Onset Time, Recovery Duration, and Drug Cost with Four Different Methods of Inducing General Anesthesia

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We compared two conventional induction techniques (thiopental and propofol), an inhaled induction with sevoflurane using a circle system, and a rebreathing method. Fentanyl 1 µg/kg was given to women undergoing 10- to 20-min procedures. Anesthesia was induced (n = 20 each) with one of the following: 1) sevoflurane and N₂O from a rebreathing bag (Sevo/Bag). A 5-L bag was prefilled with a mixture of sevoflurane 7% and N₂O 60% in oxygen. The bag was connected between the normal circle system, separated by a spring-loaded valve; 2) sevoflurane 8% and N₂O 60% from a circle system on a conventional anesthesia machine with a total fresh gas flow of 6 L/min (Sevo/Circle); 3) propofol 3 mg/kg as an IV bolus; 4) thiopental sodium 5 mg/kg as an IV bolus. Postoperative nausea and vomiting was treated with ondansetron. Induction times were comparable with each method. Recovery duration was shortest with sevoflurane, intermediate with propofol, and longest with thiopental. Induction drug costs were lowest with Sevo/Bag and thiopental, intermediate with Sevo/Circle, and highest with propofol. However, sevoflurane (by either method) caused considerable nausea and vomiting that required treatment. Consequently, total drug cost was least with thiopental, intermediate with Sevo/Bag and propofol, and greatest with Sevo/Circle. Thus, no single technique was clearly superior. Implications: Anesthetic induction techniques influence awakening time, recovery duration, and drug costs. We tested two IV methods and two inhaled techniques. However, none of the four tested methods was clearly superior to the others.

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intrinsic volume. As an alternative, we considered a 5-L bag prefilled with sevoflurane 7% in nitrous oxide 60%. This bag was connected to a valve inserted between the circle system and the face mask. Depressing the spring-loaded valve disconnected the circle system so that the patient was directly connected to the bag. Anesthesia then resulted from breathing and rebreathing from this bag (Fig. 1). We tested two conventional induction techniques (thiopental and propofol), an inhaled induction with sevoflurane using a circle system, and the rebreathing method described above. Our purpose was to evaluate the effects of induction technique on induction time, recovery characteristics, and drug cost.

Methods

With approval of the Ethics Committee of the University of Vienna and written, informed consent, we studied 80 women undergoing short gynecological procedures (e.g., hysteroscopy, curettage, cervical conic excision) with an anticipated duration of 10–20 min. All patients were aged 20–60 yr and were ASA physical status I or II.

Patients who were seriously obese, claimed allergy to any of the study drugs, were pregnant or nursing, or used opioids or sedatives were excluded. We also excluded patients who refused either IV or inhaled induction and those at risk of regurgitation.

None of the patients was premedicated. Each was preoxygenated for 1 min with 100% oxygen, and then given 1 mg/kg IV fentanyl. One of the following randomly assigned anesthetic induction techniques (thiopental and propofol), an inhaled induction with sevoflurane using a circle system, and the rebreathing method described above. Our purpose was to evaluate the effects of induction technique on induction time, recovery characteristics, and drug cost.

1. Sevoflurane and nitrous oxide from a rebreathing bag (Sevo/Bag). A 5-L bag was prefilled with a mixture of nitrous oxide 60% (0.6 minimum alveolar anesthetic concentration [MAC]) (3) and oxygen 30% that was passed through a vaporizer set to 8% sevoflurane. This produced an actual sevoflurane concentration in the bag of 7% (3.5 MAC) (4). The bag was connected between the normal circle system and the endotracheal tube, separated by a spring-loaded valve. Depressing the valve isolated the routine breathing system so that the patient breathed and rebreathed from the 5-L bag (Fig. 1).

2. Sevoflurane and nitrous oxide from a circle system on a conventional anesthesia machine (Sevo/Circle). The sevoflurane concentration on the vaporizer was set to 8% and was administered with nitrous oxide 60% in a total fresh gas flow of 8 L/min.

3. Propofol 3 mg/kg (Propofol). Propofol was given as an IV bolus.

4. Thiopental sodium 5 mg/kg (Thiopental). Thiopental was given as an IV bolus.

Lung ventilation was initially spontaneous in each case, then assisted at a rate of approximately 10 breaths/min when apnea prevailed. The specified induction method was continued until eyelid reflexes were lost, and an additional minute. A lubricated laryngeal mask was then inserted using standard technique (the cuff was slightly inflated to facilitate insertion). Additional propofol or thiopental was given if required clinically in the patients assigned to IV induction. Fresh gas flow was discontinued during laryngeal mask insertion.

Anesthesia was subsequently maintained with sevoflurane (1.2%–1.4% end-tidal concentration) in nitrous oxide 60%, using a 6-L/min fresh gas flow via a circle circuit. Patients breathed spontaneously, their breathing was assisted as necessary to maintain a Petco$_2$ near 35 mm Hg. Minimal peak airway pressures were used, consistent with maintaining physiological Petco$_2$ concentrations with a respiratory rate of 10 breaths/min. Additional fentanyl (50 μg IV) was given when it was clinically indicated.

Sevoflurane and nitrous oxide concentrations were not reduced toward the end of surgery; instead, both were abruptly discontinued when the operation was complete. After spontaneous breathing resumed and airway reflexes were reestablished, the laryngeal mask was removed. Patients were observed until they responded to command and were then transferred to the postanesthesia care unit. Postoperatively, patients were given IV boluses of the opioid piritramid as necessary for treatment of pain. Postoperative nausea and vomiting was treated by the IV administration of ondansetron (4–8 mg). Antiemetic treatment was determined by the patient’s reported sensation of nausea or when emesis or retching was observed. The treating anesthesiologists, who were blinded to group assignment and intraoperative management, based their treatments on direct patient observation and their 5-min queries (see below).

Standard morphometric and demographic characteristics of the participating patients were recorded,
along with their ASA physical status and Mallampati scores.

During induction, we recorded the number of breath-holding episodes (≥15 s). The time required for the eyelid reflex to disappear was recorded at 15-s intervals. Saturation from a pulse oximeter and concentrations of sevoflurane, oxygen, and carbon dioxide in the rebreathing bag were determined at 30-s intervals by using a Hewlett Packard M1026A gas monitor (Hewlett Packard, Boeblingen, Germany). The number of attempts at laryngeal mask insertion was recorded, along with the time elapsed since the beginning of induction. Induction time thus included the time to loss of lid reflex, 1 min additional ventilation per protocol, and the time required for laryngeal mask insertion per se.

Movement in response to laryngeal mask insertion was qualitatively graded as none, little, or major. During the maintenance phase of anesthesia, we recorded saturation from a pulse oximeter, hemodynamic responses, vaporizer setting, and end-tidal sevoflurane and carbon dioxide concentrations at 1-min intervals. Return of consciousness was determined by asking patients to open their eyes at 30-s intervals. The time elapsed between discontinuation of anesthesia and eye opening was defined as the awakening time.

Postoperative pain was evaluated at 5-min intervals using a conventional 100-mm visual analog scale (0 = no pain; 100 = most severe pain). Pain scores >50 were treated with 3 mg of IV piritramid. Fitness for discharge was evaluated using a modification (5) of the Aldrete and Kroulik (6) scoring system (Table 1). The time elapsed between discontinuation of anesthesia and a recovery score of 13 was considered the recovery duration. All postoperative measurements were performed by an investigator blinded to group assignment and anesthetic induction details.

Major outcomes were prospectively defined as induction time, recovery duration, and total drug cost. The beginning of anesthetic induction was designated elapsed time zero. Values during the maintenance phase of anesthesia were averaged first within each patient, then among the patients in each group. The average minimal oxygen saturation was similarly calculated as the average across volunteers of the minimal value in each. Drug costs were estimated from the average November 1998 United States wholesale prices, as reported by the Moffitt/Long Hospitals Pharmacy: fentanyl ($2.06 per 100 μg), thiopental ($64.68 per 5 g), propofol ($15.00 per 200 mg), sevoflurane ($1.36 per milliliter liquid), and ondansetron ($12.00 per 4 mg).

Sevoflurane use (in milliliters of liquid) was calculated by integrating the vaporizer settings and fresh gas flows over the duration of the study. Only the administered drug volumes were used in the analysis; that is, any amount wasted in unused syringes was not considered. Nitrous oxide was not included in the analysis because it is inexpensive and the total amount used was similar in each group.

Normally distributed data were compared by using one-way analysis of variance and Scheffé’s F-tests. Nominal data were compared by using χ². Results are presented as means ± SD. P < 0.05 was considered statistically significant.

### Results

Morphometric and demographic characteristics of the patients were similar in each group. Mallampati scores (7), anesthetic maintenance, and duration of anesthesia were also similar. Intraoperative mean arterial pressure, however, was significantly lower after induction with propofol than that with the other methods. Two of the patients assigned to propofol and four of the patients assigned to thiopental required supplemental doses during induction. For the patients receiving propofol, the supplemental dose averaged 80 ± 71 mg, whereas for the patients receiving thiopental, it averaged 138 ± 75 mg. Seven patients required supplemental intraoperative fentanyl (Table 2).

Induction times did not differ significantly among the four techniques. Only a single breath-holding episode was detected, and only a single mask insertion attempt

### Table 1. Fitness for Discharge Scoring System

<table>
<thead>
<tr>
<th>Activity</th>
<th>0</th>
<th>1</th>
<th>2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiration</td>
<td>No movement</td>
<td>No purposeful movement</td>
<td>Raises one arm on command</td>
</tr>
<tr>
<td>Respiration</td>
<td>Apnea</td>
<td>Dyspnea or limited breathing</td>
<td>Breaths deeply and coughs freely</td>
</tr>
<tr>
<td>SpO₂ on room air (%)</td>
<td>&lt;90</td>
<td>90–95</td>
<td>&gt;95</td>
</tr>
<tr>
<td>Consciousness</td>
<td>Unresponsive</td>
<td>Aroused to verbal stimuli</td>
<td>Fully awake</td>
</tr>
<tr>
<td>Blood pressure (% of baseline)</td>
<td>&gt; or &lt;50</td>
<td>20–50</td>
<td>0–20</td>
</tr>
<tr>
<td>Heart rate (bpm)</td>
<td>&lt;45 or &gt;120</td>
<td>45–49 or 101–120</td>
<td>50–100</td>
</tr>
<tr>
<td>Gastrointestinal tract</td>
<td>Vomiting within 30 min</td>
<td>Severe nausea and vomiting</td>
<td>Little or no vomiting</td>
</tr>
</tbody>
</table>

SpO₂ = pulse-oximeter saturation.

The total score was determined by summing the individual indicators of recovery, for which 0, 1, or 2 points were assigned. A score of ≥13 (85%) sustained for at least two measurements at 5-min intervals defined fitness for discharge.
was required in most cases. The sevoflurane concentration in the rebreathing bag decreased from 7% to approximately 3.5% after 2.5 min, whereas the inspired carbon dioxide concentration simultaneously increased to approximately 30 mm Hg; the inspired oxygen concentration remained nearly constant. The average minimal oxygen saturation exceeded 99% in each group (Fig. 2).

Patients given sevoflurane by either method required significantly less time to respond to postoperative commands than those given thiopental. Awakening was also significantly faster in the Sevo/Bag group than in patients given propofol: 6 ± 2 vs 8 ± 3 min. Initial recovery scores were comparable in the four groups. However, recovery was significantly slower in patients given thiopental than in those given sevoflurane by either method. Approximately half the patients given sevoflurane were nauseated during recovery, and approximately one-fourth vomited. In contrast, nausea was rare in the patients given thiopental or propofol, and none vomited. As a result, ondansetron was required in 10 patients given sevoflurane but in only 2 given thiopental and none given propofol.

The cost of induction drugs was lowest with the Sevo/Bag technique and thiopental, intermediate with Sevo/Circle, and highest with propofol. The cost of maintenance sevoflurane was comparable in the four groups. When the cost of postoperative ondansetron was added to induction and maintenance drug costs, the Sevo/Circle method proved significantly more expensive than thiopental. Costs were intermediate and similar with Sevo/Bag and propofol (Table 3).

**Discussion**

The novel induction technique we tested was inhalation of sevoflurane and nitrous oxide from a rebreathing bag. Because the system is sealed, the sevoflurane concentration in the bag decreased during induction as the anesthetic redistributed into the lungs and was absorbed by body tissues. Nonetheless, the concentration remained nearly 2 MAC even after 2.5 min of induction, a concentration that provided adequate anesthesia for insertion of a laryngeal mask. The carbon
Table 3. Induction and Recovery Characteristics and Cost

<table>
<thead>
<tr>
<th></th>
<th>Thiopental</th>
<th>Propofol</th>
<th>Sevo/Circle</th>
<th>Sevo/Bag</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loss of eyelid reflex (s)</td>
<td>47 ± 18‡</td>
<td>63 ± 36</td>
<td>72 ± 21*</td>
<td>52 ± 13*</td>
</tr>
<tr>
<td>Breath-holding episodes</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Laryngeal mask attempts (1/2/3/failed)</td>
<td>13/3/4</td>
<td>18/0/2</td>
<td>15/2/3</td>
<td>18/1/1</td>
</tr>
<tr>
<td>Induction time (s)</td>
<td>124 ± 45</td>
<td>140 ± 40</td>
<td>155 ± 40</td>
<td>129 ± 22</td>
</tr>
<tr>
<td>Minimal SpO₂ during induction (%)</td>
<td>99.5 ± 0.6</td>
<td>99.2 ± 0.5</td>
<td>99.4 ± 0.6</td>
<td>99.5 ± 0.6</td>
</tr>
<tr>
<td>Movement during insertion (none/little/major)</td>
<td>14/1/5</td>
<td>15/4/1</td>
<td>18/2/0</td>
<td>18/1/1</td>
</tr>
<tr>
<td>Awakening (min after sevoflurane discontinued)</td>
<td>9 ± 4‡</td>
<td>8 ± 3</td>
<td>7 ± 3*</td>
<td>6 ± 2‡</td>
</tr>
<tr>
<td>Initial recovery score</td>
<td>12.4 ± 1.7†</td>
<td>13.5 ± 0.9*</td>
<td>12.6 ± 1.2</td>
<td>13.0 ± 1.2</td>
</tr>
<tr>
<td>Recovery duration (min after discontinuing anesthesia)</td>
<td>17 ± 6‡</td>
<td>14 ± 4</td>
<td>12 ± 3*</td>
<td>11 ± 2*</td>
</tr>
<tr>
<td>Nausea/vomiting (%)</td>
<td>15/0</td>
<td>0/0</td>
<td>50‡/25</td>
<td>55†/30</td>
</tr>
<tr>
<td>Postoperative ondansetron (4 mg/8 mg)</td>
<td>2/0</td>
<td>0/0</td>
<td>6/0</td>
<td>1/3</td>
</tr>
<tr>
<td>Induction drug cost ($)</td>
<td>5.4 ± 0.9†‡</td>
<td>14.2 ± 6.1†‡</td>
<td>9.8 ± 1.2‡†</td>
<td>4.4 ± 0.2‡†</td>
</tr>
<tr>
<td>Sevoflurane maintenance ($)</td>
<td>6.7 ± 6.2</td>
<td>5.8 ± 3.1</td>
<td>8.1 ± 4.6</td>
<td>6.5 ± 5.7</td>
</tr>
<tr>
<td>Cost of ondansetron ($)</td>
<td>2.4 ± 7.4</td>
<td>0 ± 0</td>
<td>7.2 ± 11.3</td>
<td>8.4 ± 17.9</td>
</tr>
<tr>
<td>Total: induction, sevoflurane, ondansetron ($)</td>
<td>14.5 ± 9.5‡</td>
<td>20.1 ± 7.8</td>
<td>25.1 ± 12.1*</td>
<td>19.4 ± 18.1</td>
</tr>
</tbody>
</table>

Data are presented as means ± sd.
SpO₂ = pulse-oximeter saturation.
* Different from thiopental.
† Different from propofol.
‡ Different from Sevo/Circle.

Dioxide concentration simultaneously increased to approximately 30 mm Hg. Increased inspired PₐCO₂ presumably stimulated ventilation, although only a single episode of breath-holding was observed among the 80 patients who participated in the study. In contrast to the expected decrease in sevoflurane and increase in carbon dioxide, the oxygen concentration actually increased slightly during induction because gas in the rebreathing bag was diluted with oxygen expired from the patients’ lungs (which was initially near 100% oxygen). As a result, oxygen saturation remained normal throughout induction.

Induction of anesthesia was rapid and facile with each of the four tested methods, and there were no clinically important or statistically significant differences among them. This is consistent with a previous study, which indicated that laryngeal mask insertion characteristics were comparable with thiopental (4 mg/kg), propofol (2 mg/kg), and 6% sevoflurane (8). Postoperative awakening, however, was fastest in patients given sevoflurane. Prolonged awakening after propofol was expected based on the drug’s pharmacokinetics (9). However, it was surprising that awakening after propofol induction required nearly the same amount of time (10,11). Our data indicate that induction times are comparable with each tested method but that awakening after sevoflurane is faster. Recovery duration was significantly longer in patients given thiopental than in those given sevoflurane, which again is consistent with the drugs’ pharmacokinetics.

As expected, the cost of induction drugs differed significantly among the tested methods, with sevoflurane from the rebreathing bag and thiopental being the least expensive and propofol being the most expensive. However, we did not anticipate the high incidence of nausea and vomiting after sevoflurane administration and the consequent need for antiemetic therapy. Because ondansetron is so expensive, total drug cost was actually greater with sevoflurane than propofol. Thiopental, which was associated with little nausea and vomiting, was the least expensive method overall.

We studied patients undergoing extremely brief operations to maximize the effects of induction technique on induction speed, awakening time, recovery duration, and cost. The four techniques we studied were associated with statistically significant differences in some of these factors, and some of the differences were also clinically important. Nonetheless, no one technique was obviously superior; each had advantages and disadvantages. Our data thus suggest that the anesthetic induction technique for individual patients may best be chosen based on the relative importance of awakening time, recovery duration, cost, and the avoidance of nausea and vomiting.

The major limitation of our protocol is that recovery characteristics depend strongly on the type and duration of surgery. Our operations were all short; induction technique will have progressively less influence on postanesthetic recovery as the duration of surgery increases. Our thiopental and propofol results are specific for the doses we used, which were typical and have been used in numerous previous studies. However, we can assume that larger thiopental and propofol doses would produce faster and smoother inductions but slower recoveries.
An important limitation of our cost calculations is that total costs would differ substantially had we used a less expensive and equally effective (12) antiemetic such as droperidol. Because droperidol is so inexpensive, total cost would then roughly equal the sum of induction and maintenance costs. Our estimates were based on average United States wholesale pharmacy costs; costs in individual hospitals and in other countries may vary, and the variation in some cases may be substantial. Actual costs in a given hospital can be calculated by applying the appropriate ratios of actual cost to estimated cost to Table 3. Drug expenses are a relatively small fraction of the costs associated with anesthetic administration and an even smaller fraction of total surgical cost. Nonetheless, it is reasonable to use inexpensive drugs when there seems to be little benefit from more expensive ones. We also did not include the cost of the 5-L rebreathing bag in our calculation; using a disposable bag would add a small cost to the Sevo/Bag method.

In summary, induction times were similar with each of the four techniques. Recovery duration was shortest with sevoflurane, intermediate with propofol, and longest with thiopental. Induction drug costs were lowest with Sevo/Bag and thiopental, intermediate with Sevo/Circle, and highest with propofol. However, sevoflurane by either method caused the most nausea and vomiting that required treatment with ondansetron. Consequently, total drug cost was least with thiopental, intermediate with Sevo/Bag and propofol, and greatest with Sevo/Circle. No single technique was obviously superior, which suggests that the anesthetic induction technique for individual patients may best be chosen based on the relative importance of recovery duration, cost, and avoidance of nausea and vomiting.

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References