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PAEDIATRICS

Optimal dose of sufentanil in children for intubation after sevoflurane induction without neuromuscular block

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Background. We studied 63 ASA I children (age 2–8 yr) to determine the sufentanil dose needed to facilitate intubation under excellent conditions after inhalation induction with various end-tidal concentrations of sevoflurane without neuromuscular block.

Methods. Subjects were allocated randomly to receive sevoflurane end-tidal concentrations (F'_{sevo}) of 2.5%, 3%, or 3.5%. Anaesthesia was induced with sevoflurane 6% without nitrous oxide for 2 min, and then inspired sevoflurane concentration was adjusted to keep F'_{sevo} at 2.5%, 3%, or 3.5% according to the group. Subjects received i.v. sufentanil according to an 'up and down' design. Tracheal intubation by direct laryngoscopy was performed 6 min after sufentanil injection. Intubation was considered successful, if intubation conditions were excellent as determined by the laryngoscopist.

Results. The ED_{50} [effective dose for 50% of subjects; mean (SD)] of sufentanil required for excellent intubation conditions was 0.6 (0.12), 0.32 (0.10), or 0.11 (0.07) μg kg^{-1} for F'_{sevo} of 2.5%, 3%, or 3.5%, respectively. Using logistic analysis, the 95% effective dose (ED_{95}) of sufentanil was 1.02 [95% confidence intervals (CI) 0.31–1.74] μg kg^{-1}, 0.58 (95% CI 0.17–0.99) μg kg^{-1}, or 0.28 (95% CI 0.04–0.52) μg kg^{-1} for F'_{sevo} of 2.5%, 3%, or 3.5%, respectively.

Conclusions. Excellent intubation conditions could be obtained in children after inhalation induction with low sevoflurane concentrations and adjuvant sufentanil.

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Tracheal intubation after induction with sevoflurane without opioid or neuromuscular blocking drugs is routinely used in children.[1] When administered in a sufficient concentration for a long enough period, sevoflurane can produce relaxation of mandibular and laryngeal muscles to allow for laryngoscopy and intubation with good conditions without the use of a neuromuscular blocking agent.[2] The use of nitrous oxide 66% during inhalation induction decreases the concentration of sevoflurane needed to perform tracheal intubation by 40%.[3] Co-administration of remifentanil provides good-to-excellent intubating conditions 3 min after sevoflurane induction in children.[4 5]

In adults, opioids decrease the alveolar sevoflurane concentration needed to perform tracheal intubation with good or excellent conditions.[6 7] Increasing the sufentanil dose from 0.15 to 0.30 μg kg^{-1} improved the quality of intubation conditions without significant cardiovascular depression after induction with sevoflurane.[8] However, to our knowledge, there is no study investigating the optimal dose of sufentanil for tracheal intubation after inhalation induction with sevoflurane in paediatric patients. The purpose of this study was to determine the optimal dose of sufentanil required to provide excellent intubating conditions in children after sevoflurane inhalation induction at various alveolar sevoflurane concentrations.

Methods

After obtaining ethics committee approval and written informed consent from the parents, ASA I children, aged

2–8 yr, undergoing elective surgery requiring general anaesthesia were included. Exclusion criteria included disposition for malignant hyperthermia, potentially full stomach, obesity, predictive signs of difficult intubation, and history of neurological, cardiac or pulmonary disease, and hepatic or renal insufficiency.

Children were randomly assigned to receive an end-tidal sevoflurane concentration (E'_{sevo}) of 2.5% (Group 2.5%), 3% (Group 3%), or 3.5% (Group 3.5%). The anaesthesiologist who performed and rated the intubation was blinded to the sufentanil dose and the E'_{sevo} concentration. Children were premedicated with midazolam 0.3 μg kg^{-1} given orally or rectally 1 h before operation. In the operating theatre, routine non-invasive monitoring of arterial pressure, ECG, and pulse oximetry were initiated. Expired concentrations of sevoflurane, carbon dioxide (CO_2), and oxygen were measured continuously using the gas analyzer (Andros 4800®, Richmond, CA, USA) of the anaesthesia workstation (Felix®, Taema, Antony, France). After pre-oxygenation, inhalation induction was initiated via a facemask with sevoflurane 6% in oxygen without nitrous oxide with a fresh gas flow of 6 litre min^{-1}. Initially, subjects breathed spontaneously and volume-controlled ventilation was started when they became apnoeic. The tidal volume was set at 10 ml kg^{-1} to compensate for mask dead space. After loss of consciousness, the inspired sevoflurane concentration was adjusted to maintain E'_{sevo} at 2.5%, 3%, or 3.5% according to the randomization, at least 10 min before intubation to allow equilibration. Ventilatory frequency was adjusted to maintain E'_{CO_2} between 4.0 and 4.7 kPa. An i.v. line was established when pupils were in the central position, and then sufentanil was injected. Six minutes afterwards, tracheal intubation was performed with a cuffed tracheal tube.[9]

The modified Dixon's 'up-and-down' method was used to determine the sufentanil ED_{50}.[10] The response of the preceding patient determined the dose of sufentanil given to the succeeding patient in each group. The initial sufentanil doses were 0.6, 0.5, or 0.3 μg kg^{-1} in Groups 2.5%, 3%, and 3.5%, respectively. If intubation failed, the sufentanil dose for the next patient was increased by 0.1 μg kg^{-1} in Groups 2.5% and 3% and by 0.05 μg kg^{-1} in Group 3.5%. If intubation was successful, the sufentanil dose was decreased by the same amount. The quality of intubation was evaluated according to the Viby-Mogensen score (Table 1).[11] Successful intubation was defined as excellent intubating conditions, that is, all criteria were excellent. If intubation failed because of closed vocal cords, movement, or inadequate jaw relaxation, anaesthesia was deepened with i.v. propofol 1 mg kg^{-1}. Children were included until six independent pairs of consecutive subjects in which a success score followed a failure score were obtained in each group, according to Paul and Fisher.[12]

Heart rate (HR) and mean arterial pressure (MAP) were measured and recorded at the following times: just before sufentanil injection, 2 and 4 min after sufentanil injection, just before the laryngoscopy, and just after intubation.

Table 1 Assessment of intubation conditions. Excellent: all criteria are excellent. Good: all criteria are either excellent or good. Poor: presence of a single criterion listed under 'Poor'

Variables	Acceptable		Unacceptable
	Excellent	Good	Poor
Jaw relaxation	Relaxed	Not fully	Poor
Vocal cord position	Abducted	Intermediate	Closed
Vocal cord movement	None	Moving	Closing
Coughing	None	Slight	Sustained
Limb movement	None	Slight	Vigorous

Sufentanil ED_{50} enabling successful tracheal intubation was determined in each group by calculating the mean midpoint dose of six independent pairs of patients who manifested crossover from success to failure. Data were also analysed using a logistic model to calculate the sufentanil dose required to enable successful intubation in 50% and 95% (ED_{95}) of subjects.[13] ED_{95} values were calculated directly from the best-fitting logistic curves.

One-way analysis of variance and χ^2 test were used to compare patient characteristic and anaesthetic data between the groups. MAP and HR means during induction were calculated after the first crossover in each group. Mean HR and MAP variations within the groups were compared by paired Student's *t*-test. *P*-values of <0.05 were considered statistically significant. Values are expressed as mean [standard deviation (SD)] or mean [95% confidence interval (CI)] as appropriate.

Results

Sixty-three children [mean age 3.9 (1.7) yr] were enrolled in this study (Fig. 1). Groups were similar regarding other patient characteristics (Table 2).

Sufentanil ED_{50} values were 0.6 (0.12) μg kg^{-1} in Group 2.5%, 0.32 (0.10) μg kg^{-1} in Group 3%, and 0.11 (0.07) μg kg^{-1} in Group 3.5%. Dose–response data for each subject obtained by the up-and-down method are shown in Figure 2.

Sufentanil ED_{50} and ED_{95} values obtained from logistic analysis were 0.57 (95% CI 0.41–0.73) and 1.02 (95% CI 0.31–1.74) μg kg^{-1} in Group 2.5%, 0.28 (95% CI 0.16–0.39) and 0.58 (95% CI 0.17–0.99) μg kg^{-1} in Group 3%, and 0.09 (95% CI 0.02–0.16) and 0.28 (95% CI 0.04–0.52) μg kg^{-1} in Group 3.5%.

Increasing E'_{sevo} significantly decreased sufentanil ED_{50} (Fig. 3). In Group 3.5%, sufentanil ED_{50} was very low, two patients having excellent intubation conditions with sufentanil 0.05 μg kg^{-1} (Fig. 2).

Intubation conditions are shown in Table 3. They were excellent in 57% and clinically acceptable (good or excellent) in 77% of subjects. The jaw was fully relaxed in every patient during laryngoscopy. No subject experienced