Single-breath Vital Capacity Rapid Inhalation Induction in Children
8% Sevoflurane versus 5% Halothane


Background: The authors compared the speed of induction of anesthesia with sevoflurane with and without nitrous oxide with the speed of halothane and nitrous oxide using a single-breath vital capacity induction.

Methods: With informed parental consent, 51 healthy unpremedicated children aged 5–12 yr were randomized to inhale a single breath of one of three gas mixtures: 8% sevoflurane in 66% nitrous oxide, 8% sevoflurane in oxygen, or 5% halothane in 66% nitrous oxide. A blinded observer recorded the times to loss of the eyelash reflex, return of conjunctive gaze, the presence of airway reflex responses, involuntary movement, and hemodynamic responses.

Results: Forty-two children completed the study. The times (mean ± SD) to loss of the eyelash reflex with sevoflurane/nitrous oxide, 38 ± 8 s, and for sevoflurane–oxygen, 34 ± 12 s, were less than that with halothane–nitrous oxide, 58 ± 17 s (P < 0.01). Movement occurred less frequently during sevoflurane than during halothane anesthesia (P < 0.05). The times to return of conjunctive gaze and the incidence of airway reflex responses were similar among the groups. The incidence of dysrhythmias in the sevoflurane groups was less than that in the halothane group (P < 0.01).

Conclusions: Induction of anesthesia with a single breath of 8% sevoflurane with or without 66% nitrous oxide is more rapid than with 5% inspired halothane with 66% nitrous oxide in children. The incidence of movement and dysrhythmias during a single-breath induction with sevoflurane are less than they are with halothane. (Key words: Dysrhythmias; nitrous oxide; pediatrics.)

SINGLE-BREATH vital capacity inhalation induction techniques were first introduced by Bourne in 1954 but have never featured prominently in pediatric anesthesia practice. Recently this induction technique has received renewed interest with the introduction of sevoflurane into clinical practice. Single-breath inductions offer several advantages over the traditional stepwise incremental increases in the inspired concentration, including a more rapid induction of anesthesia and a decreased incidence of excitatory phenomena. Studies in children and adults have shown that high inspired concentrations of sevoflurane are well tolerated, that sevoflurane does not elicit airway reflex responses, and that sevoflurane induces anesthesia more rapidly than halothane. However, single-breath inductions with 8% sevoflurane in children have not been compared to similar inductions with 5% halothane. Accordingly, we designed the following randomized, prospective, double-blinded study in children aged 5–12 yr to compare the rate and quality of induction of anesthesia using a single-breath vital capacity inhalation induction with 8% sevoflurane with or without 66% nitrous oxide with induction with 5% halothane in 66% nitrous oxide.

Methods

After ethics committee approval, informed written consent from the parents and assent from children aged 7yr or older were obtained from 51 healthy children (age, 5–12 yr) who were fasted and scheduled for elective surgery under general anesthesia. Children were excluded from participation in the study if there was a history of significant cardiorespiratory, renal, or hepatic dysfunction, concurrent treatment with any medication known to affect myocardial performance or respiratory function, or malignant hyperthermia; if their weight exceeded 150% of the ideal; if their tympanic temperature exceeded 38°C on the day of surgery; or if they received
premedication. Children were assigned by random allocation using random-number tables to receive one of three regimens: 8% sevoflurane in 66% nitrous oxide, 8% sevoflurane in oxygen, or 5% halothane in 66% nitrous oxide.

On the day of surgery, one of the investigators showed each child how to perform vital capacity breathing: each child was instructed to inhale as deeply as possible and then to exhale maximally, at which time a face mask (without a circuit) was applied tightly to the face. The child was then instructed to inhale maximally for a second time, but this time to hold his or her breath for as long as possible. Instructions and "practice" single-breath vital capacity breaths were repeated before operation until each child had mastered the technique. A practice single-breath vital capacity induction was repeated on arrival in the operating room with a complete anesthetic circuit that had been flushed with air alone.

A blood pressure cuff, electrocardiogram pads, and pulse oximetry were administered before induction of anesthesia. Anesthesia was administered via an unscented face mask and a Jackson-Rees' modification of Ayre's T-piece that included a 2-1 reservoir bag. The circuit was primed with the designated anesthetic gas mixture, and a 5–8 l/min fresh gas flow was used. Sevoflurane was delivered via a sevotec 5 vaporizer (Ohmeda, Madison, WI) and halothane was delivered via a Fluotec 4 vaporizer (Ohmeda). The concentrations of anesthetics in the circuit were equilibrated to their target concentrations before the mask was applied to the face and were analyzed using a calibrated Datex Capnomac Ultima (Helsinki, Finland). A 20-gauge plastic cannula (Angiocath™, Becton Dickinson, Sandy, UT) was inserted into the sampling port of the elbow connector of the anesthetic circuit to sample inspired and expired gases continuously to determine when breathing resumed. No other medications were administered during this study. Loss of the eyelash reflex was assessed by gentle brushing of the eyelashes of one eyelid with a finger every 5 s after induction of anesthesia began. Unless airway obstruction or laryngospasm developed after release of the breathhold, children breathed spontaneously without assistance throughout the rest of the study with the same fresh gas flow rate and anesthetic gas composition.

The concentrations of sevoflurane, halothane, and nitrous oxide were recorded after the circuit was primed but before the face mask was applied to the face. The duration of the vital capacity breathhold and the times to loss of the eyelash reflex, return of regular respirations, and return of conjugate gaze were recorded. Respirations were considered regular when apnea and breathholding had ceased and the respiratory pattern was rhythmic. All time intervals were referenced to the beginning of the vital capacity breathhold as time zero. All airway reflex responses and any other complications were graded by a single observer who was present throughout the induction but who was blinded to the treatment assignment. Blinding was assured by isolating the observer from the anesthetic equipment and monitors using an opaque partition. Heart rate and systolic and diastolic blood pressures were recorded immediately before induction of anesthesia, at loss of the eyelash reflex, and at return of conjugate gaze. The minimum pulse oximetry and the type and duration of cardiac dysrhythmias during the study were recorded. The study concluded when conjugate gaze had returned.

Before leaving the recovery area, each child was asked whether the anesthetic gas had an odor and, if it did, whether the odor was good, bad, or did they did not know and whether they would like the same anesthetic induction for a future anesthetic.

Statistics
Sample size was based on an two-tailed alpha value of 0.05, β of 0.2, a 20-s difference in the time to loss of the eyelash reflex between sevoflurane and halothane, and a standard deviation (SD) of 16 s. This yielded 11 children per group. To account for the possibility of a smaller difference in the time to loss of the eyelash reflex between groups, of greater variances in the data, and of possible dropouts, 17 children were enrolled in each group.

Data are reported as mean ± SD unless stated otherwise. Continuous data, including the duration of the vital capacity breath, times to loss of the eyelash reflex, return of the conjugate gaze, and the inspired and expired gas concentrations were analyzed using one-way analysis of variance and the Newman-Keuls multiple-comparison test for intergroup differences. Repeated continuous data, including heart rate and blood pressure, were analyzed using repeated-measures analysis of variance and the Dunnett multiple comparisons test for intragroup differences. Nominal data, including the incidence of excitatory and airway reflex responses and the incidence of dysrhythmias, were analyzed using chi-square analysis and Fisher's exact test. $P < 0.05$ was accepted as significant.

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SINGLE BREATH INDUCTIONS WITH SEVOFLURANE

Table 1. Induction Characteristics and Evaluation

<table>
<thead>
<tr>
<th></th>
<th>Sevoflurane and Nitrous Oxide (n = 12)</th>
<th>Sevoflurane and Oxygen (n = 16)</th>
<th>Halothane and Nitrous Oxide (n = 14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of vital capacity breathhold (s)</td>
<td>23 ± 12</td>
<td>19 ± 10</td>
<td>20 ± 12</td>
</tr>
<tr>
<td>Time to loss of the eyelash reflex (s)</td>
<td>38 ± 8*</td>
<td>34 ± 12*</td>
<td>58 ± 17</td>
</tr>
<tr>
<td>Time to normal tidal breathing (s)</td>
<td>38 ± 12</td>
<td>44 ± 15</td>
<td>50 ± 20</td>
</tr>
<tr>
<td>Time to return of conjugate gaze (s)</td>
<td>118 ± 29</td>
<td>124 ± 22</td>
<td>120 ± 35</td>
</tr>
<tr>
<td>Severity of movement during induction</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>6 (51%)</td>
<td>7 (44%)</td>
<td>6 (43%)</td>
</tr>
<tr>
<td>Nonpurposeful</td>
<td>4 (33%)</td>
<td>7 (44%)</td>
<td>2 (14%)</td>
</tr>
<tr>
<td>Purposeful and/or required restraint</td>
<td>2 (16%)*</td>
<td>2 (12%)*</td>
<td>6 (43%)</td>
</tr>
<tr>
<td>How was the smell of the anesthetic?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Good</td>
<td>1 (8%)</td>
<td>3 (19%)</td>
<td>2 (14%)</td>
</tr>
<tr>
<td>Bad</td>
<td>5 (42%)</td>
<td>7 (44%)</td>
<td>7 (50%)</td>
</tr>
<tr>
<td>Neither</td>
<td>6 (50%)</td>
<td>6 (38%)</td>
<td>5 (36%)</td>
</tr>
<tr>
<td>Would you want the same technique to go to sleep again?</td>
<td>8 (67%)</td>
<td>12 (75%)</td>
<td>8 (57%)</td>
</tr>
<tr>
<td>Yes</td>
<td>4 (33%)</td>
<td>4 (25%)</td>
<td>6 (43%)</td>
</tr>
</tbody>
</table>

Data are means ± SD except where numbers of children (%).

* P < 0.01 versus halothane and nitrous oxide.
† P < 0.05 versus halothane and nitrous oxide.

Results

Of the 51 children enrolled in the study, nine (mean age, 6.8 ± 2.6 yr) did not complete the single breath induction properly and were deleted from the analysis. These nine children released their breasts and resumed respiration almost immediately after taking their breasts. None of the children who released breath rejected the mask or the anesthetic because of its odor. Of the nine children who failed to complete the breathhold, four were in the sevoflurane/nitrous oxide group, two in the sevoflurane-oxygen group, and three in halothane-nitrous oxide group. The remaining 42 children were distributed as follows: sevoflurane-nitrous oxide, n = 12; sevoflurane-oxygen, n = 16; and halothane-nitrous oxide, n = 14.

The ages (mean ± SD) of the children in the three groups were similar: sevoflurane-nitrous oxide, 8.7 ± 1.7 yr; sevoflurane-oxygen, 8.2 ± 2.3 yr; and halothane-nitrous oxide, 8.2 ± 2 yr. The weights of the children were similar: 26.3 ± 5.5 kg, 28.7 ± 10.5 kg, and 28.1 ± 7.3 kg, respectively. The ratios of boys to girls in the three groups were also similar: 9:3, 6:10, and 10:4, respectively.

Before application of the face mask, the concentration of sevoflurane in the circuit in the sevoflurane-nitrous oxide group (7.5 ± 0.3%) was significantly less than that in the sevoflurane-oxygen group (8.0 ± 0.3%, P < 0.001). The initial concentration of halothane in the halothane-nitrous oxide group was 4.5 ± 0.2%.

The duration of the vital capacity breathhold was similar among the three groups (table 1). The times to loss of the eyelash reflex in the sevoflurane groups were 20–24 s less than that in the halothane group (table 1). The times to return of conjugate gaze were similar among the three groups (table 1). Purposeful movement and movement that required restraint in the sevoflurane groups occurred less frequently than such movement in the halothane-nitrous oxide group (table 1). Although the incidence of nonpurposeful movement among the three groups did not differ significantly, the power to detect a difference with these small sample sizes was <30%. A sample size of 88 children per group would have been required to reach a significant difference between the two sevoflurane groups and the halothane group, and 325 children per group would have been required to reach a similar difference between the two sevoflurane groups. Subjective assessments of the smell of the anesthetic by the children and their willingness to receive the same induction technique again were similar among the three groups (table 1).

The incidence of moderate laryngospasm (positive pressure ventilation was required) was similar among the three groups: sevoflurane-nitrous oxide, 1 in 12...
Heart Rate

![Graph showing heart rate changes](image)

Fig. 1. Heart rate (mean ± SD) was measured before induction of anesthesia (baseline), at the time of loss of the eyelash reflex, and at the time of return of conjugate gaze in the three treatment groups: sevoflurane in 100% oxygen, sevoflurane in 66% nitrous oxide, and halothane in 66% nitrous oxide. Compared with the baseline value, heart rate increased only at the time of return of conjugate gaze in the sevoflurane-oxygen group (P < 0.01).

(8%); sevoflurane–oxygen, 3 in 16 (19%); and halothane–nitrous oxide, 2 in 14 (14%). One child in each group coughed during the induction. Pulse oximetry remained ≥94% throughout the study period in all of the children. Salivation occurred in children in all groups (sevoflurane–nitrous oxide, 3 in 12 [29%]; sevoflurane–oxygen, 3 in 16 [19%]; halothane–nitrous oxide, 4 in 14 [29%]), although none required suctioning.

Heart rate and blood pressure recorded immediately before induction of anesthesia (baseline), at loss of the eyelash reflex, and at return of conjugate gaze are presented in figures 1 and 2. The incidence of dysrhythmias in the sevoflurane groups combined (0 of 26 children or 0%) was significantly less than that in the halothane–nitrous oxide group (5 of 14 children or 36%; P < 0.01). One episode of bigeminy in the halothane–nitrous oxide group began 20 s after the start of induction, coincident with the onset of nonpurposeful movement that required restraint. The bigeminy reverted spontaneously to sinus rhythm 30 s later without hemodynamic sequelae. The remaining four episodes were hemodynamically insignificant nodal rhythms that began 110–240 s after induction of anesthesia and also resolved spontaneously within 90–360 s, respectively.

Discussion

In this study, we compared the rate and quality of a single-breath vital capacity inhalation induction with sevoflurane to that with halothane. The rate of induction measured by the time to loss of the eyelash reflex with sevoflurane with or without nitrous oxide was more rapid than with halothane, although the absolute differences were small at 20–24 s. The quality of the inductions were similar, with differences only in the incidence of movement.

The times to loss of the eyelash reflex with sevoflurane are similar to that reported with 7.5% sevoflurane in 66% nitrous oxide using a single-breath rapid inhalation induction in adults, at 41 ± 16 s7 and similar to the times to induction of anesthesia with 8% sevoflurane and spontaneous ventilation in children.13,14 The time to loss of the eyelash reflex with 5% halothane in 66% nitrous oxide in the current study is consistent with unpublished data in children. These results confirm our clinical impression that the time to induction of anesthesia with a single-breath vital capacity inhalation induction with 8% sevoflurane in children is rapid and, based on the results of this study, more rapid than it is with 5% halothane.

We postulated several mechanisms to explain the

Systemic Blood Pressure

![Graph showing blood pressure changes](image)

Fig. 2. Systolic and diastolic systemic blood pressures (mean ± SD) were measured before induction of anesthesia (baseline), at the time of loss of the eyelash reflex, and at the time of return of conjugate gaze in the three treatment groups: sevoflurane in 100% oxygen, sevoflurane in 66% nitrous oxide, and halothane in 66% nitrous oxide. Compared with the baseline values, systolic blood pressure decreased at the time of return of conjugate gaze in the sevoflurane–oxygen ("P < 0.01) and sevoflurane–nitrous oxide groups ("P < 0.05) and at both loss of the eyelash reflex and conjugate gaze in the halothane–nitrous oxide group ("P < 0.01). Compared with baseline values, diastolic blood pressure decreased at the time of return of conjugate gaze in the halothane–nitrous oxide group ("P < 0.05).
more rapid induction of anesthesia with sevoflurane than with halothane. First, the minimum alveolar concentration equivalents during a single breath wash-in of 8% sevoflurane in children may exceed those of halothane at corresponding times.\textsuperscript{9-11} Second, the difference in the wash-in between sevoflurane and halothane in children may exceed that reported in adults,\textsuperscript{15} thereby speeding the rate of equilibration of sevoflurane in the alveoli of children compared with halothane. Until the pharmacokinetic wash-in curves of sevoflurane in children have been elucidated, we cannot fully account for this effect. Third, the performance of the Sevotec 5 vaporizer may be superior to that of the Fluotec 4 vaporizer. However, we found no evidence to support this third postulate.

We were surprised that the addition of nitrous oxide to sevoflurane did not speed induction of anesthesia with the single-breath induction technique, as was shown previously with 5% halothane in children (unpublished data). We speculate that nitrous oxide exerts two opposing effects on the rate of induction of anesthesia. On the one hand, nitrous oxide may speed the rate of induction of anesthesia by the concentration effect,\textsuperscript{10} by decreasing the minimum alveolar concentration of inhalational anesthetics\textsuperscript{17} (although this effect may be attenuated with sevoflurane in children\textsuperscript{9}) and by attenuating the incidence of airway reflex responses during inhalation of a high inspired concentration of sevoflurane. However, published studies have not established a relation between the addition of nitrous oxide during a sevoflurane induction and the incidence of airway reflex responses.\textsuperscript{9,10} On the other hand, nitrous oxide may slow the induction of anesthesia as it decreases the maximum inspired sevoflurane concentration that is deliverable. This results in part from the fact that nitrous oxide dissolves in the liquid anesthetic in the vaporizer, in this case sevoflurane.\textsuperscript{18,19} On balance, 66% nitrous oxide seems to exert little or no demonstrable clinical effect on the rate of induction of anesthesia with sevoflurane when a vital capacity rapid inhalational induction is performed. Further studies are warranted to confirm these preliminary observations.

Administration of a single breath of a high inspired concentration of inhaled anesthetic is widely regarded as a greater trigger of airway reflex responses than slow stepwise gradual increases in inspired concentrations. In this study, we introduced the maximum inspired concentrations of sevoflurane and halothane that the current vaporizers can deliver into naive airways and elicited only a small incidence of airway reflex responses. These results suggest that the widespread practice of slowly increasing the inspired concentration of halothane to minimize airway reflex responses may not be justified.

A single-breath vital capacity induction requires a cooperative child who will exhale maximally, accept a tight-fitting mask to the face, and inhale a single vital capacity breath and then hold that breath for as long as possible. This is not a simple sequence for a young child to follow, as indicated by the 20% failure rate in our cohort. It has been suggested that the level of cooperation necessary to perform a single-breath vital capacity induction might preclude use of this technique in the young.\textsuperscript{2} We enrolled children as young as 5 yr because it was our experience that these children could learn to perform this single-breath induction. Although most children older than 6 yr cooperated and performed the single-breath vital capacity induction after appropriate instruction, this technique remains a challenge, particularly for young children. For those who cannot perform a vital capacity breath, administering high inspired concentrations of inhaled anesthetics while the children breathe spontaneously may be an effective alternative.\textsuperscript{14}

Cost continues to limit the use of sevoflurane in many institutions. However, cost should not encumber the use of this anesthetic as an induction agent. Based on an hourly acquisition cost of $35 for sevoflurane and $1 for halothane both at fresh gas flows of 6 l/min and 1 minimum alveolar concentration, the cost of a 1-min flush of an Ayre's t piece circuit and a 2-min induction with sevoflurane is approximately $1.75 and with halothane it is $0.20. These costs compare favorably with the cost of an intravenous induction with sodium thiopental in a 25-kg child of $0.88, but they are one half of less of the cost an intravenous induction with propofol, at $3.33. These costs confirm that a single-breath vital capacity induction with sevoflurane is inexpensive and fiscally competitive with other induction techniques.

In conclusion, when a single-breath vital capacity induction is performed in children with 8% sevoflurane, with or without 66% nitrous oxide, loss of the eyelash reflex is more rapid and the incidence of movement and dysrhythmias is less frequent with sevoflurane than with 5% halothane in 66% nitrous oxide.

References


