

Substitution of Isoflurane by Sevoflurane Toward the End of Long Surgeries Is Cost Effective

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ABSTRACT

The lower solubility of sevoflurane allows a more rapid emergence from anesthesia than after anesthesia with more soluble but less expensive anesthetic isoflurane. Cost control in anesthesia is no longer an option; it is a necessity. We substitute sevoflurane for isoflurane toward the end of anesthesia for operations longer than 3 hours in an attempt to combine the cost effectiveness of isoflurane with rapid emergence from sevoflurane.

Sixty patients undergoing long abdominoplastic and ENT surgeries were randomly equally divided into three groups: group I (isoflurane group), group II (crossover group) where isoflurane was substituted by sevoflurane during the last 30 minutes of the operation and group III (sevoflurane group). A fresh gas flow of 2 L/min as 60% N₂O in O₂ was used for maintenance of anesthesia. Consumption of volatile anesthetics was measured by weighing the vaporizers with a precision weighing machine and recovery variables were recorded. The times for spontaneous breathing, times to opening eyes, squeeze a finger on command, times for extubation, orientation, times to read Aldrete score ≥ 9 and time to discharge from PACU, all these times were significantly longer in isoflurane group than the crossover and sevoflurane groups and no significant difference between crossover and isoflurane groups. Cost was significantly higher in sevoflurane group (1.242 EP per minute anesthesia). The costs among the other two groups did not differ significantly (0.319 EP/min for isoflurane group and 0.344 EP/min for crossover group). So sevoflurane based anesthesia was associated with the highest costs and faster recovery. In conclusion, by changing from isoflurane to sevoflurane toward the end of long anesthesia, we can accelerate recovery and decrease its expenditures without compromising the measured patient outcomes.

INTRODUCTION

Cost containment is an important issue in medicine today and the ability to control costs and maintain quality patient care, presents a challenge to practitioners.

The relatively low solubility of newer inhaled anesthetics such as sevoflurane and desflurane allows rapid elimination after their use is discontinued. This results in an earlier emergence than with the older anesthetics with higher solubilities, such as isoflurane. However, their higher cost may offset this potential advantage of newer anesthetics.⁽¹⁾

Patients undergoing abdomino-plastic, ENT and maxillofacial surgeries are more liable to suffer inadequate lung ventilation due to splinting of the diaphragm and airway obstruction, respectively. These problems are minimized by more rapid recovery from anesthesia and consequently early establishment of respiratory functions.

Also, as the duration of anesthesia increases, emergence becomes increasingly dependent on total tissue uptake of the inhalational anesthetic agent, which is a

function of agent solubility, the average concentration used, and the duration of exposure to the anesthetic. So early emergence is expected by substitution of highly soluble volatile anesthetic by less soluble volatile anesthetic toward the end of long surgeries.⁽²⁾

In an attempt to combine the advantage of the more rapid recovery of sevoflurane with the advantage of the lesser cost of isoflurane, we substitute sevoflurane for isoflurane toward the end of anesthesia for operations longer than 3 hours, to determine whether this substitution would accelerate recovery and decrease the cost than when using isoflurane or sevoflurane alone, respectively.

PATIENTS AND METHODS

The study was done in the Main University Hospital of Menofiya and it was approved by the local ethics committee. After informed consent, 60 ASA status I-II patients aged 20-60 yr, undergoing long abdomenoplastic, maxillofacial or ENT surgeries, were enrolled in

this study. The patients were randomly categorized into three groups to receive isoflurane, isoflurane changed to sevoflurane in last 30 min or sevoflurane as a maintenance anesthetic. Exclusion criteria were renal insufficiency creatinine >1.5 mg/dL, liver dysfunction (aspartate aminotransferase >40 U/L, alanine aminotransferase >40 U/L), abuse of alcohol and drugs, and documented coronary or valvular heart diseases

All patients were premedicated with 1-2 mg midazolam I.V. 30 min. before the start of anesthesia. The patients were randomly categorized into three groups:

- * In **Group 1** (isoflurane group) (n= 20), anesthesia was induced by using 1 ug/kg fentanyl, 0.5 mg/kg atracurium, and 2 mg/kg propofol. Anesthesia was maintained by isoflurane, which was titrated to the clinical effects (step wise increase in dose when heart rate increased >70 bpm, systolic blood pressure increased >10mmHg or sweating occurred). Fentanyl was also added when anesthesia seemed inadequate. Atracurium was added as needed to maintain a single twitch on the neurostimulator (Train of four (ToF)).
- * **Group 2** (crossover or shift group) (n= 20), the same procedure for induction and maintenance of anesthesia was used, except that isoflurane was substituted by sevoflurane during the last 30 minutes of the operation for maintenance of anesthesia.
- * **Group 3** (sevoflurane group) (n=20), the same procedure for induction and maintenance of anesthesia was used, except that sevoflurane was administered for maintenance of anesthesia.

All patients were mechanically ventilated with 60% N₂O in oxygen to maintain SaO₂ >95% (continuous oximetry). Ventilation patterns were adjusted to keep end-expiratory CO₂ between 35 and 40 mmHg (continuous capnography). A constant fresh gas flow of 2 L/min was used during maintenance (steady state) of anesthesia in all groups. Crystalloids and colloids solutions were infused in all patients as needed. At the end of the surgical procedure, the residual neuromuscular blockade was reversed with I.V. neostigmine and glycopyrrolate. The vaporizer was turned off, and the fresh gas flow was increased to 2 L/min. Crystalloids and colloids solutions were infused in all patients as needed. At the end of the surgical procedure, the residual neuromuscular blockade was reversed with I.V. neostigmine and glycopyrrolate. The vaporizer was turned off, and the fresh gas flow was increased to 2 L/min.

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- Fixed costs for anesthesia machines and monitoring equipment or other overhead costs (e.g. hospital overheads) were not taken into consideration.
- Mechanical ventilation was continued until the return of spontaneous ventilation. The trachea was extubated when adequate spontaneous ventilation tidal volume >4 ml/kg, and patient response to verbal command were established. The time for spontaneous breathing and for extubation were recorded.
- Recovery endpoints were defined as follows:
 1. Emergence: time from discontinuation of anesthesia delivery (i.e. vaporizer turned off) to opening of eyes.
 2. Response to commands: time from discontinuation of anesthesia delivery to correct response to verbal commands (e.g. hand squeeze).
 3. Orientation: time from discontinuation of anesthesia delivery to orientation (e.g., stating name and date of birth or current location).
 4. Time to reach Aldrete score \geq 9. Aldrete score assess SpO₂ (or color), consciousness, circulation, respiration and motor activity, where 0= minimal score and 10= best score.
 5. Time to discharge from the PACU with the following discharge criteria: fulfilled easy arousability, full orientation, the ability to maintain and protect the airway, stable vital signs for at least 30

minutes, the ability to call for help if necessary and no obvious surgical complications (such as active bleeding).

- Data are presented as mean SD. Statistics were performed using SPSS (Statistical Package for Social Sciences) software, version 10.1. P values <0.05 were considered significant.

RESULTS

- Demographics and operative data: (Table I)
Demographics including number of patients age, body weight, body height did not differ statistically between the three groups.
 - The duration of anesthesia administration did not differ statistically between the three groups (Table I).
 - Recovery variables: (Table II)
 - Times for spontaneous breathing was significantly longer in isoflurane group than the cross over and sevoflurane groups and no significant difference between cross over and sevoflurane group.
 - Times for extubation was significantly longer in isoflurane group than crossover and sevoflurane groups and no significant difference between crossover and sevoflurane group.
 - Times to opening eyes was significantly longer in isoflurane group than the crossover and sevoflurane groups and no significant difference between crossover and sevoflurane groups.
 - Times to squeeze a finger on command was significantly longer in isoflurane group than the cross-over group and sevoflurane group and no statistically significant difference between crossover group and sevoflurane group.
 - Times for orientation was significantly longer in isoflurane group than crossover group and sevoflurane, but no significant difference between the crossover and sevoflurane group.
 - Times to reach Aldrete score > 9 was statistically significant longer in isoflurane group than cross-over and sevoflurane group but no significant difference between crossover group and sevoflurane group.
 - Time to discharge from PACU there was no significant difference between the three groups.
 - The SPO₂, EtCO₂ and hemo-dynamic parameters were within normal throughout the procedures.
 - Cost of consumed volatile anesthetic drugs.(Table III)
 - * In isoflurane group the total volume of isoflurane in the 20 cases was 848.8 ml and mean volume used per one minute anesthesia was 0.2 ml/minute with total cost of 1356.8 Egyptian pound per 20 cases and cost of 0.319 EP per minute anesthesia.
 - * In crossover group the total volume of isoflurane consumed in 20 cases was 680 ml in addition to sevoflurane 180 ml and a mean volumes used/min anesthesia were 0.2 and 0.3 ml/min respectively with a total cost of 1376 Egyptian pound per 20 case and a cost of 0.344 EP per minute anesthesia.
 - * In sevoflurane group the total volume of sevoflurane consumed in 20 cases was 1248 ml and mean volume used/min anesthesia was 0.3 ml/min with a total cost of 4992 EP and a cost of 1.242 EP/minute.
- So the cost of consumed volatile anesthetics was significantly higher in sevoflurane group than crossover and isoflurane groups and no significant difference between cross over and isoflurane group.

Table I: Demographics and Intraoperative data of the studied groups

	Isoflurane group	Crossover group	Sevoflurane group
Number M/F	20 (10/10)	20 ±(9/11)	20±(11/9)
Age (yr)	33±18	38 ±28	36±21
Body weight (kg) Mean SD	81.7±13	79.3±11	83.9±14
Body height (cm) Mean SD	171±9.2	173±12	169±11.9
Duration of anesthesia administration (min) Mean SD	212.2±40	201.1±37	208.6±50

Table II: Recovery parameters in the studied groups

	Isoflurane group	Crossover group	Sevoflurane group
Time to spontaneous breathing (min)	18.5±9.7*	12.7±6.5	11.2±7.3
Time to opening eyes on command (min)	19.7±8.1*	14.1±7.4	13.3±6.2
Time to squeeze a finger on command (min)	21.4±10.3*	15.3±6.9	14.8±7.8
Time for extubation (min)	22.7 9.9*	16.4±8.5	15.1±7.9
Time for stating name on command (min)	27.4±12.1*	20.3±9.1	18.1±9.7
Time to reach Aldrete score >9 (min)	32.5±14.1*	23.2±11.8	21.1±9.7
Time to discharge from PACU (min)	64.7±19.2	60.3±17.2	59.7 81

where * significant difference (p<0.05).

Table III: Cost of consumed volatile anesthetic drugs in the studied groups.

	Isoflurane group	Isoflurane-Sevoflurane group	Sevoflurane group
Total use of anesthetics in all patients (ml)	848.8	680 + 180	1248
Volume of anesthetics per minute (ml)	0.2	0.2 + 0.3	0.3
Total cost of inhalational anesthetics vaporized for all operations (EP)	1356.8	1376	4992*
cost of inhalational anesthetics/ minute (EP)	0.319	0.344	1.242*

where * significant difference (p<0.05)

DISCUSSION

Today, the financial consequences of treating patients seem to be as important as the medical consequences. Although several innovative techniques have been developed in anesthesia e.g. introduction of new volatile anesthetics, standard anesthetic regimens are still used because of fear of increasing costs. It is challenging to reduce the costs of anesthesia while maintaining or even improving quality.⁽⁴⁾ Sevoflurane and desflurane are reported to have an improved recovery profile compared to the older volatile anesthetics because of lower blood gas solubility. However, at equivalent fresh gas flow rates, sevoflurane and desflurane

cost 2-3 times more than equipotent concentrations of isoflurane. Therefore, to justify the increased expense of the newer volatile anesthetics a clear cost: benefit ratio need to be shown.⁽⁵⁾

During anesthesia, fresh gas flow must be frequently changed; low flow rates require too long for equilibration to a new concentration. For example, immediately after tracheal intubation and before skin incision, flow rate and end-tidal concentrations are modified to increase the depth of anesthesia rapidly. Thus, we measured the consumption of volatile anesthetics with the help of precision weighing machine, which is able to record changes up to 0.1 g although the

vaporizers individually weigh up to 10 kg. This technique allows precise measurement of the consumed liquid quantity of inhaled anesthetics.⁽⁴⁾

The major findings of this study are that when using partial rebreathing system, substituting a less soluble anesthetic (sevoflurane) for a more soluble anesthetic (isoflurane) for the last 30 minutes of a more than 180-minute anesthesia produces a substantial (significant) improvement in early recovery and better respiratory parameters than when using isoflurane alone and on the other hand less cost than when using sevoflurane alone, so we can gain the advantages of sevoflurane (rapid recovery) and isoflurane (low price).

In agreement with our study Ebert et al⁽⁶⁾ found significant differences in early recovery endpoints between sevoflurane and isoflurane anesthesia. In patients anesthetized with sevoflurane, emergence from anesthesia occurred an average of 3.3 min earlier, and orientation occurred 4 min earlier than in patients anesthetized with isoflurane. This kinetic advantage of sevoflurane over isoflurane would be particularly manifest in surgery of longer duration (three to five hours) leading to earlier recovery.

Also, Gauthier et al⁽⁷⁾ found that patients who received sevoflurane as their maintenance anesthetic for long-duration neurological surgery had a faster emergence than patients who received isoflurane.

Wissing et al,⁽⁸⁾ stated that the apparent volumes of distribution were clearly smaller for sevoflurane than isoflurane and this was most pronounced for the peripheral volume. Distribution from the central to the peripheral compartment was much more rapid for isoflurane than for sevoflurane, whereas the redistribution was only slightly greater for sevoflurane than isoflurane. This difference may be explained by a 30% longer mean duration of isoflurane anesthesia.

Gong et al.,⁽¹⁾ concluded that in rats breathing from a non-rebreathing system,

substitution of desflurane for isoflurane toward the end of anesthesia improved early recovery but produced a much smaller improvement in later recovery.

Substitution of sevoflurane for isoflurane toward the end of long operations as we did in our study potentially decreased the risk of nephrotoxicity associated with long duration anesthesia with sevoflurane where Eger et al⁽⁹⁾ found that sevoflurane undergoes biodegradation to inorganic fluoride and degradation by carbon dioxide absorbents to vinyl ether called "Compound A". Both inorganic fluoride and compound A can produce renal injury.⁽¹⁰⁾

Early recovery with substitution of sevoflurane for isoflurane toward the end of anesthesia than after isoflurane alone is very important in certain situations e.g. abdominoplastic surgeries where patients are usually obese and plication of the abdominal wall splints the diaphragm which if associated with respiratory center depression due to delayed recovery from anesthetic can lead to severe hypoventilation and hypoxia. Also in maxillofacial and ENT operations, we usually need early recovery from anesthesia where the patient can adequately maintain his airway.⁽¹¹⁾

Cost control in anesthesia is no longer an option; it is a necessity.⁽⁴⁾ In the present study we demonstrated that substitution of sevoflurane for isoflurane toward the end of long operations decreased the cost of anesthetics than when using sevoflurane all over the procedures. This is because in our institution sevoflurane to isoflurane pricing ratio is 3:1.

In agreement with our study Ries et al⁽¹²⁾ found that volatile consumption and cost were greater for sevoflurane anesthesia than with isoflurane because of the four-fold sevoflurane-to- isoflurane cost difference that was the product of two ratios, the ratio of consumption, 2:1; and the ratio of institutional price, 2:1.

In contrast to our study Boldt et al⁽⁶⁾ found that the cost of the new inhaled anesthetics sevoflurane and desflurane did not differ from those of a standard, isoflurane-based anesthesia regimen, this may be due to the nearly equal prices of equal volumes of sevoflurane and isoflurane in their institution where 250 ml sevoflurane price was \$155 and 250 ml isoflurane price was \$142.

Lockwood and White,⁽¹³⁾ in agreement with our study stated that isoflurane is almost certain to be much less expensive than desflurane and sevoflurane and that sevoflurane would cost the same as desflurane and if a closed system is used isoflurane is almost certain to be less expensive than sevoflurane and would probably be less expensive than desflurane.

CONCLUSION

In conclusion, by changing from isoflurane to sevoflurane toward the end of long anesthesia, we can accelerate recovery and decrease in expenditures without compromising the measured patient outcomes.

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