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Optimal bolus dose of alfentanil for successful tracheal intubation during sevoflurane induction with and without nitrous oxide in children†

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Background. The goals of this study were to determine the effective bolus dose of alfentanil required for successful tracheal intubation during inhalation induction using sevoflurane 5% without neuromuscular block in children, and whether nitrous oxide reduces these doses.

Methods. Fifty paediatric patients, aged 3–10 yr, were randomly assigned to one of the two groups. Subjects received either sevoflurane 5% in oxygen 100% (O_2 group, n=25) or sevoflurane 5% in oxygen 40% and nitrous oxide 60% (N_2O group, n=25) through a face mask. One minute after inhalation induction, a predetermined dose of alfentanil was injected over 15 s. The alfentanil dose was determined using Dixon's up-and-down method, starting from alfentanil 14 μg kg^{-1}. The trachea was intubated 3 min after inducing anaesthesia.

Results. The ED_{50} [95% confidence interval (CI)] of alfentanil for successful tracheal intubation was 11.5 (9.9–13.1) and 8.6 (7.4–9.8) μg kg^{-1} in the O_2 and N_2O groups, respectively. The ED_{50} of the N_2O group was significantly lower than that of the O_2 group (P=0.0146). From isotonic regression, 50% effective dose (ED_{50}) (95% CI) of alfentanil in the O_2 and N_2O groups was 11.4 (9.9–13.0) and 6.5 (5.0–8.1) μg kg^{-1}, respectively.

Conclusions. The effective bolus dose of alfentanil for successful tracheal intubation was 11.5 μg kg^{-1} in 50% of children during inhalation induction using sevoflurane 5% without neuromuscular blocking agent. Addition of nitrous oxide 60% in oxygen reduced the effective alfentanil dose by 25%.

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Sevoflurane is frequently used for inhalation induction of anaesthesia and tracheal intubation in children without the use of neuromuscular blocking drugs.[1] During sevoflurane inhalation induction, the addition of an opioid has been shown to allow rapid tracheal intubation[2 3] and decrease the target cerebral concentration of sevoflurane needed to perform tracheal intubation in children,[4] and therefore reduces some side-effects associated with the use of high-concentration sevoflurane. Nitrous oxide also decreases the minimum alveolar concentration of halogenated anaesthetics, and Swan and colleagues[5] reported that nitrous oxide and sevoflurane suppress the responses to tracheal intubation in a linear and additive manner in children.

To date, there are no reports of the bolus dose of alfentanil for successful tracheal intubation during sevoflurane inhalation induction in paediatric patients. The purpose of this study was to determine the bolus dose of alfentanil to provide successful tracheal intubation during inhalation

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induction using sevoflurane 5% and oxygen 100% with or without nitrous oxide in the absence of neuromuscular blocking agent in children.

Methods

This study was approved by the institutional review board, and written informed consent for the study was obtained from the parents. Fifty children, ASA I or II, aged 3–10 yr, undergoing general anaesthesia for short elective surgery lasting <1 h were enrolled. Children with a history of reactive airway disease and a suspected difficult airway were excluded.

To prevent the possible delay in time to intubation, a 24 G cannula was inserted in the dorsum of the hand and a dextrose 5% in NaCl 0.2% solution was infused before arriving in the operating theatre. Once in the operating theatre, all subjects were monitored with ECG, pulse oximeter, and a non-invasive arterial pressure device. The end-tidal concentration of CO_2 and sevoflurane was measured continuously at the elbow of the breathing circuit using a precalibrated gas monitor (at a sampling flow rate of 250 ml min^{-1}). The subjects were randomized using a computer-generated sequence of random numbers and allocated to one of the two groups using a sequential sealed envelope technique. Subjects received either oxygen 100% (O_2 group, n=25) or oxygen 40% and nitrous oxide 60% (N_2O group, n=25) during induction. Glycopyrrolate 0.004 mg kg^{-1} was administered before inducing anaesthesia. According to their group, a semi-closed anaesthetic circuit was primed with sevoflurane 5% in oxygen 100%, or sevoflurane 5% in oxygen 40% and nitrous oxide 60% for 2 min. Inhalation induction was initiated via a face mask with a fresh gas flow rate of 5 litre min^{-1}. Initially, the subjects breathed spontaneously, and ventilation was assisted manually to maintain an end-tidal CO_2 of 4.25–4.79 kPa when they became apnoeic. One minute after beginning inhalation induction, a predetermined dose of alfentanil was injected over 15 s. Three minutes after the beginning of inhalation induction, the trachea was intubated with a cuffed tracheal tube.

The bolus dose of alfentanil for each subject was determined by the response of the previously tested subject using the up-and-down sequential allocation method of Dixon and Massey[6] (2 μg kg^{-1} as a step size). The first subject was tested at alfentanil 14 μg kg^{-1} in each group. If intubation failed, the alfentanil dose was increased by 2 μg kg^{-1}. If it was successful, it was then decreased by 2 μg kg^{-1}. The anaesthesiologist who performed and assessed the intubating conditions was unaware of the alfentanil dose and the use of N_2O. Blinding to the treatment group was assured by an opaque partition placed between anaesthetic machine and the observer. Intubation conditions were evaluated according to a scoring system described by Viby-Mogensen and colleagues[7] (Table 1). Successful intubation was defined as excellent or good intubating conditions. Rocuronium 0.3 mg kg^{-1} was administered in the case of unacceptable intubating conditions due to strong movement, inadequate jaw relaxation, closed vocal cords, or sustained coughing. Any evidence of chest wall rigidity, such as difficulty in ventilation, wheezing, changing compliance, or change in the slope of the end-tidal CO_2 waveform, was noted. Clinically significant hypotension or bradycardia, defined as >30% decrease in mean arterial pressure (MAP) or heart rate (HR) compared with baseline at anaesthetic induction, respectively, was treated with atropine or ephedrine as appropriate. MAP, HR, Sp_{O_2}, end-tidal CO_2, and sevoflurane concentrations were recorded at anaesthetic induction, and before and 1 min after intubation.

Table 1 Assessment of intubating conditions. Intubating conditions: Excellent, all criteria are excellent; Good, all criteria are either excellent or good; Poor, the presence of a single criterion listed under 'poor'

Variables	Intubating conditions		
	Acceptable		Unacceptable
	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	Diaphragm	Sustained (>10 s)
Movement of the limbs	None	Slight	Vigorous

Statistical analyses

Statistical analyses were performed using SAS 9.1 for Windows (SAS Institute Inc., Cary, NC, USA). Data are expressed as mean (SD) or number of subjects. The 50% effective dose (ED_{50}) of alfentanil was defined as the alfentanil dose at which there was a 50% probability of successful tracheal intubation. The up-and-down sequences were analysed using the formula reported by Dixon and Massey,[6] which enabled the ED_{50} to be calculated with a 95% confidence interval (CI). Data were also subjected to isotonic regression estimators for calculating the ED_{50} and ED_{95} and the 95% CI in each group. An adjusted response probability was easily calculated by the pooled-adjacent-violators algorithm (PAVA) and the CI was estimated by a bootstrapping approach.[8] The subject characteristics and induction profiles were compared using Student's t-test. Changes in haemodynamic data were compared by repeated-measures ANOVA. A P-value of <0.05 was considered significant. The sample size was calculated based on the assumed standard deviation of the alfentanil dose from a previous study.[9] Twenty-four patients were required in each group to detect a mean difference of alfentanil 2 μg kg^{-1} between the groups at a power of 0.9 and a P-value of 0.05. The sample size was increased to 50 patients to allow for dropouts.

Results

A total of 48 subjects completed the study; one from each group showed severe excitation during induction and were excluded from the statistical analyses (Fig. 1).