Sevoflurane Induction Procedure: Cost Comparison Between Fixed 8% Versus Incremental Techniques in Pediatric Patients

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This study compared 2 well-accepted and safe methods of pediatric inhalation induction using sevoflurane. Incremental and fixed 8% induction methods were evaluated for economic outcomes by comparing the amount of liquid sevoflurane consumed. We also tried to establish the relation between cost of induction and demographic parameters in both groups. One hundred pediatric patients scheduled for ophthalmologic examination under anesthesia were randomly divided into 2 equal groups. The amount of sevoflurane consumed in both groups was computed using the Dion method. Although the time to loss of consciousness was significantly lower using the 8% method (75.98 vs 135 seconds), the liquid sevoflurane consumption using the incremental method (2.25 mL) was almost half that of the fixed 8% method (4.46 mL). The overall procedural cost of induction (loss of consciousness plus intravenous cannulation and insertion of a laryngeal mask airway) was also almost double using the fixed 8% method. Use of the incremental method preferably over the fixed 8% method could save almost $18 US for each procedure. The volume of sevoflurane consumed during anesthesia induction was found to be independent of age, weight, or sex of pediatric patients. Both induction methods proved to be equally safe and acceptable to the patients.

Keywords: Anesthesia, anesthesia cost, induction methods, pharmacoeconomics, sevoflurane.

The last 2 decades have seen revolutionary advances in anesthesia with the introduction of newer and safer drugs. Sevoflurane is one such drug that has replaced its predecessors and emerged as the inhalation anesthetic of choice for multiple indications. As an induction agent, sevoflurane is not associated with a pungent odor, airway irritation, or hemodynamic instability, and thus it is widely accepted by not only patients but also anesthesia providers. Compared with previously used agents such as halothane, the limitation of using sevoflurane is the associated cost. Cost is even more important when sevoflurane is used in high concentrations and at high fresh gas flows, as in pediatric inhalation induction.

There are 2 well-described and tested methods of sevoflurane induction in the literature: the fixed 8% method and the incremental method. Both these methods have been shown to be equally safe and acceptable; however, no literature is available comparing costs associated with these methods.

Materials and Methods

• Patients. After approval of the study protocol from our institution’s ethical review committee, 100 pediatric patients (age range, 1 to 8 years) scheduled for ophthalmologic examination under anesthesia were included in the study. A written, informed parental consent was obtained for participation in the study. The patients were divided into 2 groups of 50 each using a computer-generated table of random numbers. Patients with the following conditions were excluded from the study: known seizure disorder, craniofacial abnormalities/difficult airway, cardiopulmonary or neuromuscular defects, hepatic or renal insufficiency, and expected difficult intravenous (IV) cannulation (eg, dark complexion, obese).

The 2 groups were labeled on the basis of the method of induction used. Group 1 underwent incremental sevoflurane induction. Group 2 had 8% sevoflurane induction.

All children in both groups were premedicated with midazolam, 0.5 mg/kg orally, about 30 minutes before the induction of anesthesia. A parent or guardian accompanied the child into the operating room to allow the child to remain calm and cooperative for inhalation induction. Before induction, pulse oximetry and electrocardiogram monitoring were attached. All patients were anesthetized using an anesthesia workstation (Draeger Primus, Draeger...
Medical), and a vaporizer (Draeger Vapor 2000, Draeger Medical) was used to deliver sevoflurane.

- **Procedure.** For each group, inhalation induction was initiated using a face mask. The time until loss of consciousness was noted in seconds using a stopwatch by an assistant. Loss of consciousness was defined by loss of eyelash reflex and adequate jaw relaxation. The remaining procedure is described for each group.

- **Group 1.** The sevoflurane vaporizer dial initially was set at 1% (in a 1:1 oxygen:nitrous oxide mixture) with a total fresh gas flow of 6 L/min. The sevoflurane concentration was incrementally increased by 1% every 3 breaths. This was done until the vaporizer setting reached 8% or until loss of consciousness (whichever occurred earlier). After loss of consciousness, the sevoflurane concentration setting on the vaporizer was decreased to 4%. An IV line was secured by a resident physician assisting the anesthesia provider, following which an optimal-sized laryngeal mask airway (The LMA Classic, Teleflex Inc) was inserted.

- **Group 2.** After priming the circuit with 8% sevoflurane in 50% nitrous oxide at a flow of 6 L for 1 minute, inhalation induction was initiated. After loss of consciousness, the sevoflurane dial concentration was reduced to 4%. An IV line was secured by a resident assistant assisting the anesthesia provider, and an optimal-sized LMA (The LMA Classic) was inserted. The total duration until successful insertion of the LMA was noted in seconds.

The placement of an LMA was attempted only after ensuring proper depth of anesthesia, which was adjudged by loss of jaw tone and centralization of the pupils. If there was failure to adequately place the LMA on the first attempt, the time for repeated attempts was included in the induction time.

It was made sure that the resident placing the IV line was the same person or had similar level of experience; thus, skill of cannulation did not confound the results. The same was applied for the anesthesia provider inserting the LMA. Therefore, the possibility of confounding insertion times due to difference in expertise level was minimized.

- **Calculations.** The total amount of sevoflurane consumed was calculated using the Dion equation as follows:

\[
\text{Amount of Liquid Sevoflurane Used} = \frac{PFTM}{2.412d}
\]

where

- \(P\) = Vaporizer dial concentration in percent
- \(F\) = Total fresh gas flow in liters per minute
- \(T\) = Time for which the concentration \(P\) was set in minutes
- \(M\) = Molecular mass of sevoflurane in grams
- \(D\) = Density of liquid sevoflurane in grams per milliliter

The fixed variables used in the equation for the present study were as follows:

- \(F = 6\) L/min
- \(d (at 21°C) = 1.52\) g/mL

After substitution of these fixed variables, the equation can be rewritten as

\[
\text{Total Sevoflurane Used} = 2.62 + 0.00546(8 \times t) + 4(t_{IV} + t_{LMA})
\]

where \(t_{IV}\) and \(t_{LMA}\) are times for IV cannulation and successful LMA placement.

- **Group 1.** The time (duration) for each concentration was labeled as \(T_1, T_2, T_3, T_4, T_5, T_6, T_7, T_8\) in seconds for corresponding concentrations of 1%, 2%, 3%, and so on until 8%.

Total liquid sevoflurane used was calculated as

\[
0.00546(T_1 + 2T_2 + 3T_3 + 4T_4 + 5T_5 + 6T_6 + 7T_7 + 8T_8 + 4t_{IV} + 4t_{LMA})
\]

where \(t_{IV}\) and \(t_{LMA}\) are times for IV cannulation and successful LMA placement.

- **Group 2.** The time for priming was 1 minute at a sevoflurane concentration of 8%. Thus, sevoflurane can be calculated as follows:

\[
\text{Sevoflurane Liquid Used While Priming} = 0.00546(\text{Sevoflurane Percentage} \times \text{Time of Priming in seconds}) = 2.62\ \text{mL}
\]

From these equations, the total amount of liquid sevoflurane was calculated during each induction. The cost of induction finally was calculated by multiplying the volume of liquid sevoflurane consumed and the cost of each milliliter of sevoflurane available in the market. The cost of sevoflurane varies throughout the world; thus, we used the amount of sevoflurane consumed as a surrogate for procedural cost in our analysis. This would allow our findings to be interpreted universally, irrespective of local cost of liquid sevoflurane. The cost of oxygen and nitrous oxide consumed is negligible compared with that of the inhalation agent. Thus, oxygen and nitrous oxide cost was not included in the calculations for estimation of procedural cost.

**Results**

The data obtained were analyzed using statistical analysis software (SPSS version 20, IBM SPSS) for Macintosh. The degree of statistical significance was set at 95%, allowing an \(\alpha\) error of 5% for the expressed results. The normality of data was verified using the Kolmogorov-Smirnov test, and variances were compared using the Levene test for equality of variance.

Demographic variables were statistically comparable between both groups (Table 1). The mean age (± standard deviation) of children in group 1 was 3.17 ± 1.83 years and in group 2 was 3.42 ± 1.81 years. Both groups had male predominance, with 66% and 62% male patients in group 1 and group 2, respectively. The mean liquid sevoflurane consumed during the induction procedure in group 1 and group 2 was 3.09 ± 1.50 mL and 6.13 ± 1.11 mL.
mL, respectively. These volumes were compared using an independent-samples Student t test, and the difference (2.18 ± 0.26 mL) was found to be highly significant, with a P value of < .001. To simulate actual clinical practice where priming is often done before use of the fixed 8% method, it was found that priming the circuit consumed 2.62 mL of liquid sevoflurane in each procedure. The median sevoflurane consumption was 3.55 mL and 5.94 mL in groups 1 and 2, respectively. Table 2 shows the comparison of time of “loss of consciousness” and “IV cannulation + LMA insertion,” with the corresponding amount of sevoflurane consumed in both groups.

The present cost of generic liquid sevoflurane is approximately $6 US per milliliter. On this basis, the mean cost of sevoflurane consumed during a fixed 8% method was found to be $36.78 ± $6.67 and $18.54 ± $9 using the incremental method. This would amount to a savings of approximately $18.24 per induction procedure done via the incremental method.

No statistically significant correlation between the volumes of sevoflurane consumed could be found for age (Pearson correlation coefficient = 0.030, P = .77; Figure 1) or for weight (Pearson correlation coefficient = 0.038, P = .7704; Figure 2). The correlation coefficients in individual groups for the above variables are shown in Table 2. In group 1, the mean volume of sevoflurane consumed by boys and girls was 3.78 ± 1.25 mL and 4.37 ± 1.89 mL, respectively. In group 2, the mean sevoflurane consumption in boys was 6.29 ± 1.28 mL and was 5.93 ± 0.73 mL in girls. The difference between consumption values for boys and girls in each group was found to be statistically nonsignificant; thus, no relation between consumption and gender was found. Three patients in each group required insertion of an LMA more than once; hence, the sevoflurane consumed for them was found to be much higher than the rest of the patients in the corresponding group (Figure 3).

**Discussion**

The major limiting factor in the use of sevoflurane in the developing world has been the economic factors associated with the agent. Multiple studies have compared costs associated with the use of different inhalation agents, and further comparisons have been made between inhalation and intravenous anesthesia. Inhalation induction using sevoflurane has been shown to be more economical and almost equally rapid compared with propofol-based total intravenous anesthesia.3 The quality of induction with sevoflurane, along with its ability to generate optimal conditions for LMA insertion without supplemental opioids or muscle relaxants, has also been well documented.4

An ideal inhalation induction technique besides being rapid and comfortable for the patient should be economical. To achieve rapidity, use of vital capacity breaths with 8% sevoflurane is a more popular method of induction compared with the conventional incremental induction. Sevoflurane used in high concentrations is known to be safe and is not associated with substantial hemodynamic instability.5 Comparisons between induction using “tidal volume” and “vital capacity” breathing in high sevoflurane concentration (8%) have shown that vital capacity breathing is rapid and is associated with a lower incidence of involuntary movements and coughing.6 This “vital capacity breath” induction is primarily limited to adults only because initiation of vital capacity breathing on demand by the anesthesia provider cannot be achieved in the pediatric population. In comparison studies, high-concentration induction and incremental induction in a pediatric population at tidal volume breathing have proved to be equally safe.7 The rapidity of induction in terms of a few seconds, as expected in a high-concentration group, can be practically more useful in an uncooperative child during induction; however, this can be easily offset by calming the child using adequate preoperative sedation. Thus, the marginally increased induction time in a sedated child is not likely to have significant impact when it is compared with the higher cost of sevoflurane.

**Table 1. Comparison of Demographic Variables Between Groups**

<table>
<thead>
<tr>
<th>Demographic variable</th>
<th>Group 1 (n = 50)</th>
<th>Group 2 (n = 50)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y (mean ± SD)</td>
<td>3.17 ± 1.83</td>
<td>3.42 ± 1.81</td>
</tr>
<tr>
<td>Male/female</td>
<td>33/17</td>
<td>31/19</td>
</tr>
<tr>
<td>Weight, kg (mean ± SD)</td>
<td>11.40 ± 3.90</td>
<td>11.70 ± 3.12</td>
</tr>
</tbody>
</table>

Abbreviation: SD, standard deviation.

Both groups were statistically comparable (all P values > .05).

**Table 2. Comparison of Time and Sevoflurane Consumption During Induction Procedure in Both Groups**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Fixed 8% group</th>
<th>Incremental group</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time (s) – IV cannulation + LMA insertion</td>
<td>79.22 ± 56.88</td>
<td>70.50 ± 44.69</td>
<td>.396</td>
</tr>
<tr>
<td>Sevoflurane (mL) – IV cannulation + LMA insertion</td>
<td>1.73 ± 1.24</td>
<td>1.46 ± 0.94</td>
<td>.395</td>
</tr>
<tr>
<td>Time (s) – Loss of consciousness</td>
<td>75.98 ± 18.99</td>
<td>135.38 ± 19.61</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Sevoflurane (mL) – Loss of consciousness</td>
<td>4.46 ± 0.73</td>
<td>2.25 ± 0.63</td>
<td>&lt; .001</td>
</tr>
</tbody>
</table>

Abbreviations: IV, intravenous; LMA, laryngeal mask airway.

Data are mean ± standard deviation.
consumed in expediting the induction.

As both these methods are known to be clinically safe, the choice of using one over the other must be governed by the cost-benefit ratio. In the present study the average cost of anesthesia induction using the 8% method on a per case basis was almost 100% more than the incremental method (mean consumption in group 1 = 3.09 mL vs 6.13 mL in group 2). However, in the fixed 8% method, 2.62 mL was consumed during each procedure for priming the circuit alone. Not priming before induction would have possibly shown a lower sevoflurane consumption, but it would not have simulated actual clinical practice, where priming is often recommended before high-concentration induction. In fact, the advantage of high-concentration induction is the rapidity with which anesthesia can be induced in patients; not priming the circuit prolongs the induction time by consuming time to build up concentration in the circuit. Thus, it would defeat the purpose for which high-concentration induction is used.

The strategy to conserve inhalation agent during the induction phase is likely to be most efficient because, during this phase, inhalation agents are used at high concentration and at high flows. The advantage gained by quicker induction of the high-concentration method should be evaluated against the cost paid to achieve the goal. These concerns become all the more important in developing countries where gross domestic product toward health is limited and the cumulative costs become great.

The present study aimed to evaluate only costs associated with the induction methods; we did not analyze the associated complications or the ease of LMA insertion in detail. However, since the same anesthesiologist was involved in airway management, it was observed that both methods were comparable in terms of ease of LMA insertion. In both groups, 3 patients required LMA insertion twice, and these were the patients who consumed more...
than the average amount of sevoflurane (see Figure 3). The number of adverse events was also similar. The most common problem noted was temporary breath holding in both groups, which resolved spontaneously. One patient in the high-concentration group experienced laryngospasm and was excluded from analysis because of change in the management plan.

Most of the cost of inhalation induction is attributed to the amount of inhalation agent consumed. To quantify the amount of liquid inhalation vapor used, various methods have been employed previously. One of the direct methods is to weigh the anesthesia vaporizer before and after the procedure and to attribute the difference to the amount of agent consumed. In fact, this is one of the most accurate methods of measuring vapor consumption and is used in calibration of vaporizers during the manufacturing process. However, weighing machines with such a high degree of sensitivity are not routinely available. The values obtained for weight of liquid agent consumed are very small, and measurements are subject to errors. Each milliliter of liquid sevoflurane at operating room temperature produces 182.7 mL of sevoflurane vapor. With the density of sevoflurane being 1.52 g/mL, an error in measuring the vaporizer weight by just 1.5 g will make a difference of approximately 180 mL of gaseous sevoflurane. Volumetric measurements of residual liquid sevoflurane in the vaporizer after each case also suffer a high degree of error; even 1 mL of measurement error (residual volume of liquid on emptying the vaporizer) will again be magnified 180× in the estimation of used vapor. Also, the amount of liquid sevoflurane consumed in each procedure was very small. Emptying sevoflurane vaporizer and measuring the volume of residual liquid is likely to be subject to errors because of residual volume of sevoflurane in the vaporizer (due to surface tension).

Another popular method to calculate the amount of liquid anesthetic agent is the Dion equation. It can be used to calculate amount in liquid consumed for any inhalation agent once its molecular mass and density are known. The physical properties of sevoflurane are well known, and thus its consumption under anesthesia can be calculated using the Dion method. The Dion formula has already been validated previously in multiple cost analyses. Once the amount of liquid agent consumed is known, the calculation of cost can be done by prices of agents available on the market.

For the improved accuracy of our measurements, we used the Draeger Vapor 2000 series sevoflurane vaporizer at a fresh gas inflow of 6 L/min. These vaporizers (known to be devoid of any pumping/pressurizing effect) are calibrated at 5 to 6 L during the manufacturing process, and their output is most accurate at these fresh gas flow rates. The anesthesia workstation Draeger Primus uses electronic flow meters that estimate fresh gas flows using hot wire anemometry and is known to be highly accurate.

The price of nitrous oxide in comparison to inhalation agents is very small and can be considered as negligible in a cost analysis. The cost of volatile inhalation agents account for approximately 20% of total anesthetic drugs used during surgery. Cutting down on consumption of inhalation agents can significantly lower total costs without compromising patient safety. A study by Lampotang et al showed that just by conservative use of inhalation agents, the United States could save approximately $100 million a year. These cost savings are even more important for developing nations with limited health resources, where wasteful expenditures are undesirable.

Conclusion

The incremental method of sevoflurane induction is associated with almost half the cost compared with the fixed 8% method. The volume of sevoflurane consumed during anesthesia induction is independent of age, weight, or sex of pediatric patients.

REFERENCES


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