optimal dose in their study. It provides acceptable intubating conditions in 80% patients without significant cardiovascular depression, and no airway complications was reported. Similarly, in another study performed by De Fátima De Assunção Braga *et al.*,[25] 3 mg/kg propofol preceded by 3 μg/kg fentanyl provided acceptable intubating conditions in 80% of the patients without significant hemodynamic changes. However, it is not surprising that induction by propofol and short-acting opioids without sevoflurane was associated with less ideal intubating conditions than those achieved with sevoflurane combined with adjuvants.[6,26]

In the present study, we ensured that an adequate depth of anesthesia at the time of laryngoscopy likely influenced the intubating conditions for tracheal intubation. The doses of propofol were chosen owning to the concept that doses <2 mg/kg in children seem likely to only partially suppress cough reflex.[6,23] We suggested that an increase in the propofol dose from 2 to 3 mg/kg improved the degree of coughing significantly which may be attributed to the apneic, and the suppressive effect of propofol on upper airway reactivity and the muscle tone,[18,25,27] whereas the beneficial effect of fentanyl is mainly related to the depressant effects on laryngeal reflexes, and its antitussive effect so that it blunts the pressor responses and prevents the bucking during tracheal intubation.[15]

In the current study, although both doses of propofol along with fentanyl were associated with a significant decrease in MAP following induction, this fall was within clinically acceptable limits and the usual increase in HR following tracheal intubation was significantly less in patients who received 3 mg/kg propofol. We did not find the doses of propofol to be associated with any episode of severe bradycardia or hypotension. The incidence of hypotension could be partially attributed to many factors, including variations of circulatory effects in anesthetic agents, volume status of the child, and presence of surgical stimulation. However, this study was conducted in healthy children and might not be well tolerated in some sick children.

A various scoring system for assessing intubating conditions have been used in previous studies.[8,18,25] However, we used the scoring system of Viby-Mogensen *et al*.,[19] which included limb movements for better assessment. The key reason for the discrepancy of our results from those results in previous studies might be related to the different study designs: patient population, sample size, premedication given, type of adjuvant induction agents, doses, the timing and sequence of drug administration, and finally the subjective criteria used to evaluate the quality of intubating conditions by different assessment scores.

In the current study, excellent intubating conditions were chosen to be our primary outcome based on the results of Mencke *et al*.,[22] who suggested that laryngeal morbidities such as postoperative hoarseness and vocal cords sequelae could be attributed to less than excellent intubating conditions. A report by Combes *et al.*[28] demonstrated that tracheal intubation without neuromuscular blocking agent is associated with more frequent adverse postoperative upper airway symptoms and adverse hemodynamic events if laryngoscopy and intubation are attempted under inadequate conditions. In the present study, we did not report any significant airway complication associated with the used techniques.

### Limitation

First, no control group (receiving only sevoflurane) was included in this study design as sevoflurane induction alone produces inadequate intubating conditions. Second, potential limitation was that we did not compare sevoflurane group with a muscle relaxant as some procedures were cochlear implant surgeries and others were short procedures precluding the use of a muscle relaxant. Finally, premedication may contribute to the quality of intubating conditions, and the results of the current study might be quite different in other unpremeditated children. However, all of our patients received the same premedication with oral midazolam; therefore, we do not consider the premedication to be a relevant factor of intubating conditions.

## Conclusion

Our results suggest that the administration of 3 mg/kg propofol preceded by 2 μg/kg fentanyl provides a higher proportion of excellent intubating conditions compared with 2 mg/kg propofol preceded by 2 μg/kg fentanyl during sevoflurane induction in healthy, premedicated children without muscle relaxants. We recommended the use of this regimen where tracheal intubation is necessary but muscle relaxing agents is undesirable.

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Nil.

### Conflicts of interest

There are no conflicts of interest.

## References


1. Blair JM, Hill DA, Wilson CM, Fee JP. Assessment of tracheal intubation in children after induction with propofol and different doses of remifentanil. Anaesthesia 2004;59:27-33.
2. Woods AW, Allam S. Tracheal intubation without the use of neuromuscular blocking agents. Br J Anaesth 2005;94:150-8.
3. Erhan E, Ugur G, Alper I, Gunusen I, Ozyar B. Tracheal intubation without muscle relaxants: Remifentanil or alfentanil in combination with propofol. Eur J Anaesthesiol 2003;20:37-43.
4. Inomata S, Watanabe S, Taguchi M, Okada M. End-tidal sevoflurane concentration for tracheal intubation and minimum alveolar concentration in pediatric patients. Anesthesiology 1994;80:93-6.
5. Inomata S, Nishikawa T. Determination of end-tidal sevoflurane concentration for tracheal intubation in children with the rapid method. Can J Anaesth 1996;43:806-11.
6. Aouad MT, Yazbeck-Karam VG, Mallat CE, Esso JJ, Siddik-Sayyid SM, Kaddoum RN. The effect of adjuvant drugs on the quality of tracheal intubation without muscle relaxants in children: A systematic review of randomized trials. Paediatr Anaesth 2012;22:616-26.
7. Blair JM, Hill DA, Bali IM, Fee JP. Tracheal intubating conditions after induction with sevoflurane 8% in children. A comparison with two intravenous techniques. Anaesthesia 2000;55:774-8.
8. Eikermann M, Hunkemöller I, Peine L, Armbruster W, Stegen B, Hüsing J, *et al*. Optimal rocuronium dose for intubation during inhalation induction with sevoflurane in children. Br J Anaesth 2002;89:277-81.
9. Oberer C, von Ungern-Sternberg BS, Frei FJ, Erb TO. Respiratory reflex responses of the larynx differ between sevoflurane and propofol in pediatric patients. Anesthesiology 2005;103:1142-8.
10. Lerman J, Sikich N, Kleinman S, Yentis S. The pharmacology of sevoflurane in infants and children. Anesthesiology 1994;80:814-24.
11. Vakkuri A, Yli-Hankala A, Särkelä M, Lindgren L, Mennander S, Korttila K, *et al*. Sevoflurane mask induction of anaesthesia is associated with epileptiform EEG in children. Acta Anaesthesiol Scand 2001;45:805-11.
12. Inomata S, Kihara S, Yaguchi Y, Baba Y, Kohda Y, Toyooka H. Reduction in standard MAC and MAC for intubation after clonidine premedication in children. Br J Anaesth 2000;85:700-4.
13. Swan HD, Crawford MW, Pua HL, Stephens D, Lerman J. Additive contribution of nitrous oxide to sevoflurane minimum alveolar concentration for tracheal intubation in children. Anesthesiology 1999;91:667-71.
14. Cagiran E, Eyigor C, Balcioglu T, Uyar M. Tracheal intubation in intellectually disabled patients: Clinical usefulness of remifentanil and sevoflurane without a muscle relaxant. J Int Med Res 2013;41:1632-8.
15. Katoh T, Nakajima Y, Moriwaki G, Kobayashi S, Suzuki A, Iwamoto T, *et al.* Sevoflurane requirements for tracheal intubation with and without fentanyl. Br J Anaesth 1999;82:561-5.
16. Kwak HJ, Kim JY, Min SK, Kim JS, Kim JY. Optimal bolus dose of alfentanil for successful tracheal intubation during sevoflurane induction with and without nitrous oxide in children. Br J Anaesth 2010;104:628-32.
17. Soulard A, Babre F, Bordes M, Meymat Y, Sztark F, Cros AM. Optimal dose of sufentanil in children for intubation after sevoflurane induction without neuromuscular block. Br J Anaesth 2009;102:680-5.
18. Lerman J, Houle TT, Matthews BT, Houck J, Burrows FA. Propofol for tracheal intubation in children anesthetized with sevoflurane: A dose-response study. Paediatr Anaesth 2009;19:218-24.
19. Viby-Mogensen J, Engbaek J, Eriksson LI, Gramstad L, Jensen E, Jensen FS, *et al*. Good clinical research practice (GCRP) in pharmacodynamic studies of neuromuscular blocking agents. Acta Anaesthesiol Scand 1996;40:59-74.
20. Politis GD, Frankland MJ, James RL, ReVille JF, Rieker MP, Petree BC. Factors associated with successful tracheal intubation of children with sevoflurane and no muscle relaxant. Anesth Analg 2002;95:615-20.
21. Devys JM, Mourissoux G, Donnette FX, Plat R, Schauvliège F, Le Bigot P, *et al.* Intubating conditions and adverse events during sevoflurane induction in infants. Br J Anaesth 2011;106:225-9.
22. Mencke T, Echternach M, Kleinschmidt S, Lux P, Barth V, Plinkert PK, *et al.* Laryngeal morbidity and quality of tracheal intubation: A randomized controlled trial. Anesthesiology 2003;98:1049-56.
23. Siddik-Sayyid SM, Taha SK, Aouad MT, Abdallah FW, Al Alami AA, Kanazi GE. Propofol 2 mg/kg is superior to propofol 1 mg/kg for tracheal intubation in children during sevoflurane induction. Acta Anaesthesiol Scand 2011;55:535-8.
24. Gupta A, Kaur R, Malhotra R, Kale S. Comparative evaluation of different doses of propofol preceded by fentanyl on intubating conditions and pressor response during tracheal intubation without muscle relaxants. Paediatr Anaesth 2006;16:399-405.
25. De Fátima De Assunção Braga A, Da Silva Braga FS, Potério GM, Filier PR, Cremonesi E. The effect of different doses of propofol on tracheal intubating conditions without muscle relaxant in children. Eur J Anaesthesiol 2001;18:384-8.
26. Simon L, Boucebci KJ, Orliaguet G, Aubineau JV, Devys JM, Dubousset AM. A survey of practice of tracheal intubation without muscle relaxant in paediatric patients. Paediatr Anaesth 2002;12:36-42.
27. Glen JB. Animal studies of the anaesthetic activity of ICI 35868. Br J Anaesth 1980;52:731-42.
28. Combes X, Andriamifidy L, Dufresne E, Suen P, Sauvat S, Scherrer E, *et al.* Comparison of two induction regimens using or not using muscle relaxant: Impact on postoperative upper airway discomfort. Br J Anaesth 2007;99:276-81.