

การศึกษาเปรียบเทียบระหว่างยา desflurane และ sevoflurane ในเทคนิคการดมยาสลบโดยใช้อัตราการไหลของก๊าซรวมต่ำในผู้ป่วยที่มีน้ำหนักเกินมาตรฐาน

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Abstract: Low - flow Anesthesia in Overweight Patients: Comparison between Desflurane and Sevoflurane.

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Background: This study aimed to study the kinetic behaviors of desflurane compared with sevoflurane during high - flow wash - in, 1L - flow maintenance and early recovery profile in overweight adult patients. **Methods:** Forty unpremedicated adult patients (Aged 18 - 65, BMI 25 - 35) were enrolled to receive either desflurane or sevoflurane anesthesia. After induction of anesthesia, desflurane 4% or sevoflurane 1.5% in a fresh gas flow of 6 L/min ($N_2O:O_2 = 3:3$) was administered via an absorber circuit. After 10 minutes, the inflow was decreased to 1 L/min ($N_2O:O_2 = 0.5:0.5$)

and desflurane or sevoflurane was then switched to 5% or 2% respectively, and maintained throughout the surgery. At the end of the procedure, the vaporizer was turned off and the inflow was back to 6 L/min of O_2 . Delivered concentration (FD), inspired concentration (FI) and end - tidal concentration (FA) of the anesthetics were measured and recorded from start until extubation. The times from discontinuation of the anesthetics to eye opening on command and extubation were also recorded. **Results:** During high - flow wash - in, the FA/FI were comparable between the two groups with the ratios of

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0.89 + 0.05 vs 0.88 + 0.02 at minute 10. While in low - flow maintenance, the FI of both groups gradually increased with corresponding increases of FA. During the 1st hour of low flow, the FA/FI were not significantly different with the ratios of 0.91 + 0.03 vs 0.89 + 0.02 at minute 60. When back to high flow of O₂ at the end of surgery, desflurane was washed out faster than sevoflurane. There were significant differences between groups with respects to the time to eye opening on command (5.20 ± 1.72 vs 6.73 ± 2.10 min, p = 0.008) and time to extubation (6.62 ± 0.40

vs 8.63 ± 0.45 min, p = 0.002). **Conclusions:** In overweight adult patients, desflurane and sevoflurane provide comparably fast wash-in during the 1st hour of 1 L/min maintenance flow. However, desflurane has faster wash-out and provides faster early recovery.

Keywords: *Anesthetic technique, low - flow anesthesia, overweight, desflurane, sevoflurane*

Introduction

In Thailand, desflurane is a rather new fluorinated anesthetic agent. With its very low blood - gas partition coefficient (0.42) and low oil - gas partition coefficient (27.2), it should allow rapid wash - in and rapid emergence. These would be of benefits to obese patients, in whom the impacts of the coefficients should increase as the duration of anesthesia and body weight increase.¹ Because of the low potency and high price of desflurane, a low - flow technique is recommended. To date, very few low - flow anesthesia in obese patients have been reported. This prospective, randomized, controlled study aimed to study the kinetic behaviors of desflurane compared with sevoflurane during high - flow wash - in, low-flow maintenance, wash - out, and early recovery profile in adult obese patients when no sedative premedication had been used.

Methods

After obtaining approval from the ethical committee of the Faculty, 40 adult patients (ASA

physical status I - II, aged 18 - 65, BMI 25 - 35) scheduled for elective surgery under general endotracheal anesthesia were included in the study. Pregnancy and laparoscopic surgery were excluded. The night before surgery, all eligible patients received oral ranitidine 150 mg. One hour before surgery, ranitidine 50 mg. and metoclopramide 10 mg. were given intravenously. No sedative was given preoperatively. After arrival in the operating room, patient were allocated randomly to receive either desflurane or sevoflurane by means of computer - generated 1 block randomization numbers sealed in an opaque envelope. Standard monitoring (non - invasive automated blood pressure, electro - cardiography and pulse oximetry) was used throughout the study. After induction and intubation with propofol and succinylcholine, 4% desflurane or 1.5% sevoflurane in a fresh gas inflow of 6 L/min (N₂O:O₂ = 3:3) was administered via an absorber circuit in conjunction with rocuronium and fentanyl. Ventilator setting was adjusted to keep the ETCO₂ between 35 - 40 mmHg. An

infrared gas analyzer (AG 90RK, Nihon Kohden) was used to measure the concentration of CO₂, desflurane and sevoflurane. Ten minutes later, the inflow was decreased to 1 L/min (N₂O:O₂ = 0.5:0.5), and the delivered concentration of desflurane or sevoflurane was set to 5% or 2% respectively and maintained throughout the surgery. At the end of surgery, the anesthetic was switched off and the inflow was increased to 6 L/min of O₂. Atropine and neostigmine were then given to antagonize the effect of rocuronium.

Delivered concentration (F_D), inspired concentration (F_I) and end-tidal concentration (F_A) were measured from the start of the anesthetic until extubation and recorded by the attending anesthesiologist who was not in the study team. The measurements were done at the interval of 1 minute during high - flow wash-in, 10 minutes during low - flow, and 30 seconds during wash - out. At the end of surgery, the times to eye opening on command and extubation, patient's ability to state his name on arrival at the recovery unit and discharge time were recorded by another blinded investigator. Continuous data are presented as mean ± SD, whereas categorical data as n, per cent. Statistical analysis was performed using Student's t - test or Fisher's exact test where appropriated. A *P* value of less than 0.05 was considered statistically significant.

Results

There was no difference in demographic data as well as the anesthesia time between desflurane and sevoflurane groups. (Table 1) During high - flow wash - in, the F_A/F_I were comparable between the 2 groups with the ratios of 0.89 ± 0.05 vs 0.88 ± 0.02 at minute 10. While in low-flow maintenance, the F_I of both groups gradually increased with corresponding increases of F_A. The F_A at the end of the 1st hour was 4.2 ± 0.05 for desflurane and 1.78 ± 0.01 for sevoflurane. During the 1st hour of low flow, the F_A/F_I were not significantly different with the ratios of 0.91 ± 0.03 vs 0.89 ± 0.02 at minute 60. When back to high flow of O₂ at the end of surgery, desflurane was washed out faster than sevoflurane during the 1st minute with the F_A/F_I of 0.35 ± 0.05 vs 0.42 ± 0.08, *P* = 0.002, but not different afterwards. The recovery was faster in sevoflurane group with respects to the times to eye opening on command (312.3 ± 103.1 vs 403.7 ± 126.1 sec, *P* = 0.008) and extubation (397.0 ± 24.1 vs 518.0 ± 27.0 sec, *P* = 0.002). (Table 2) All patients in both groups could state their names on arrival at the recovery unit and the discharge times were similar (2 hours, the compulsory minimal stay time in the recovery unit).

Table 1 Patient characteristics and duration of anesthesia. Data are shown as mean (SD), number and percent.

	Desflurane (N = 20)	Sevoflurane (N = 20)	P value
Age (yr)	44.2 (11.7)	44.1 (9.8)	0.860
Sex (N, %)			
Male	3 (42.9)	4 (57.1)	0.672
Female	17 (51.5)	16 (48.5)	
Weight (kg)	73.2 (11.2)	71.2 (9.1)	0.694
Height (cm)	156.2 (7.6)	157.3 (9.5)	0.682
BMI (kg/m ²)	29.7 (2.8)	28.4 (1.9)	0.079
ASA (N, %)			
I	10 (47.6)	11 (52.4)	0.752
II	10 (52.6)	9 (47.4)	
Anesthesia time (min)	141 (10)	155.3 (14.5)	0.422

Table 2 Recovery times (seconds), shown as mean (SD); and ability to state name at the recovery room, in percent

	Desflurane (N = 20)	Sevoflurane (N = 20)	P value
Time to eye opening	312.3 (103.1)	403.7 (126.1)	0.008
Time to extubation	397.0 (24.1)	518.0 (27.0)	0.002
Ability to state name	100	100	

Discussion

Certain pathophysiological changes in obese patients make the requirements that before extubation, this group of patients should be awake and alert, and the muscle relaxant has been adequately reversed in order to avoid the potential risk of post-operative hypoxemia.¹ In obese patients, the effects of blood-

gas and oil-gas partition coefficients on the kinetic behaviors of an inhaled drug will be greater as the duration of anesthesia and body weight increase. Desflurane is a fluorinated anesthetic agent with very low blood-gas partition coefficient (0.42) and low oil-gas partition coefficient (27.2). These should allow rapid wash-in and rapid emergence, even in

obese patients. The 4% and 1.5% F_I of desflurane and sevoflurane will give roughly equipotent concentrations at equilibrium. The fresh gas flow of 1 L/min was chosen because it was the lowest recommended flow for sevoflurane. Sevoflurane undergoes temperature dependent degradation by baralyme and soda lime and forms compound A which can lead to kidney damage. The threshold for renal injury in humans is approximately 150 ppm - hours of exposure to Compound A. Patient exposure to compound A is increased with low fresh gas flow and high sevoflurane concentrations. Kobayashi et al² reported that, using a fresh gas flow of 1 L/min with soda lime and 1-3% F_I of sevoflurane, maximum Compound A concentration in the circuit was 28.0 (10.0) ppm. This would render a safe use of sevoflurane for approximately 5 hours. In the study of Groudine et al,³ there were no differences in the renal effects of sevoflurane and isoflurane in surgical patients undergoing 1 L/min anesthesia for up to 8 hours. Even in patients with renal insufficiency, low - flow sevoflurane anesthesia is considered safe. Conzen et al⁴ studied in patients with stable renal insufficiency and demonstrated the safety of low - flow (1L/min) sevoflurane anesthesia [3.1(2.4) MAC - hours]. Maximal inspiratory compound A in this study was 18.9(7.6) ppm resulting in an average total compound A exposure of 44.0 (30.6) ppm/hr and no kidney function alterations were found. Regarding desflurane, it has been used with safety even in closed circuit with minimal or metabolic flow. One major concern is that desiccated CO_2 absorbent and inhaled

anesthetics interaction can lead to the production of CO in the anesthetic circuit (desflurane > isoflurane). For the utmost safety, calcium hydroxide - based CO_2 absorbents are therefore preferable since they are chemically inert and do not degrade sevoflurane to compound A, or degrade other inhaled anesthetics to CO_2 .

The results of this study showed comparable kinetic profiles between desflurane and sevoflurane during the initial 10 minutes of high flow wash - in and the 1st hour of 1 L/min maintenance flow in overweight patients. These, in part, conformed with those of La Colla et al⁵ which reported that, during high flow, F_A/F_I of both anesthetics were not significantly different until the 15th minute and afterwards. The initial wash - in is more affected by the cardiac output and alveolar - to - venous partial pressure difference rather than the blood solubility. However, our study demonstrated that 1 L/min maintenance flow would have decreased the magnitude of impact of blood solubility on the wash - in resulting in comparable F_A/F_I through the 1st hour. In contrast, the wash - out of desflurane was faster, particularly in the 1st minute, which resulted in shorter early recovery times. In the non - obese population, a faster recovery desflurane compared with sevoflurane was demonstrated in many previous studies.⁶⁻⁸ Many studies^{5, 9-11} also demonstrated the same results in morbidly obese patients, though, using high - flow technique. This would be of clinical benefits in patients who are at risks of post - operative airway obstruction and aspiration. The faster wash - out of desflurane can

be explained by its lower blood solubility and less tissue deposit. The effects of tissue deposit would be greater as the duration of anesthesia increases particularly in obese patients. In fact, the recovery times could have been shorter if we used the ultra - short acting opioid, remifentanyl in stead of fentanyl. Nonetheless, the recovery of cognitive function and discharge times from recovery room was not different in both groups. These conformed with the study of Nathanson et al⁷ done in outpatient group. Clinically, the rapid wash - in may be of less significance compared with the rapid wash - out since it can be easily compensated for by an increase of F_D while the latter counts solely on the clearance which depends on the amount of tissue deposit and ventilation.

The potency of desflurane is quite low, its MAC is approximately 6%. Because of its high price and low potency, a low - flow technique is recommended. Furthermore, this technique renders body temperature preservation, increased airway humidity and reduction of environmental pollution.¹² However, cautions should be exercised in patients with history of heavy smoking, alcoholism, starvation, sepsis, cardiac dysfunctions, poorly controlled diabetes mellitus and morbid obesity, particularly in minimal or metabolic-flow technique. In this study during 1 L/min flow with 5% desflurane, the F_A gradually increased from 3.5% to 4.2% by the end of 1st hour with the F_A/F_I ratio of 0.91.

We selected the F_D of 5% because it was easy for dial setting and yielded the final F_A of around 4%. Seemingly, the F_A of 4% might be more than enough, however, we would like to make sure that the provided anesthesia depth could cover almost all the procedures since the bispectral analyzer had not been used.

There were some limitations of this study. First, a second gas effect from N_2O could have affected the kinetic behaviors of volatile anesthetics, particularly during wash - in. Second, bispectral analyzer was not used hence the anesthesia level might have been too deep and affected the recovery. Third, the use of a long - acting opioid, fentanyl, might have effect on the recovery as well, if not carefully titrated. However, it was supposed that both desflurane and sevoflurane groups had been equally affected by these factors.

Conclusion

In unpremedicated overweight patients, desflurane and sevoflurane provided comparable fast wash - in under 1 L/min flow of anesthesia. Although desflurane rendered shorter early recovery times, the discharge times from the recovery room were not different. We recommend the F_D of 5% for desflurane and 2% for sevoflurane during 1 L/min of maintenance flow as an economical and safe practice where the facilities are limited.

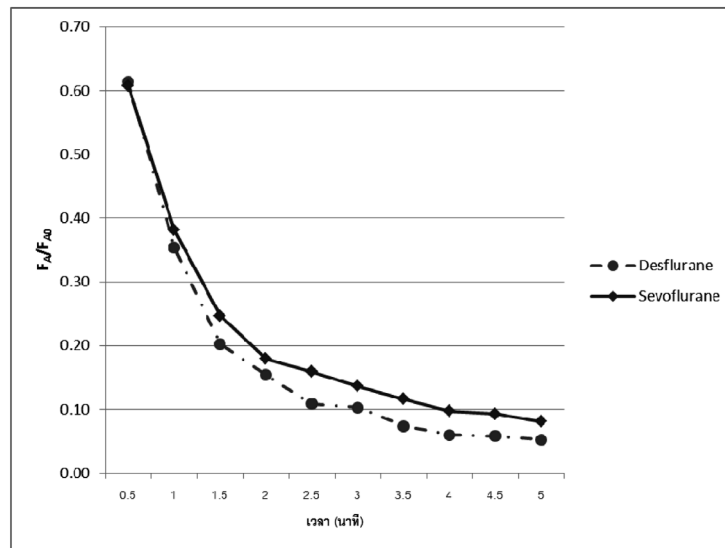


Figure 1 Wash - out curves of desflurane and sevoflurane in overweight patients after 1 L/min flow of anesthesia

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