Sevoflurane Consumption During Inhalational Induction in Children: A Randomized Comparison of Minute Ventilation-Based Techniques With Standard Fixed Fresh Gas Flow Technique

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This study was done to ascertain the optimum fresh gas flow (FGF) offering the best balance between rapid induction and minimal waste in pediatric patients. Forty-five children (weighing 10-20 kg) undergoing elective procedures under general anesthesia were randomly assigned into 3 groups: 0.5 minute ventilation (MV), MV, and S (FGF = 6 L/min). After priming the pediatric closed circuit, anesthesia was induced using a face mask with 8% sevoflurane in 100% oxygen (Draeger Primus Vista 120 anesthesia machine) at FGF-determined MV per group allocation. After loss of eyelash reflex (time 1 [T1]), intravenous cannulation (T2) and laryngeal mask airway (LMA) placement (T3) were done. Total sevoflurane consumed during induction (measured using logbook function) was the primary outcome. The cost of sevoflurane, any reflex movement, tachycardia (heart rate change > 20%), or additional propofol boluses required were also recorded. Sevoflurane consumption (3.8 vs 5.8 vs 9.2 mL) and cost of sevoflurane (104.2 vs 199.4 vs 312.8 rupees) were lowest in group 0.5 MV (P < .001). There was no difference in hemodynamic parameters, movement on cannulation/LMA insertion, and rescue propofol boluses required. For pediatric sevoflurane induction, half the MV-based FGF provided similar anesthetic conditions for LMA insertion with minimum sevoflurane consumption.

Keywords: Children, fresh gas flow, inhalation induction, sevoflurane consumption.

Sevoflurane is widely used for painless, rapid inhalational induction of anesthesia in children.1 The technique commonly used in children involves delivery of sevoflurane at the maximum vaporizer dial setting (8%) and a high fresh gas flow rate (4-8 L/min) via a rebreathing system until the patient loses consciousness.2,3 Following the loss of consciousness, the sevoflurane concentration is titrated to maintain anesthesia.

The rationale for using the highest dial setting of sevoflurane is to achieve sufficient alveolar concentration for unconsciousness as early as possible. However, there is no recommendation regarding the fresh gas flow (FGF) that should be used during induction in children. A high FGF reduces the time required to achieve the desired sevoflurane concentration in the circuit-patient system. However, high FGF leads to waste of anesthetic gases, making it uneconomical4 and leading to environmental pollution.5 On the other hand, if the FGF is too low, the time taken to achieve desired inhalational agent concentration in the system would be too long, thus reducing operating room turnover and increasing the stress of induction on the child.

The rate of delivery of an anesthetic agent to the lungs depends on the minute alveolar ventilation.6 Thus, if we can tailor the FGF during induction to the patient’s minute ventilation (MV), we can achieve the desired balance between rapid induction and minimal waste. This study has been designed to ascertain the MV-based FGF that offers the best balance between rapid induction and minimal waste in pediatric patients.

Methods
This parallel, randomized controlled trial was registered with the Clinical Trials Registry–India (registration No. CTRI/2016/12/007608) before the recruitment of the first patient. The study period was January 1, 2017, through April 30, 2017. After informed parental consent and ethics committee approval, 45 children weighing 10 to 20 kg, scheduled to undergo superficial procedures under general anesthesia with LMA, were randomly divided into 3 groups, as explained later in this section: MV, 0.5 MV, and S. All the children underwent preanesthetic evaluation for systemic illness, recent upper respiratory tract infection, and any important family history. Patients were excluded from the study if they had substantial cardiovascular, neurologic, pulmonary, or genetic disorders; anticipated difficult airway (high arched palate, retrognathia, micrognathia, short neck, malar hypoplasia, adenotonsillar hypertrophy, oral swellings, or growths in head and
neck area); history of upper respiratory tract infection in the previous 2 weeks; anticipated difficult intravenous (IV) access; and known allergy to anesthetic agents.

Standard fasting guidelines were followed before the patient was taken to the operating room. Oral midazolam, 0.25 mg/kg, was administered to each child 30 minutes before being wheeled inside the operating room. Computer-generated random numbers were maintained in sequentially numbered sealed envelopes to randomly assign the children into 3 groups. The anesthesiologist who was not involved in the trial any further handed over the envelope to the anesthesiologist conducting the case. Both the patient and the outcomes assessor were blinded to the group allocation. An anesthesia machine with integrated hemodynamic and gas monitoring system (Draeger Primus Vista 120, Draeger Inc) was used in all cases.

**Anesthesia Procedures.** Before the induction, the pediatric closed circuit with a 1-L reservoir bag was flushed of any residual anesthetic gases. Thereafter, the circuit was primed with 8% sevoflurane in 100% oxygen (O2) at 6 L/min for 30 seconds, the Y piece connected to the endotracheal tube was occluded, and the adjustable pressure-limiting valve was set at 10 cm H2O. The MV was calculated for each patient based on his or her weight using the Radford nomogram. The anesthesia induction was then started via face mask with 8% sevoflurane in 100% O2 at FGF according to group allocation as follows: FGF = MV in group MV; FGF = half the MV in group 0.5 MV, and FGF = 6 L/min in group S.

The time of application of the face mask onto the child’s face was taken as time zero (T0). Once the child was calm, the electrocardiogram leads, pulse oximeter probe, and noninvasive blood pressure cuff were attached. The anesthesiologist checked the eyelash reflex every 5 seconds by gentle brushing of the eyelashes of one eyelid with his finger. After the loss of eyelash reflex, the sevoflurane vaporizer dial setting was reduced to 5%. The inspired and end-tidal sevoflurane concentrations, the minimum alveolar concentration (MAC) of sevoflurane, and the end-tidal carbon dioxide concentration were measured with a multigas analyzer. The anesthesiologist ensured an adequate depth of anesthesia.

**Figure 1. CONSORT Flow Diagram**

Abbreviations: CONSORT, Consolidated Standards of Reporting Trials; FGF, fresh gas flow; mV or MV, minute ventilation; S, standard fresh gas flow at 6 L/min.
in each child before attempting IV cannulation (loss of limb muscle tone) and LMA placement (regular respiration, jaw relaxation, and trapezius squeezing test). Any coughing, movement, or tachycardia (heart rate rise by > 20% compared with before LMA insertion) during LMA insertion was noted. In case of any movement during attempted LMA insertion, a rescue bolus injection of propofol bolus of 1 mL/kg was administered.

After induction, the sevoflurane was switched off, isoflurane was started, and other drugs were administered according to requirements of the surgery. The total amount of sevoflurane consumed in milliliters during induction was recorded from the “logbook” function of the anesthesia machine at the end of the anesthetic by setting the ventilator to standby mode.

An independent assistant recorded the T1 (time from T0 to loss of eyelash reflex), T2 (time from T0 to IV cannula insertion), and T3 (time from T0 to LMA placement); total sevoflurane consumption during induction; and incidence of cough, movement, or tachycardia at the time of LMA insertion.

### Statistical Analysis.

Data were analyzed using statistical analysis software (IBM SPSS version 20.0 for Windows, IBM Corp). A Kruskal-Wallis nonparametric test was applied to compare the time and sevoflurane consumption among the 3 groups. Post hoc pairwise comparisons were made using the Mann-Whitney U test for the parameters found significant in the Kruskal-Wallis test. The P value .017 (0.05/3) was considered significant in the Mann-Whitney U test due to Bonferroni correction. One-way analysis of variance was applied for comparing the heart rate among the 3 groups with a post hoc Tukey test for multiple comparisons. The complication proportions among the 3 groups were performed using the χ² test, and the Fisher exact test was applied for pairwise comparison. The sample size was calculated using an open source calculator (StatsToDo) for 3-group analysis. Considering 2 mL to be a significant difference and the population SD to be 1.5 mL, with an α error of .05 and a power of 80%, a sample size of 12 patients per group was required. After accounting for 25% dropouts, a sample size of 15 per group was considered.

### Results

A total of 60 patients were screened for inclusion, of which 10 did not meet the inclusion criteria and 5 declined to participate in the study. A total of 45 patients were randomly assigned to the 3 groups to participate in the trial (Figure 1). Demographic parameters were comparable among the 3 groups except for gender distribution, which was statistically significant in favor of the boys (Table 1; P = .004).

There was no significant difference in time taken for loss of eyelash reflex (T1), IV cannula insertion (T2), and LMA insertion (T3; see Table 1). The median sevoflurane consumption in group 0.5 MV was significantly lower compared with both group MV and group S (Figure 2, Table 1). The heart rate was comparable at times T1, T2, and T3 in the 3 groups (Figure 3).

The incidence of tachycardia and movement on IV cannula and LMA insertion, airway complications, and need for rescue propofol were comparable among the 3 groups (Table 2).

### Discussion

In the present study, the techniques used in each of the 3 groups were equally effective in providing satisfactory conditions for LMA insertion. However, sevoflurane consumption was significantly lower in group 0.5 MV compared with both group MV and group S.

Sevoflurane is one of the most attractive agents for pediatric day care procedures performed using anesthesia because of the sweet smell, smooth induction characteristics, low blood-gas partition coefficient resulting in
rapid induction and recovery, and wide cardiorespiratory safety profile. It provides an optimal condition for insertion of supraglottic devices with minimum requirement for muscle relaxants and IV anesthetics. However, financial cost and environmental impact of sevoflurane remain the major limiting factors. Thus, any measure that can reduce sevoflurane consumption without compromising the quality of anesthesia is desirable, especially for developing countries.

There have been many studies analyzing the effectiveness of various measures to reduce the financial and environmental cost of anesthesia, such as the application of price list stickers on vaporizers, bispectral index–guided anesthesia maintenance, and automated control of end-tidal anesthetic gas concentration. Eschertzhuber et al observed a more than 60% reduction in anesthesia cost with the use of sevoflurane at low FGF (0.5 L/min) withuffed endotracheal tubes, as opposed to uncuffed tubes requiring higher flows. These methods deal with the reduction of sevoflurane consumption during the maintenance phase of anesthesia. However, a large portion of sevoflurane consumption (and waste) occurs during inhalational induction. No known previous study had assessed the feasibility of using low FGF during anesthesia induction with sevoflurane, and whether such an approach can result in a significant reduction in financial cost and environmental impact of anesthesia.

For the precise pharmacoeconomic assessment of inhalational agents, accurate measurement of the volume of sevoflurane consumed in milliliters during the anesthetics is required. The difference in the weight of vaporizer before and after the anesthetic is considered the gold standard for measurement of its consumption.

However, this technique is cumbersome and impractical. The Draeger Primus anesthesia workstation calculates the sevoflurane consumption accurately by using some unrevealed proprietary technique and displays it on logbook at the end of the anesthetic. Biro et al compared the volatile agent consumption as displayed on a Draeger Primus workstation with the gold standard method of weighing the vaporizer. They concluded that the automatically displayed values in logbook were precise estimates of sevoflurane and desflurane consumption and can be reliably used to estimate the economic impact of inhalational anesthesia. We used this logbook function to estimate the consumption of sevoflurane by 3 techniques during induction and found that the sevoflurane consumption was minimum in the 0.5 MV group (see Figure 3). Despite a lower consumption of sevoflurane, the times to loss of consciousness (T1), IV cannula insertion (T2), and LMA insertion (T3) were comparable in the 3 groups (see Table 1). The priming of the circuit with 8% sevoflurane at high gas flows ensured the filling up of the equipment dead space with anesthetic gases and expedited the induction. Priming of the anesthesia circuit with a high concentration of inhalational agents has been recommended earlier to achieve a faster induction. If we assume that the delivery apparatus (circuit volume 800 mL + soda lime chamber 600 mL + reservoir bag 1,000 mL) was fully saturated in 30 seconds, the total volume of sevoflurane vapor present in the primed circuit would be 2,400 mL. However, this technique is cumbersome and impractical.
across various countries. However, considering the fact that there was a mean difference of 6 mL per case between group 0.5 MV and group S, an FGF of 0.5 MV for induction would be potentially more economical. This cost reduction may be great, especially for developing nations.

Moreover, considering the environmental impact of sevoflurane, 1 mL of sevoflurane liquid produces 182 mL of sevoflurane gas at 20°C temperature and 1 atmosphere pressure (molar weight = 200 g, specific gravity = 1.52). Thus, a median difference of 6 mL per case of liquid sevoflurane, for 10 cases per day, would equate to a reduction of 1.1 L per day of “greenhouse” gas emission. With the 20-year global warming potential of sevoflurane being 349, this is equivalent to a reduction of 384 L of carbon dioxide production, from a single case alone. 16

Our study had some limitations. The objective depth of anesthesia monitoring using indexes such as the bispectral index or entropy was not performed during induction. However, MAC and a surrogate indicator (incidence of tachycardia, movement, and cough) revealed no difference in the 3 groups. Second, there was a difference in gender distribution in the 3 groups. However, the sevoflurane consumption is unaffected by the gender, so this would not have affected our results. 4 Also, the same pediatric circuits with a 1-L reservoir bag were primed with 8% sevoflurane for a constant time and FGF to ensure a similar sevoflurane volume is used and to achieve priming quickly. If we subtract the sevoflurane used for priming from the total consumption, still the difference would remain significant because the groups differed only in the sevoflurane use according to the varied FGF. The results may vary if we were to use an unprimed circuit, start induction with nitrous oxide, or alter the circuit or the reservoir bag volume or the concentration of sevoflurane. Finally, the fresh gas flow of 0.5 MV was chosen arbitrarily. Although it yielded the greatest economy without compromising the quality of induction, the ideal FGF may be still lower and needs to be studied.

**Conclusion**
The use of half of the predicted MV as fresh gas flow, as opposed to standard fresh gas flow, during sevoflurane induction using a primed circuit, significantly reduces sevoflurane consumption and waste, without affecting the quality of anesthesia. Thus, it reduces the economic and environmental burden of anesthesia.

### Table 2. Complications, Movement on IV Cannula or LMA Insertion, and Additional Propofol Boluses Requirement

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Group 0.5 MV (n=15)</th>
<th>Group MV (n=15)</th>
<th>Group S (n=15)</th>
<th>P valuea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complications (tachycardia/laryngospasm/breath holding/bradycardia/none)</td>
<td>1/1/2/1/9</td>
<td>1/0/1/0/13</td>
<td>1/1/0/0/13</td>
<td>.601</td>
</tr>
<tr>
<td>Movement at IV cannula insertion</td>
<td>4</td>
<td>4</td>
<td>3</td>
<td>&gt; .999</td>
</tr>
<tr>
<td>Movement at LMA insertion</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>&gt; .999</td>
</tr>
<tr>
<td>Propofol bolus</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>&gt; .999</td>
</tr>
</tbody>
</table>

Abbreviations: IV, intravenous; LMA, laryngeal mask airway; MV, minute ventilation; S, standard fresh gas flow at 6 L/min.
a χ2 test.

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**DISCLOSURES**

The authors have declared no financial relationships with any commercial entity related to the content of this article. The authors did not discuss off-label use within the article. Disclosure statements are available for viewing upon request.