Int J Clin Exp Med 2018;11(6):5548-5555
www.ijcem.com /ISSN:1940-5901/IJCEM0068310

Original Article

Effect of administration time in obese patients on speed of recovery and risk of rehypnotization following recovery from different inhaled anesthetics: a computational simulation

Lijun Wang, Yirong Cai

Department of Anesthesiology, The Eye, Ear, Nose and Throat Hospital of Fudan University, Shanghai 200031, China

Received October 31, 2017; Accepted March 23, 2018; Epub June 15, 2018; Published June 30, 2018

Abstract: Incomplete airway obstruction often occurs after emergence in obese patients. It may result in rehypnotization if subsequent hypoventilation occurs. Herein, GasMan® simulations were used for examining the effect of administration time on the speed of recovery and risk of rehypnotization following recovery in obese patients. Three different weights of patients, 70 kg, 120 kg and 120 kg with more fat (120 mF) were utilized. Isoflurane, sevoflurane, or desflurane were administered to attain flow of vessel-rich group (F_{VRG}) of 1 minimum alveolar concentration (MAC) for 2 h, 4 h, 6 h, 8 h and 10 h in all groups. At the end of the time, administration of the agent was terminated, and fresh gas flow was increased to 5 L/min. The time for F_{VRG} to reach 0.3 MAC (MAC_{awake}) was determined, following which, several degrees of hypoventilation were instituted (VA of 0.25 and 0.5 L/min) to determine whether F_{VRG} would increase above 0.3 MAC (rehypnotization). The awake time was prolonged with the extension of anesthesia time and increasing weight of the patients (isoflurane > sevoflurane > desflurane with the same weight and anesthesia time). Rehypnotization occurred in all groups except SEV 0.5 and DES 0.5 groups (70 kg, 2 h). The rehypnotization time was decreased with the extension of anesthesia time in all groups (desflurane > sevoflurane > isoflurane, irrespective of V_A = 025 or 0.5 L/min). The changes in fat volume affected neither the awake time in sevoflurane and desflurane nor the rehypnotization time except in isoflurane at 2 h anesthesia. These GasMan® simulations confirmed that desflurane is adequate for fast recovery and will additionally reduce the risk of rehypnotization in a prolonged surgery in obese patients.

Keywords: Computational simulation, inhaled anesthetics, rehypnotization, obese patients

Introduction

Inhaled volatile anesthetic agents remain the most widely accepted anesthetics for the maintenance of general anesthesia due to their ease of administration, availability of end-tidal agent monitoring, and predictable intraoperative and recovery characteristics. Isoflurane, sevoflurane, and desflurane are the three commonly used inhaled volatile anesthetic agents.

Sevoflurane is a fluorinated ether inhalational agent with low blood/gas partition coefficient (0.6). Its insolubility provides rapid onset and offset allowing early postoperative recovery [1]. However, with prolonged administration, the recovery times may be delayed resulting in the loss of its advantages [1, 2]. Desflurane is a volatile anesthetic known to have early recovery from anesthesia due to low blood solubility, blood-gas (0.42), and tissue-blood partition coefficients resulting in a more rapid wash-in and wash-out as compared to the other known volatile anesthetics [3]. Isoflurane is still widely used in the clinic as it is cost-effective and more beneficial in neurosurgery than the other inhalational anesthetics. Currently, the number of obese patients presenting for general anesthesia is increasing. However, the effect of administration time on the speed of recovery between the three anesthetic agents has not yet been elucidated in such patients.

Moreover, incomplete airway obstruction often occurs after emergence, especially in obese patients. Low alveolar ventilation leads to

Table 1. GasMan® settings and parameters

Anesthetic	Solubility				Volatility	Circuit
	Blood	VRG	Muscle	Fat		
Isoflurane	1.3	2.1	4.5	70	196	Semi
Sevoflurane	0.65	1.1	2.4	34	183	Semi
Desflurane	0.42	0.54	0.97	13	209	Semi

VRG: vessel-rich group, including the central nervous system (CNS).

Table 2. Parameters of 3 different weights in GasMan®

Weight (kg)	Volumes (L)					Metabolism		Flow Percentages		
	ALV	VRG	MUS	FAT	VEN	VA	CO	VRG	MUS	FAT
70	2.5	6.0	33.0	14.5	1.0	4	5	76%	18%	6%
120	4.29	10.29	56.57	24.86	1.71	5.993	7.491	76%	18%	6%
120 mF	4.29	10.29	46.57	34.86	1.71	5.993	7.491	76%	18%	6%

ALV, alveoli; VRG, vessel-rich group, including the CNS; MUS, muscle; VEN, venous; VA, alveolar ventilation; CO, cardiac output.

rehypnotization, which might be detrimental if not noticed immediately. Nonetheless, the risk of rehypnotization following recovery in obese patients with different inhaled volatile anesthetics cannot be compared to that in the clinical setting. Therefore, we used GasMan® simulations to help demonstrate and clarify the following two issues: does the administration time affect the speed of recovery in obese patients with inhaled volatile anesthetic agents and is the risk of rehypnotization different when subsequent hypoventilation occurs?

Materials and methods

The hypotheses mentioned above were tested using simulations by GasMan® (Version 4.2 Med Man Simulations, Inc., Chestnut Hill, MA, USA). GasMan® is a physiology-based model of inhaled anesthetic uptake and distribution, commercially available as a computer program used for education [3, 4] and during induction and emergence from anesthesia [5].

GasMan® is based on a 6-compartment model: alveolar functional residual capacity (FRC) and vessel-rich group (VRG) that includes the brain, muscle, arterial blood, venous blood, and fat compartments with an additional compartment for the anesthetic circuit. The equilibration among these compartments presumably follows first-order kinetics for partial pressure or tension based on the blood/gas and tissue/gas solubility and tissue perfusion with arterial blood. Inter-tissue diffusion, drug metabolism, and ventilation/perfusion variation in the lungs are not simulated [6]. GasMan® settings and parameters are summarized in **Table 1**. In the current study, we investigated 3 anesthetics: isoflurane, sevoflurane, and desflurane at 3 different weights each: 70 kg, 120 kg and 120 kg with more fat (120 mF). Thus, there were 9 groups: isoflurane and 70 kg (ISO 70), sevoflurane and 70 kg (SEV 70), desflurane and 70 kg (DES 70), isoflurane and 120 kg (ISO 120), sevoflurane and 120 kg (SEV 120), desflurane and 120 kg (DES 120), isoflurane and 120 kg with more fat (ISO 120 mF), sevoflurane and 120 kg with more fat (SEV 120 mF) and desflurane and 120 kg with more fat (DES 120 mF). The volume, metabolism, and flow percentages in 70 kg and 120 kg were used at default settings by GasMan®. The muscle (MUS) and fat (FAT) volumes were changed in the 120 mF group. These parameters are listed in **Table 2**. The effect of age on minimum alveolar concentration (MAC) is ignored. The MAC values used in our GasMan® simulations were as follows: desflurane 6%, sevoflurane 2%, and isoflurane 1.2%.

In GasMan®, isoflurane, sevoflurane, or desflurane were administered to attain an F_{VRG} (representing F_{CNS}) of 1 MAC for 2 h, 4 h, 6 h, 8 h and 10 h, respectively. At the end of the time, administration of the agent was terminated, and FGF (fresh gas flow) was increased to 5 L/min to wash-out the residual anesthetic. We determined the time for the F_{VRG} to reach 0.3 MAC, which was considered as MAC_{awake}. In addition, the awake time for each agent with 3 different weights was recorded. After F_{VRG} had reached MAC_{awake}, several degrees of hypoventilation were instituted (VA 0.25 and 0.5 L/min) such that each group was divided into 2 subgroups according to the alveolar ventilation. The course of F_{VRG} was observed, and an increase in F_{VRG} > 0.3 MAC was considered as the evidence of rehypnotization.

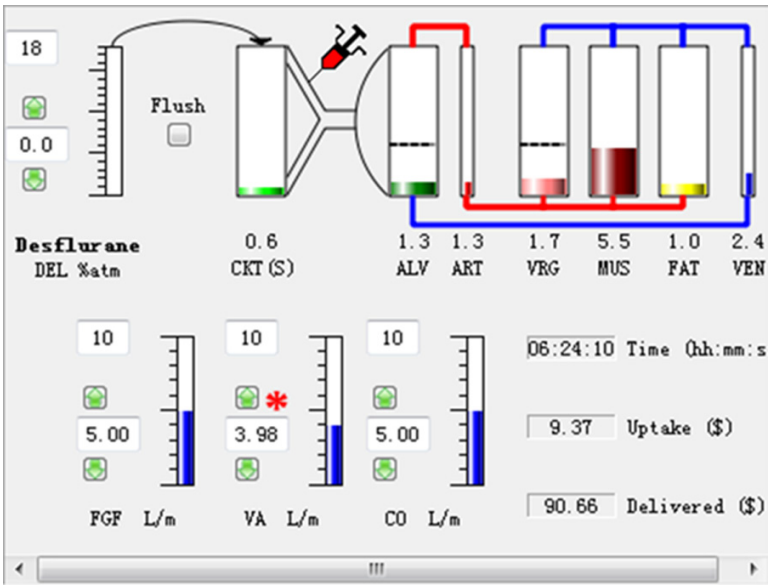

Figure 1. A representative screen shot of a running simulation.

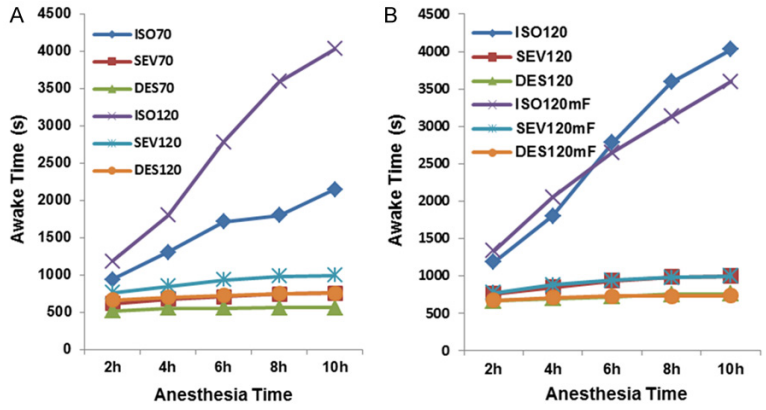

Figure 2. Comparison of awake time in different groups. ISO 70: isoflurane and 70 kg; SEV 70: sevoflurane and 70 kg; DES 70: desflurane and 70 kg; ISO 120: isoflurane and 120 kg; SEV 120: sevoflurane and 120 kg; DES 120: desflurane and 120 kg; ISO 120 mF: isoflurane and 120 kg with more fat; Sev 120 mF: sevoflurane and 120 kg with more fat; DES 120 mF: desflurane and 120 kg with more fat. A. Comparison of awake time with 70 kg and 120 kg for different anesthesia times. B. Comparison of awake time with 120 kg and 120 kg more fat for different anesthesia times.

Results

A representative screen shot of a running simulation is illustrated in **Figure 1**. Time for F_{VRG} to reach 0.3 MAC (awake time) was prolonged with the extension of anesthesia time in the presence of isoflurane. Among the 3 anesthetics, the order of the awake time was isoflurane > sevoflurane > desflurane with the same weight and same anesthesia time. The awake time with isoflurane was obviously longer than the other two anesthetics. In the case of the same anesthetic and anesthesia time, the awake time in the 120 kg group was longer than that in the 70 kg group. The awake time in ISO 120 was shorter than that in ISO 120 mF at 2 h and 4 h. However, it was longer at 6 h, 8 h and 10 h. The changes in fat volume did not affect the awake time in sevoflurane and desflurane (**Figure 2**).

The low alveolar ventilation (VA of 0.25 and 0.5 L/min) after F_{VRG} reached MAC_{awake} leads to rehypnotization in all groups except in SEV 0.5 and DES 0.5 groups with the weight of 70 kg for anesthesia time of 2 h (**Table 3**). **Figures 3-5** display comparison of rehypnotization time in the 70 kg, 120 kg and 120 mF groups. The rehypnotization time was decreased with the extension of anesthesia time in all groups. Irrespective of the alveolar ventilation of 0.25 or 0.5 L/min, the rehypnotization time was desflurane > sevoflurane > isoflurane. **Figure 3** shows that the rehypnotization time was similar to that of desflurane for different anesthesia times (regardless of 4 h or 10 h). In addition, a severe airway obstruction occurred (VA = 0.25 L/min), the rehypnotization time was longer with desflurane than isoflurane or sevoflurane. In obese patients (120 and 120 mF kg), the rehypnotization time was sevoflurane > desflurane for 2 h anesthesia and the rehypnotization time displayed a sudden decrease in the SEV 0.5 group in the case of 2-4 h anesthesia. After 4 h, the trend lines were almost similar (**Figures 4** and **5**).

Figures 6-8 shows the comparisons of rehypnotization time with different weights in isoflu-

Table 3. Rehypnotization times in each group with different anesthesia times

Weight (kg)	Groups	Rehypnotization time (s)				
		2 h	4 h	6 h	8 h	10 h
70	ISO 0.25	148	121	63	47	43
	SEV 0.25	415	133	97	89	84
	DES 0.25	425	182	170	163	155
	ISO 0.5	166	123	72	49	46
	SEV 0.5	-	197	122	105	104
	DES 0.5	-	287	263	231	220
120	ISO 0.25	137	60	52	51	51
	SEV 0.25	355	138	97	84	80
	DES 0.25	279	186	144	143	140
	ISO 0.5	156	63	54	58	64
	SEV 0.5	1089	164	112	94	89
	DES 0.5	557	234	171	167	159
120 mF	ISO 0.25	87	63	55	59	54
	SEV 0.25	282	119	95	84	83
	DES 0.25	219	185	157	147	146
	ISO 0.5	93	66	64	62	57
	SEV 0.5	1087	144	104	89	87
	DES 0.5	358	220	192	169	160

ISO 0.25, isoflurane and V_A 0.25 L/min; SEV 0.25, sevoflurane and V_A 0.25 L/min; DES 0.25, desflurane and V_A 0.25 L/min; ISO 0.5, isoflurane and V_A 0.5 L/min; SEV 0.5, sevoflurane and V_A 0.5 L/min; DES0.5, desflurane and V_A 0.5 L/min. The symbol "-" indicates no rehypnotization in this group.

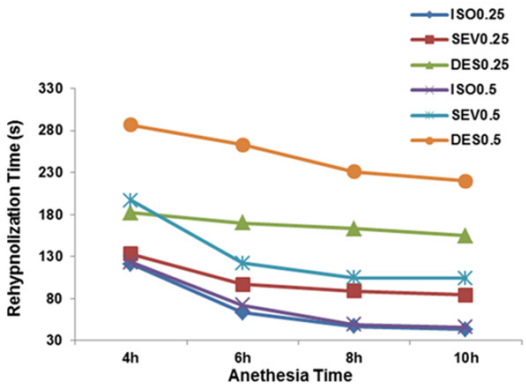

Figure 3. Comparison of rehypnotization times in the 70 kg group. ISO 0.25: isoflurane and V_A 0.25 L/min; SEV 0.25: sevoflurane and V_A 0.25 L/min; DES 0.25: desflurane and V_A 0.25 L/min; ISO 0.5: isoflurane and V_A 0.5 L/min; SEV 0.5: sevoflurane and V_A 0.5 L/min; DES 0.5: desflurane and V_A 0.5 L/min.

rane, sevoflurane, and desflurane. For isoflurane, the rehypnotization time in obese patients was shorter than that in normal patients (70 kg) at 2 h, 4 h and 6 h irrespective of the VA of 0.25 or 0.5 L/min. For sevoflurane, when the VA was 0.25 L/min, the rehypnotization time in obese patients was shorter than that in normal patients only at 2 h and approximately equivalent to the other four time points. However, if the VA was 0.5 L/min, the rehypnotization time in obese patients was shorter than that in normal patients at 4 h, 6 h, 8 h and 10 h, respectively. The trend lines in desflurane were similar to that of sevoflurane. The changes in the fat volume in obese patients did not affect the rehypnotization time distinctly except in isoflurane for 2 h anesthesia.

Discussion

GasMan® is based on a physiological model of uptake and distribution of volatile anesthetics [7]. Since the current design does not allow data export to a spreadsheet for obtaining the complete wash-out curves, we could only compare the single-point GasMan predictions with the wash-out curves. The emergence from general anesthesia with a potent inhaled anesthetic occurs in 50% of the patients when F_{CNS}, reflected in the GasMan® program by F_{VRG}, decreases below the threshold MAC_{awake}, which was defined as 0.3 MAC. The driving force to decrease F_{VRG} is a decrease in F_a (alveolar concentration), and GasMan® presumes that at the level of the alveolar-capillary interface, an instantaneous virtual equilibration between blood and alveolar gas occurs such that $F_a = F_A$ (the end-expired concentrations). Therefore, it is the decrease in F_A that results in a decreased F_{CNS}.

Our study showed that the awake time was prolonged with the extension of anesthesia time. However, these changes were not obvious with desflurane. The fat solubility of anesthetics plays a critical role in the time to wake up. The blood-gas solubility was a more crucial factor influencing the emergence time than fat solubility [8]. The new fluorinated agents have ma-

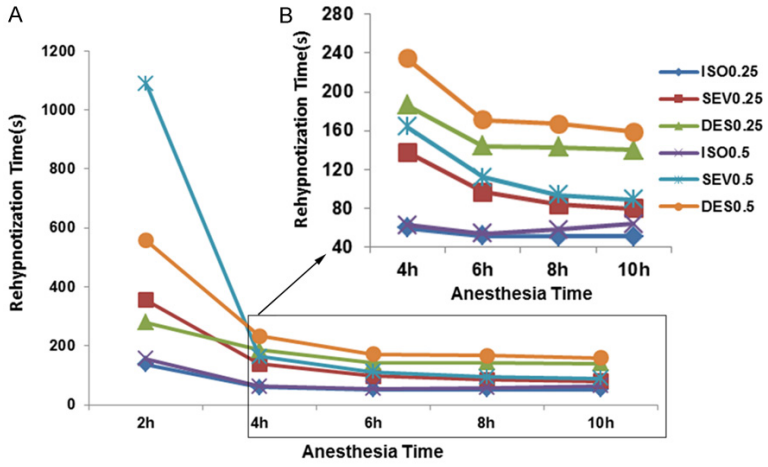

Figure 4. Comparison of rehypnotization time in the 120 kg group. A. Comparison of rehypnotization time in 120 kg group with anesthesia time 2 h, 4 h, 6 h, 8 h and 10 h. B. Comparison of rehypnotization time in 120 kg group with anesthesia time 4 h, 6 h, 8 h and 10 h. ISO 0.25: isoflurane and V_A 0.25 L/min; SEV 0.25: sevoflurane and V_A 0.25 L/min; DES 0.25: desflurane and V_A 0.25 L/min; ISO 0.5: isoflurane and V_A 0.5 L/min; SEV0.5: sevoflurane and V_A 0.5 L/min; DES 0.5: desflurane and V_A 0.5 L/min.

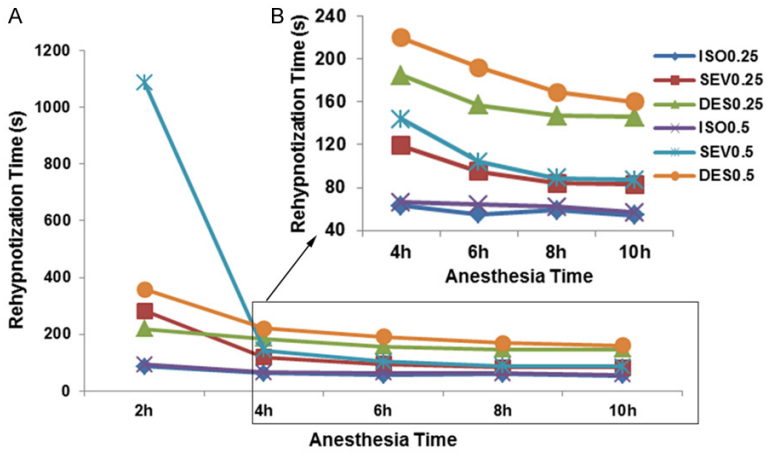

Figure 5. Comparison of rehypnotization times in the 120 kg group with more fat. A. Comparison of rehypnotization times in the 120 mF group with anesthesia time 2 h, 4 h, 6 h, 8 h and 10 h. B. Comparison of rehypnotization times in the 120 mF group with anesthesia time 4 h, 6 h, 8 h and 10 h. ISO 0.25: isoflurane and V_A 0.25 L/min; SEV 0.25: sevoflurane and V_A 0.25 L/min; DES 0.25: desflurane and V_A 0.25 L/min; ISO 0.5: isoflurane and V_A 0.5 L/min; SEV 0.5: sevoflurane and V_A 0.5 L/min; DES 0.5: desflurane and V_A 0.5 L/min.

rkedly improved the quality and the time required for recovery as compared to the previous inhalation anesthetics. Especially, desflurane is a new fluorinated anesthetic agent with an extremely low blood-gas partition coefficient (approximately 30% less than sevoflurane) and low oil-gas partition coefficient (about 64% less than sevoflurane), which allows rapid modification of the anesthetic plan and emergence at the end of surgery [9]. Desflurane has lower solubility in blood than sevoflurane, and a prolonged duration of surgery might lead to large differences in recovery outcomes. Meta-analysis by Ebert et al. compared sevoflurane with isoflurane and the recovery time did not differ in studies with surgeries < 1 h. Nevertheless, in studies with surgeries lasting 1-3 h, the recovery time was shorter in the sevoflurane groups and significantly shorter in those lasting 3-5 h [10].

Our data confirm the previous evidence in obese patients undergoing general surgery and provided new evidence on the advantages of desflurane, especially after prolonged administration [11]. A prospective, randomized, double-blind study by La Colla et al. enrolled 28 unpremedicated obese patients and showed that desflurane provided a faster wash-in and washout than sevoflurane, which might be attributed to a large amount of tissue deposits and high blood-gas partition coefficient of sevoflurane, causing a slower rate of decrease in both arterial circulation and lungs [12]. Bilotta et al. obtained a similar conclusion in overweight and obese patients undergoing craniotomy [13]. Desflurane exhibited a significantly lower blood/gas partition coefficient than sevoflurane or isoflurane [14], which resulted in a short recovery time in morbidly obese patients undergoing prolonged surgery. A systematic review and meta-analysis of randomized controlled trials indicated that postoperative recovery was significantly faster after desflurane than sevoflurane, isoflurane, or propofol anesthesia in obese patients [15]. McKay et al. compared the recovery times with desflurane *vs*. sevoflurane

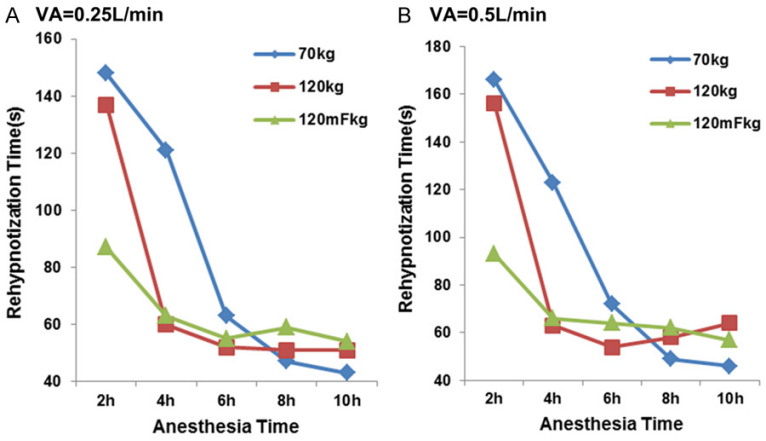

Figure 6. Comparison of rehypnotization times with different weights in isoflurane. A. Comparison of rehypnotization times with different weights in isoflurane with anesthesia time 2 h, 4 h, 6 h, 8 h and 10 h (VA = 0.25 L/min). B. Comparison of rehypnotization times with different weights in isoflurane with anesthesia time 2 h, 4 h, 6 h, 8 h and 10 h (VA = 0.5 L/min).

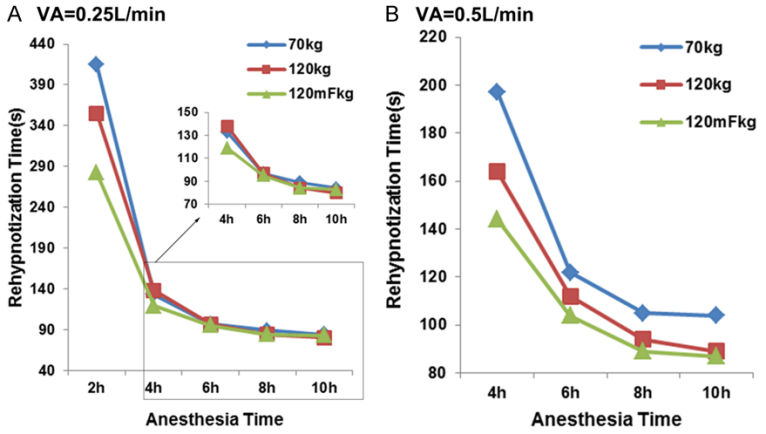

Figure 7. Comparison of rehypnotization times with different weights in sevoflurane. A. Comparison of rehypnotization times with different weights in sevoflurane with anesthesia time 2 h, 4 h, 6 h, 8 h and 10 h (VA = 0.25 L/min). B. Comparison of rehypnotization times with different weights in sevoflurane with anesthesia time 4 h, 6 h, 8 h and 10 h (VA = 0.5 L/min).

for maintaining the anesthesia in patients with BMIs ranging from 18.3-40.2 kg/m^2 and various durations of surgery. The study determined that a prolonged duration of sevoflurane anesthesia significantly extend the airway reflex recovery time, whereas desflurane anesthesia had only a minimal effect on the airway recovery time. These results were in agreement with that of our study. We observed short durations to awakening and extubation with sevoflurane and desflurane as compared to isoflurane, and the patients would face difficulty in awakening from isoflurane anesthesia for ≥ 4 h, especially in obese patients. This phenomenon indicated that sevoflurane and desflurane are both less soluble in muscle and fat as compared to isoflurane and will be washed out more rapidly.

Clinically, obese patients are prone to airway obstruction after emergence [16]. These patients are at an increased risk for episodes of postoperative desaturation, despite supplemental oxygen therapy [17], which might be detrimental owing to hypoventilation that could lead to rehypnotization, thereby threatening the patients' life. Rehypnotization is caused by a large amount of agent being brought into the alveoli from the peripheral tissues such as the muscle, fat, and venous blood than the amount of agent that is removed from the alveoli by VA (alveolar ventilation). When F_A > MAC_{awake}, rehypnotization will occur eventually. The amount of agent delivered to the alveoli depends on the amount of agent released by each tissue group, and the agents with high tissue solubility may result in an increased F_A than agents with a lower solubility. In the case of desflurane, low tissue solubility results in relatively less desflurane returned to the alveoli than is cleared by the lungs even in the presence of mild-moderate hypoventilation. However, with isoflurane, relatively more agent is released by the tissues, and therefore, even mild hypoventilation results in rehypnotization. The current GasMan® simulation shows that hypoventilation after initial recovery not only reduces the speed of reduction in FVRG but also increases F_{VRG} above MAC_{awake} values, resulting in rehypnotization. Lower blood and tissue solubility of the agent reduces the risk of rehypnotization when hypoventilation occurs. Eger et al. stated that recovery is faster with agents with low solubility and that isocapnic hyperventilation can hasten the recovery [6,

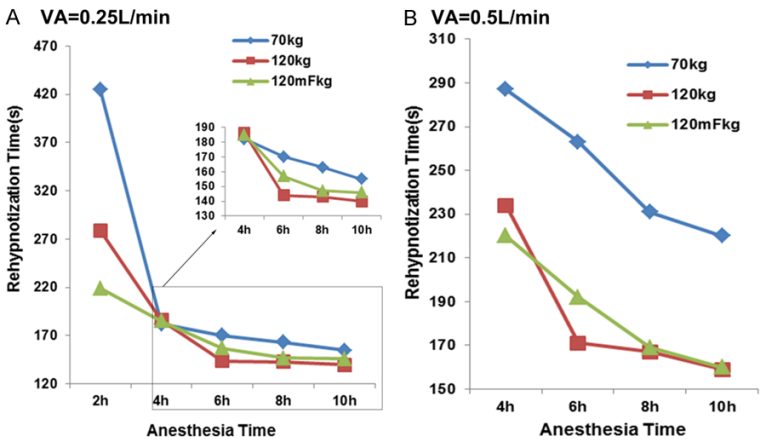

Figure 8. Comparison of rehypnotization times with different weights in desflurane. A. Comparison of rehypnotization times with different weights in desflurane with anesthesia time 2 h, 4 h, 6h, 8 h and 10 h (VA = 0.25 L/min). B. Comparison of rehypnotization times with different weights in desflurane with anesthesia time 4 h, 6 h, 8 h and 10 h (VA = 0.5 L/min).

18], and that hypoventilation can result in an increased F_A. Furthermore, to the best our knowledge, the present observations regarding the effects of subsequent hypoventilation on rehypnotization have not yet been described explicitly.

We found out that in obese patients (120 and 120 mF kg), the order of rehypnotization time was sevoflurane > desflurane for anesthesia 2 h, which might be attributed to the lower blood-gas partition coefficient of desflurane as compared to sevoflurane such that the drug concentration in the peripheral tissue was increased rapidly. When the administration time was short, sevoflurane in the peripheral tissue did not reach saturation. Once the tidal volume was reduced, an excess of desflurane from peripheral tissue to vessel-rich group was present than sevoflurane. Therefore, the rehypnotization time was sevoflurane > desflurane. In the case of prolonged administration duration, both sevoflurane and desflurane in peripheral tissue reach saturation. Desflurane is clarified clearance rapidly, and hence, the rehypnotization time was sevoflurane < desflurane. Moreover, our study showed that changes in the fat volume affected neither the awake time in sevoflurane and desflurane nor the rehypnotization time except in isoflurane at 2 h anesthesia.

The limitations of this study are inherent in computational simulations, and the assumptions of the model used. First, the patients' height cannot be set in GasMan® system. Therefore, we only change the weight and not BMI (body mass index) in obese patients. Second, GasMan® is a computer software only for simulating the trend of anesthesia. It does not show the exact point, resulting in slight variations between different computers or different system versions. Third, our simulations used arbitrarily designated values for hypoventilation after emergence as the clinical values for this threshold are rarely known. Furthermore, our model ignored the metabolism and inter-compartment diffusion. In addition, the effects of body habitus (more or less muscle and fat mass) necessitate further studies. Herein, we observed that the altered fat volume did not affect the awake time in sevoflurane and desflurane. However, we can speculate that an increase in the size of the muscle group increases the risk of rehypnotization with hypoventilation after recovery as an excess of the agent will be availed by the muscle group for redistribution. Although the results of the present study, with its controlled assumptions, provide a general framework for future clinical research, these observations based on a simulation will have to be substantiated by well-controlled clinical studies.

In summary, this computational simulation study provides insights into the effect of administration time on the speed of recovery and the risk of rehypnotization following recovery. These GasMan® simulations theoretically confirm that the use of new, less soluble agents is useful for fast recovery and will additionally reduce the risk of rehypnotization. Compared to the other inhaled anesthesia agents, desflurane is more advantageous in a prolonged surgery in obese patients. However, well-controlled clinical studies are yet required to validate these simulations.

Disclosure of conflict of interest

None.

Address correspondence to: Yirong Cai, Department of Anesthesiology, The Eye, Ear, Nose and Throat Hospital of Fudan University, Shanghai 200031, China. E-mail: caiyirong@eentanesthesia.com

References

[1] Duffy CM and Matta BF. Sevoflurane and anesthesia for neurosurgery. J Neurosurg Anesthesiol 2000; 12: 128-139.

[2] Eger EI 2nd, Gong D, Koblin DD, Bowland T, Ionescu P, Laster MJ and Weiskopf RB. The effect of anesthetic duration on kinetic and recovery characteristics of desflurane versus sevoflurane, and on the kinetic characteristics of compound A, in volunteers. Anesth Analg 1998; 86: 414-421.

[3] Philip JH. Gas Man--an example of goal oriented computer-assisted teaching which results in learning. Int J Clin Monit Comput 1986; 3: 165-173.

[4] Garfield JM, Paskin S and Philip JH. An evaluation of the effectiveness of a computer simulation of anaesthetic uptake and distribution as a teaching tool. Med Educ 1989; 23: 457-462.

[5] Bouillon T and Shafer SL. Hot air or full steam ahead? An empirical pharmacokinetic model of potent inhalational agents. Br J Anaesth 2000; 84: 429-431.

[6] Eger EI 2nd and Shafer SL. Tutorial: context-sensitive decrement times for inhaled anesthetics. Anesth Analg 2005; 101: 688-696, table of contents.

[7] Dean JM. GasMan. MD Comput 1986; 3: 537.

[8] Arain SR, Barth CD, Shankar H and Ebert TJ. Choice of volatile anesthetic for the morbidly obese patient: sevoflurane or desflurane. J Clin Anesth 2005; 17: 413-419.

[9] Juvin P, Vadam C, Malek L, Dupont H, Marmuse JP and Desmonts JM. Postoperative recovery after desflurane, propofol, or isoflurane anesthesia among morbidly obese patients: a prospective, randomized study. Anesth Analg 2000; 91: 714-719.

[10] Ebert TJ, Robinson BJ, Uhrich TD, Mackenthun A and Pichotta PJ. Recovery from sevoflurane anesthesia: a comparison to isoflurane and propofol anesthesia. Anesthesiology 1998; 89: 1524-1531.

[11] Vallejo MC, Sah N, Phelps AL, O'Donnell J and Romeo RC. Desflurane versus sevoflurane for laparoscopic gastroplasty in morbidly obese patients. J Clin Anesth 2007; 19: 3-8.

[12] La Colla L, Albertin A, La Colla G and Mangano A. Faster wash-out and recovery for desflurane vs sevoflurane in morbidly obese patients when no premedication is used. Br J Anaesth 2007; 99: 353-358.

[13] Bilotta F, Doronzio A, Cuzzone V, Caramia R, Rosa G and Group PS. Early postoperative cognitive recovery and gas exchange patterns after balanced anesthesia with sevoflurane or desflurane in overweight and obese patients undergoing craniotomy: a prospective randomized trial. J Neurosurg Anesthesiol 2009; 21: 207-213.

[14] Yasuda N, Targ AG, Eger EI 2nd, Johnson BH and Weiskopf RB. Pharmacokinetics of desflurane, sevoflurane, isoflurane, and halothane in pigs. Anesth Analg 1990; 71: 340-348.

[15] Liu FL, Cherng YG, Chen SY, Su YH, Huang SY, Lo PH, Lee YY and Tam KW. Postoperative recovery after anesthesia in morbidly obese patients: a systematic review and meta-analysis of randomized controlled trials. Can J Anaesth 2015; 62: 907-917.

[16] Philippi-Hohne C. Anaesthesia in the obese child. Best Pract Res Clin Anaesthesiol 2011; 25: 53-60.

[17] Ahmad S, Nagle A, McCarthy RJ, Fitzgerald PC, Sullivan JT and Prystowsky J. Postoperative hypoxemia in morbidly obese patients with and without obstructive sleep apnea undergoing laparoscopic bariatric surgery. Anesth Analg 2008; 107: 138-143.

[18] Eger EI and Saidman LJ. Illustrations of inhaled anesthetic uptake, including intertissue diffusion to and from fat. Anesth Analg 2005; 100: 1020-1033.