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Effects of reduction of carrier gas flow rate on sevoflurane and isoflurane consumption and costs

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Abstract

Purpose. To evaluate whether sevoflurane and isoflurane consumption would be actually halved by halving the carrier gas flow rate, as predicted by a theoretical model, we measured the consumed volume of liquid sevoflurane and isoflurane and total costs of anesthetic gas at carrier gas flow rates of 3 and 6 l·min^{-1}.

Methods. Eighty patients of ASA physical status I or II were randomly assigned to one of four groups: sevoflurane at 3 or 6 l·min^{-1} and isoflurane at 3 or 6 l·min^{-1}. Anesthesia was induced with thiamylal and maintained with sevoflurane or isoflurane, as well as with nitrous oxide in oxygen. The consumption of sevoflurane and isoflurane was measured by weighing the bottle of liquid agent, which was greater in the groups receiving 6 l·min^{-1} gas than in those receiving 3 l·min^{-1}.

Results. Halving the carrier gas flow rate reduced the consumption of sevoflurane by 41.8% and that of isoflurane by 52.6%. It also reduced the total cost by 44.3% for sevoflurane and 49.2% for isoflurane.

Conclusion. Halving the carrier gas flow rates halved the consumption of isoflurane but not of sevoflurane, indicating that factors other than carrier gas flow rates are involved in determining consumption in the clinical setting.

Key words: Anesthetic cost, Isoflurane, Sevoflurane, Carrier gas flow

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Introduction

Theoretical models are commonly used to determine the consumption of volatile anesthetics [1]. However, the theoretical values may differ from the actual ones because of rather complex factors involved in the clinical setting. The consumed volume of liquid volatile anesthetics is dictated by the individual characteristics of the anesthetics and the rate of carrier gas flow [2]. Other individual characteristics, such as the minimum alveolar concentration (MAC) and the blood–gas partition coefficient, also partly determine the consumption of volatile anesthetics. Theoretically, sevoflurane would be consumed at a rate approximately 1.78 times that of isoflurane because the MACs for sevoflurane and isoflurane are 2.05% and 1.15%, respectively (2.05/1.15 = 1.78) [3,4]. The depth of anesthesia is, however, controlled more easily and quickly with sevoflurane than with isoflurane, because the blood–gas partition coefficient of sevoflurane (0.63) is less than that of isoflurane (1.4). Because of this difference between sevoflurane and isoflurane, sevoflurane should be consumed at a rate less than 1.78 times that of isoflurane for the same carrier gas flow rate.

The volume of volatile anesthetic used is also directly proportional to carrier gas flow rate; decreasing the rate lowers the consumption of anesthetics. This relationship is particularly important for anesthetics with high MACs. Low-flow anesthesia is, therefore, recommended for economic and environmental reasons [5]. One major drawback of low-flow anesthesia is that the depth of anesthesia is less easily adjusted. Halving the carrier gas flow rate would double the time needed to reach the desired inspired concentration of an anesthetic, and would increase even more the time needed to achieve the desired end-tidal concentration of an anesthetic. A volatile anesthetic with a lower blood–gas partition coefficient would, therefore, accelerate any increase of end-tidal concentration of the anesthetic

more than that of an anesthetic with a higher coefficient when low-flow anesthesia is employed. Consequently, reducing the rate of flow should reduce the rate of consumption of sevoflurane more than that of isoflurane.

We measured the consumed volume of liquid sevoflurane and isoflurane at two different carrier gas flow rates, 6 and 3 l·min^{-1}. In addition, we calculated the total costs of both anesthetics and carrier gases delivered at the two carrier gas flow rates. We tested the hypotheses that (1) the consumption of sevoflurane would be less than 1.8 times that of isoflurane at the same carrier gas flow rate, and (2) halving the carrier gas flow rate would be of greater benefit with sevoflurane than with isoflurane.

Materials and methods

With the approval of the research committee of Kushiro Municipal General Hospital and after obtaining informed consent from the patients, we studied 80 patients of ASA physical status I or II, who were between 20 and 65 years old and who were scheduled for elective oropharyngeal or oral procedures under general anesthesia. The patients were randomly assigned to one of four groups of 20 patients each by drawing shuffled coded envelopes: sevoflurane at 6 l·min^{-1} carrier gas flow (Sevo-6), sevoflurane at 3 l·min^{-1} carrier gas flow (Sevo-3), isoflurane at 6 l·min^{-1} carrier gas flow (Iso-6), and isoflurane at 3 l·min^{-1} carrier gas flow (Iso-3). All patients received 2.5 mg midazolam and 0.5 mg atropine intramuscularly for premedication.

Anesthesia was induced with 3 mg·kg^{-1} thiamylal and 0.1 mg·kg^{-1} vecuronium, and was followed by mask inhalation of sevoflurane or isoflurane (up to 2.5 MAC of the inspired concentration) and nitrous oxide (4 l·min^{-1}) in oxygen (2 l·min^{-1}). After endotracheal intubation, the lungs were mechanically ventilated at 10 breaths·min^{-1} to maintain end-tidal carbon dioxide tension between 35 and 40 mmHg. Anesthesia was maintained with either sevoflurane or isoflurane, and 66% nitrous oxide in oxygen at total fresh gas flows of either 3 or 6 l·min^{-1}. In the Sevo-3 and Iso-3 groups, however, the total fresh gas flow was kept at 6 l·min^{-1} for the first 8 min of the anesthetic course to achieve the desired level of anesthesia quickly [4]. All patients were monitored with intermittent noninvasive blood pressure measurements and continuous electrocardiography. Heart rate (HR) and systolic blood pressure (SBP) were measured before the induction of anesthesia and every 5 min during anesthesia. An Ohmeda RGM (respiratory gas monitor) 5250 (Ohmeda, Salt Lake City, UT, USA) was used to monitor continuous capnography, inspired and end-tidal concentrations of anesthetics, and hemoglobin oxygen saturation. We used a semiclosed anesthetic circuit system (Excel 110, Ohmeda, Salt Lake City, UT, USA) equipped with SevoTec 5 and IsoTec 5 continuous flow vaporizers (Ohmeda, BOC Health Care, West Yorkshire, UK). Two anesthetists participated in this study: one to administer the anesthetic, and the other to measure the consumption. The goal of the anesthetist was to provide an adequate depth of anesthesia only by adjusting the inspired concentration of sevoflurane or isoflurane according to the changes of hemodynamic parameters (hypotension, hypertension, bradycardia, or tachycardia). If not treated by sevoflurane or isoflurane alone, nicardipine or ephedrine was administered to keep the blood pressure within the appropriate range. No opioids or regional blocks were used.

We assessed the hemodynamic variability to confirm that comparable levels of anesthesia were administered to all groups. The variability of HR and SBP was evaluated by the coefficient of variation, calculated by dividing the standard deviation by the mean value of each measurement of HR or SBP for 120 min, and expressed as a percentage.

The consumption of sevoflurane or isoflurane was measured at 30, 60, and 120 min after administration. At the beginning of anesthesia, a vaporizer was filled with the volatile agent and refilled at 30, 60, and 120 min after the start of administration. The bottle of liquid agent was weighed on an electronic scale before and after refilling. The volume of liquid agent consumed was calculated by dividing the weight loss of the bottle by the density of the agent (isoflurane, 1.510 g·ml^{-1}; sevoflurane, 1.525 g·ml^{-1}). The hourly consumption was calculated on the basis of the results at 120 min. The total cost of anesthetic, including nitrous oxide, oxygen, and either sevoflurane or isoflurane, was calculated using the following formula:

$$S = C1 \cdot A + C2 \cdot F1 \cdot T + C3 \cdot F2 \cdot T,$$

where S is total cost, C1 is the cost of the liquid agent (¥·ml^{-1}), C2 is the cost of oxygen (¥·l^{-1}), C3 is the cost of nitrous oxide (¥·l^{-1}), A is the volatile anesthetic consumed at three time points (ml), T is duration of usage (min), F1 is oxygen flow (l·min^{-1}), and F2 is nitrous oxide flow (l·min^{-1}). We added ¥159 to the Sevo-3 and Iso-3 groups because we used carrier gas flow rates of 6 l·min^{-1} for the first 8 min. In our hospital, both sevoflurane and isoflurane cost ¥107.4·ml^{-1}, oxygen costs ¥0.24·l^{-1}, and nitrous oxide costs ¥19.84·l^{-1}. We did not consider the other costs, such as equipment, other medications, and personnel expenses.

Patient characteristics and hemodynamic variability were analyzed using the chi-square test or one-way analysis of variance. The consumption of sevoflurane and isoflurane was analyzed using two-way analysis of

variance with comparisons between the groups receiving 6 and 3 l·min^{-1} carries gas flow rates, and between the sevoflurane and isoflurane groups with the same carrier gas flow rates. All data are presented as mean ± SD, with significance defined as $P < 0.05$.

Results

The demographic characteristics of the 80 patients are summarized in Table 1. The four groups did not differ significantly in age, sex, height, weight, or type of surgical procedure. Four patients with sevoflurane and six patients with isoflurane received nicardipine to treat hypertension, and one patient with isoflurane received ephedrine to treat hypotension after endotracheal intubation. No patients received nicardipine or ephedrine during surgery. Intraoperative hemodynamic values are summarized in Table 2. They are comparable between the groups. No intergroup differences were observed in the variability of HR and SAP ($P = 0.162$ and $P = 0.545$, respectively).

Anesthetic consumption in the four groups is summarized in Table 3. Significantly more sevoflurane than isoflurane was consumed, irrespective of carrier gas flow rate ($P < 0.001$). In the Sevo-6 group, sevoflurane consumption was approximately 1.2 times greater than that of isoflurane. Halving the carrier gas flow lowered the consumption of both anesthetics ($P < 0.001$), and the average consumption of sevoflurane and isoflurane per hour was reduced by 41.7% and 52.6%, respectively. The consumption of sevoflurane was almost 1.5 times greater than that of isoflurane at a carrier gas flow rate of 3 l·min^{-1}.

Table 1. Demographic and surgical characteristics of patients undergoing oral or oropharyngeal surgery with sevoflurane and isoflurane anesthesia at high- or low-flow rates

	Sevoflurane		Isoflurane	
Characteristic	6 l·min^{-1} ($n = 20$)	3 l·min^{-1} ($n = 20$)	6 l·min^{-1} ($n = 20$)	3 l·min^{-1} ($n = 20$)
Demographics				
Age (yr)	41 ± 11	47 ± 11	44 ± 12	46 ± 10
Weight (kg)	64 ± 13	61 ± 10	64 ± 11	59 ± 10
Height (cm)	163 ± 8	162 ± 8	161 ± 9	160 ± 11
Sex (M/F)	12/8	12/8	12/8	10/10
Type of operation (n)				
Total sinusectomy	8	8	8	9
Neck tumor removal	6	10	8	5
Thyroidectomy	2	1	1	3
Extraction of third molar	1	1	3	2
Mandibular fracture repair	3	0	0	1

Data are mean ± SD or number. There were no significant differences between groups.

Table 2. Perioperative variability of heart rate and systolic blood pressure in four groups 120 min after initiation of anesthesia

	Sevoflurane		Isoflurane	
Variable	6 l·min^{-1} ($n = 20$)	3 l·min^{-1} ($n = 20$)	6 l·min^{-1} ($n = 20$)	3 l·min^{-1} ($n = 20$)
Heart rate				
Maximum (bpm)	111 ± 13	112 ± 14	119 ± 20	108 ± 17
Minimum (bpm)	75 ± 14	71 ± 11	71 ± 15	68 ± 10
CV (%)	9.7 ± 3.1	11.5 ± 5.4	12.6 ± 5.1	12.4 ± 4.1
Range of CV	3.1 – 15.0	5.2 – 29.5	5.1 – 25.6	4.1 – 23.5
Systolic blood pressure				
Maximum (mmHg)	155 ± 18	153 ± 25	161 ± 24	150 ± 19
Minimum (mmHg)	100 ± 10	96 ± 12	96 ± 24	99 ± 12
CV (%)	11.3 ± 3.4	12.5 ± 4.5	12.9 ± 6.4	11.0 ± 4.4
Range of CV	3.4 – 21.9	4.5 – 22.9	5.7 – 27.7	4.3 – 23.1

CV, Coefficient of variation. Data are means ± SD. There were no significant differences between groups.

Table 3. Consumption of sevoflurane and isoflurane at three time points after initiation of anesthesia

	Sevoflurane consumption (ml)		Isoflurane consumption (ml)[a]	
Time (min)	6 l·min^{-1}	3 l·min^{-1}[b]	6 l·min^{-1}	3 l·min^{-1}[b]
30	26.2 ± 6.3	17.5 ± 3.8	20.3 ± 5.9	10.2 ± 3.6
60	45.3 ± 8.0	28.5 ± 5.0	37.2 ± 7.8	17.3 ± 4.8
120	80.7 ± 13.4	47.0 ± 5.9	66.2 ± 12.2	31.4 ± 8.0
Rate of consumption (ml·h^{-1})	40.3 ± 6.7	23.5 ± 2.9	33.1 ± 6.2	15.7 ± 4.0

Data are mean ± SD.
[a] Difference between sevoflurane and isoflurane groups with the same carrier gas flow rate, $P < 0.001$.
[b] Difference between 3 and 6 l·min^{-1} carrier gas flow rate groups with the same anesthetic, $P < 0.001$.

The total costs for the four groups are shown in Fig. 1. The total costs consisted of the costs of the anesthetics (sevoflurane or isoflurane) and the carrier gases (nitrous oxide and oxygen), but not the costs of equipment or drugs administered during anesthesia. The mean total hourly costs in the Sevo-6 and Sevo-3 groups were ¥9123 and ¥5077, respectively. The mean total hourly costs in the Iso-6 and Iso-3 groups were ¥8345 and ¥4240, respectively. Halving the carrier gas flow rate reduced costs by 44.3% and 49.2% for sevoflurane and isoflurane anesthesia, respectively. At carrier gas flow rates of both 6 and 3 l·min^{-1}, the mean hourly cost of sevoflurane anesthesia was significantly higher than that of isoflurane anesthesia ($P < 0.001$ for both comparisons). The hourly costs of nitrous oxide and oxygen were ¥4790 and ¥2554 for high-flow and low-flow rates, respectively, which were 52.5% and 50.3% of the total costs for the Sevo-6 and Sevo-3 groups, respectively, and 57.4% and 60.2% of the total costs for the Iso-6 and Iso-3 groups, respectively.

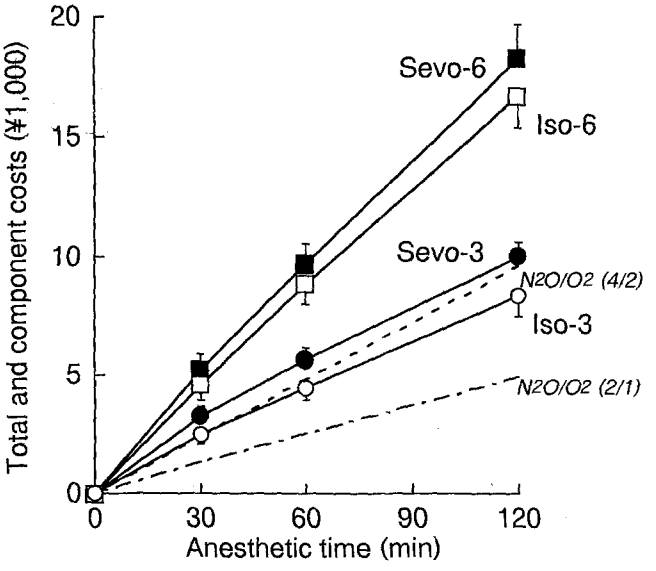

Fig. 1. Total and component costs of anesthetics and carrier gases. Low-flow rates were significantly ($P < 0.001$) less expensive than high-flow rates for both anesthetics. Sevoflurane was significantly ($P < 0.001$) more expensive than isoflurane at both flow rates. The total cost was lowered by reducing the carrier gas flows, which decreased costs by 44.3% and 49.2% in the sevoflurane and isoflurane groups, respectively. The dotted and dashed lines represent the costs of the carrier gas alone, which consists of 4 l·min^{-1} nitrous oxide/2 l·min^{-1} oxygen and 2 l·min^{-1} nitrous oxide/1 l·min^{-1} oxygen. The cost of the carrier gas amounted to half the total anesthetic cost. Results are presented as means ± SD

Discussion

We compared the consumption of sevoflurane and isoflurane at two different total gas flow rates, 6 and 3 l·min^{-1}, using a popular semiclosed anesthesia system. Although decreasing the carrier gas flow rate provided an acceptable quality of anesthesia, decreasing the consumption of sevoflurane and isoflurane compared with the conventional high-flow anesthesia technique, this strategy was less effective with sevoflurane anesthesia than with isoflurane anesthesia.

One of our initial hypotheses was that the consumption of sevoflurane would be less than 1.78 times that of isoflurane. As expected, the actual consumption of sevoflurane was approximately 1.2 times greater than that of isoflurane. Because sevoflurane has a lower blood–gas partition coefficient than isoflurane, the depth of anesthesia can be more rapidly adjusted, which may decrease the consumption of sevoflurane.

We also hypothesized that, in terms of savings in consumption, decreasing the carrier gas flow rate would be more beneficial in sevoflurane anesthesia than in isoflurane anesthesia. However, our results showed that the consumption ratio of sevoflurane to isoflurane was greater in the 3 l·min^{-1} carrier gas flow groups (1.49) than in the 6 l·min^{-1} groups (1.21). In addition, the difference in consumption between 6 l·min^{-1} and 3 l·min^{-1} was always smaller during sevoflurane than isoflurane anesthesia. Halving the carrier gas flow rate decreased the consumption of isoflurane more than that of sevoflurane.

Assuming that sevoflurane and isoflurane are identical except for different MACs, the consumption of sevoflurane should be 1.8 times greater than that of isoflurane. Because the average consumption of isoflurane was 33.1 ml·h^{-1} when the carrier gas flow rate was 6 l·min^{-1}, sevoflurane should have been consumed at a rate of 59.6 ml·h^{-1}. The actual rate of consumption of sevoflurane, however, was 40.3 ml·h^{-1}, only 1.2 times that of isoflurane. More than 30% of sevoflurane consumption could be saved at a carrier gas flow rate of 6 l·min^{-1}, probably because sevoflurane has a smaller blood–gas partition coefficient and produces a depth of anesthesia that can be adjusted more quickly than that of isoflurane. When the carrier gas flow rate was halved, the actual consumption of isoflurane decreased to 15.7 ml·h^{-1}. If the above assumption was used, 28.3 ml·h^{-1} of sevoflurane should have been consumed at a carrier gas flow rate of 3 l·min^{-1}. The actual consumption of sevoflurane at the 3 l·min^{-1} carrier gas flow rate was 23.5 ml·h^{-1}, a 17% reduction, which was smaller than that at a carrier gas flow rate of 6 l·min^{-1}.

Why does sevoflurane reduce savings at low-flow rates compared with high-flow rates? First, during low-flow anesthesia, the time needed for the inspired and the end-tidal concentrations of the anesthetic to approximate the delivery concentration (vaporizer setting) is increased compared with high-flow anesthesia. To compensate for this delay, anesthetists often raise the delivery concentration above that required. Isoflurane, however, can induce hypertension and tachycardia when the inspired concentration is rapidly elevated [6,7]. In contrast, sevoflurane does not have this side effect [8,9]. As a result, when comparing the MAC equivalents, the delivery concentration of sevoflurane from the vaporizer may be greater than that of isoflurane during 3 l·min^{-1} carries gas flow. This greater concentration might explain why the consumption ratio of sevoflurane to isoflurane was greatest after 30 min of anesthesia at a carrier gas flow rate of 3 l·min^{-1}. Second, the consumption of an anesthetic would also depend on how soon the anesthetic could treat hyperdynamic responses induced by surgical stimulation. Low-flow anesthesia would worsen this ability compared with high-flow anesthesia. However, isoflurane would hardly be influenced by attenuating the ability during low-flow anesthesia, because isoflurane would have a lower ability than sevoflurane, even during high-flow anesthesia. This low ability of isoflurane might explain why decreasing the carrier gas flow rate was less beneficial in sevoflurane anesthesia than in isoflurane anesthesia. Finally, at a carrier gas flow rate of 6 l·min^{-1}, less sevoflurane was consumed than expected. This lesser consumption might also explain why the savings in sevoflurane were less than the savings in isoflurane at a carrier gas flow rate of 3 l·min^{-1}. Nevertheless, decreasing the carrier gas flow rate should provide great savings in anesthetic during both sevoflurane and isoflurane anesthesia.

The total costs of the volatile anesthetics and the carrier gases are shown in Fig. 1. As expected, halving the carrier gas flow rate lowered the total anesthetic costs during both sevoflurane and isoflurane anesthesia. Interestingly, half the total anesthetic cost is for nitrous oxide and oxygen. Therefore, decreasing the carrier gas flow rate, especially that of nitrous oxide, contributes greatly to cost savings in anesthesia.

The carrier gas flow rate can be reduced to 0.5 l·min^{-1} or less, because oxygen consumption in anesthetized patients is expected to be approximately 110 ml·min^{-1}·m^{-2} [10]. This relationship suggests that the anesthetic dose can be further reduced by decreasing the carrier gas flow to a minimum. However, the use of the minimum flow rate is limited in clinical practice. First, to produce general anesthesia at flows below 1 l·min^{-1}, new equipment is required, such as closed-circuit anesthesia systems and anesthetic agent monitors. Second, when used in a low-flow circle system at carrier gas flow rates below 2 l·min^{-1}, sevoflurane may increase the concentration of compound A, potentially causing renal injury [11].

The major criticism of our study design relates to the fact that the use of volatile anesthetics might depend on the individual anesthetist and the type of surgery. In clinical settings, it would be hard to standardize the surgical stimuli and the level of the depth of anesthesia. We believe that these variations could be partially compensated for by employing the same anesthetist and selecting patients undergoing similar types of surgery. Furthermore, the comparable variability of HR and SBP could prove that comparable depths of anesthesia were achieved in the groups.

In conclusion, the consumption of sevoflurane was 1.2 times that of isoflurane when a conventional semiclosed anesthesia system was used at a carrier gas flow rate of 6 l·min^{-1}. Although halving the carrier gas flow rate lowered the consumption of both anesthetics, the savings in volatile expenditure were not strictly proportional to

the decrease in the carrier gas flow rate, as a result of pharmacological properties of the agents. Other factors, such as the differences in vaporizer setting patterns between the two anesthetics, also help determine the consumption of anesthetics.

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