의학석사 학위논문

A Pharmacodynamic Model of Tidal Volume and Inspiratory Sevoflurane Concentration in Children during Spontaneous Breathing

자발호흡을 하는 소아에서 일회호흡량과 세보플루란 농도의 약력학 모형

2020 년 2 월

서울대학교 대학원
의학과 마취통증의학 전공
강 표 윤

A thesis of the Degree of Master of Science

자발호흡을 하는 소아에서 일회호흡량과 세보플루란 농도의 약력학 모형

A Pharmacodynamic Model of Tidal Volume and Inspiratory Sevoflurane Concentration in Children during Spontaneous Breathing

February 2020

Department of Anesthesiology and Pain Medicine
Seoul National University College of Medicine
Pyoyoon Kang

Abstract

A Pharmacodynamic Model of Tidal Volume and Inspiratory Sevoflurane Concentration in Children during Spontaneous Breathing

Pyoyoon Kang
Department of Anesthesiology and Pain Medicine
The Graduate School
Seoul National University

Purpose: High concentrations of sevoflurane depress tidal volume (TV) during spontaneous ventilation. The purpose of this study was to identify clinical variables that affect the relationship between TV and sevoflurane concentration, and to establish a population pharmacodynamic modelling approach to TV and sevoflurane concentration in children.

Methods: A prospective observational study involving 48 patients (≤ 6 years of age) scheduled to undergo general anesthesia using laryngeal mask airway was performed. When the inspiratory sevoflurane concentration reached 2vol%, the vaporizer was

increased to 4vol% for 5 min, then sevoflurane was decreased to 2vol% for 5 min. During the study period, TV, end-tidal carbon dioxide, and sevoflurane concentration were recorded every 30 s. Pharmacodynamic analysis using a sigmoid E_max model was performed to assess the TV-sevoflurane concentration relationship.

Results: TV decreased with increasing inspiratory sevoflurane concentrations. Hysteresis between the TV and sevoflurane concentration was observed and was accounted for when the model was developed. Initial TV and maximal reduction in TV was related to body weight. The ɣ and k_{eo} were 8.78 and 2.27 min^{-1}, respectively.

Conclusion: Changes in TV were correlated with sevoflurane concentration with spontaneous breathing during sevoflurane anesthesia. The initial and maximal TV were related to body weight; in a pediatric population.

Keywords: children, sevoflurane, spontaneous breathing, tidal volume

Student number: 2017-26753

CONTENTS

List of Tables and Figures

INTRODUCTION

During general anesthesia, spontaneous breathing has been commonly used in pediatric populations along with mechanical ventilation. Spontaneous breathing has its own benefits with regard to silent spaces compared with anesthesia and mechanical ventilation.[1] In contrast, previous studies have reported that spontaneous breathing can result in high end-tidal carbon dioxide concentration (E_TCO_2) and reduction in tidal volume (TV).[2,3] Therefore, if the TV and E_TCO_2 are acceptable under the appropriate surgical anesthetic depth or concentration, spontaneous breathing may be beneficial in pediatric patients undergoing procedures requiring general anesthesia; moreover, it would be possible to guarantee the safety of neuromuscular blockade during anesthesia.

Sevoflurane has been the most popular volatile anesthetic for children undergoing procedures requiring general anesthesia. In addition, it is very common practice for children with spontaneous breathing using laryngeal mask airway to undergo sevoflurane anesthesia. Basically, volatile anesthetics increase the frequency of breathing and decrease TV as the concentration of anesthetic increases.[4] Therefore, pediatric anesthesiologists can easily observe reductions in TV while maintaining spontaneous breathing during sevoflurane anesthesia.

Population pharmacokinetic and pharmacodynamic (PD) models are important tools for summarizing drug dose, concentration, and effect relationships. If we assume that sevoflurane concentration is a drug concentration and TV is an effect, it would be possible to develop a PD model to explain the relationship between sevoflurane and TV in children during spontaneous breathing anesthesia.

In this study, we aimed to identify clinical variables affecting the

relationship between sevoflurane concentration and TV, and to establish a population PD model for sevoflurane concentration and TV during general anesthesia in a pediatric population.

METHODS

Patient recruitment and anesthetic methods

The present study was approved by the Institutional Review Board of Seoul National University Hospital (Seoul, Korea; 1803-068-929) and registered at http://register.clinicaltrials.gov (NCT03491839). Each participant was given a verbal explanation of the study and was offered the opportunity to ask questions about the protocol. Informed consent was obtained from one parent or guardian of each patient. Verbal consent was obtained from all patients. All procedures adhered to the principles of the Declaration of Helsinki and its subsequent revisions.

A total of 48 patients (age range, 1 month to 6 years), who underwent surgery under sevoflurane anesthesia were screened and enrolled in the present study. Patients who underwent planned mechanical ventilation, had an expected surgical time > 2 h, underwent airway surgery, had an American Society of Anesthesiologists physical status ≥ 3, formerly premature infant, infants < 44 weeks post-conception age, or emergency case status, were excluded.

All patients were fasted according to current practice guidelines from the American Society of Anesthesiologists. Recruited patients did not receive premedication. After arrival to the operating room, electrocardiogram (ECG), heart rate (HR), non-invasive blood pressure (NIBP) at 1 min intervals, peripheral oxygen saturation (SpO_2), and E_TCO_2 were monitored during induction. Preoxygenation was performed and anesthesia was induced using thiopental sodium (5-6 mg/kg for children < 3 years of age) or propofol (2-2.5 mg/kg for patients ≥ 3 years of age), and the patients spontaneously breathed a mixture of 8 vol% sevoflurane and 100% oxygen. A supraglottic airway device was inserted after confirming muscle relaxation using the trapezius squeeze test.[5]

anesthesia was maintained using 2 vol% of inspiratory sevoflurane after commencement of surgery, with a fraction of inspired oxygen of 0.4. An axillary temperature probe was placed to monitor body temperature, which was maintained > 35.5°C during the 10 min study period.

Study protocol

After stabilization the inspiratory sevoflurane concentration and end-tidal sevoflurane concentration (C_{ET}) at a vaporizer setting of 2 vol% of sevoflurane, the setting of the vaporizer was changed to 4 vol% of sevoflurane and maintained at this setting for 5 min. The setting of the vaporizer was then turned to 2 vol% of sevoflurane and maintained for an additional 5 min. During the study period (i.e., 10 min), all vital signs (ECG, HR, NIBP at 2.5 min intervals, SpO_2, TV, C_{ET}, and temperature) were closely monitored and recorded every 30 s. After the study period, all patients were liberally anesthetized by the attending anesthesiologists.

Data analysis[6,7] and model selection

The C_{ET} and the corresponding TV and E_TCO_2 were recorded every 30 s over the 10 min study period. The end-tidal sevoflurane concentration and TV, along with patient characteristics, were used to develop a PD model using nonlinear mixed-effects modelling software (NONMEM version VII; GloboMax, Hanover, MD, USA). The model provides estimates of a population's mean parameters, inter-individual random variabilities, and residual random effects. The PD model was run using the first-order conditional estimation method with inter-individual-residual interaction (FOCEI) to determine parameter estimates. To account for delays between the C_{ET} and

the sevoflurane concentration at the effect site (C_e), an effect compartment was modelled. It was assumed that the C_{ET} was linearly linked to C_e, which was estimated using the following equation:

$$dC_e/dt = (C_{ET}-C_e)\times k_{e0}$$

in which k_e0 is the first-order rate constant determining the equilibrium between the C_{ET} and C_e. The C_e over time was calculated as the convolution of the C_{ET} over time with the disposition function of the effect site. The convolution was based on a "connect-the-dots" approach previously described by Schnider et al.[8] The k_{e0} was estimated by minimizing the area of the hysteresis loop of the TV data versus the C_{ET}. An individual k_{e0} value was calculated on the basis each patient's particular TV ramp. The relationship between the C_e and TV was modelled using a sigmoid E_{max} model, as follows:

$$\text{sigmoid } E_{max} \text{ model: } E = E_0+(E_{max}-E_0)\times C_e^{\gamma}/(C_{e50}^{\gamma}+C_e^{\gamma})$$

in which E_0 is the initial TV, E_{max} is the smallest TV, C_{e50} is the effect-site sevoflurane concentration required to obtain 50% of maximum decrement of TV, and γ is the steepness of the concentration-response relation curve. Inter-individual variability in E_0, E_{max}, C_{e50}, γ, and k_{e0} was modelled using an exponential error model. Residual intra-individual variability was modelled using the additive error model. The basic population model without covariates was modelled first, and additional covariates of sex, age, height, weight, or appropriate body indices were explored successively to determine their impact on estimates of the model parameters. NONMEM computed the minimum objective

function value (OFV), the statistical equivalent of the -2 log likelihood of the model. A level of 0.05, which corresponds to a reduction in the OFV of 3.84 (chi-squared distribution, degrees of freedom = 1; $P < 0.05$), was used to distinguish between hierarchical models.

Model evaluation and validation

After building the final model, its performance was evaluated and validated. An internal bootstrap validation was performed using fit4NM version 4.6.0 (Eun-Kyung Lee and Gyu-Jeong Noh; http://fit4NM.org).[9] The medians and 2.5% to 97.5% percentiles of the bootstrap parameter estimates were compared with the final parameter estimates. The predictive performance of the final model was evaluated with the predictive checks using fit4NM version 4.6.0.

Statistical analysis

Statistical analyses were performed using SPSS version 23.0 (IBM Corporation, Armonk, NY, USA) for Windows. Data are expressed as mean ± standard deviation for normally distributed continuous variables, median (interquartile range [25 th -75th percentile]) for non-normally distributed continuous variables, and counts and percentages for categorical variables.

RESULTS

Patient characteristics are summarized in Table 1. A total of 50 patients were recruited, of whom 48 completed the study. Data from 2 patients were excluded due to an incomplete recording of data. During the study period, there were no significant hypertensive, hypotensive, bradycardia, tachycardia, or desaturation events.

Each study was commenced after a steady state of inspiratory sevoflurane concentration and C_{ET} at 2 vol% of sevoflurane vaporizer was reached; operators controlled the dial of the vaporizer from 2vol% to 4vol% of sevoflurane concentration and vice versa. Data were collected from different operating rooms, and the initial and target inspiratory sevoflurane concentration varied with the 2 or 4vol% from the vaporizer after steady state was reached. On average, the initial C_{ET} was 1.93 and the highest C_{ET} was 4.10. In addition, the average E_TCO_2 during the study period was 44 mmHg, and the lowest and highest E_TCO_2 were 24 mmHg and 66 mmHg, respectively. Sevoflurane concentration increased or decreased ahead of the changes in TV, which demonstrated hysteresis.

The time course of sevoflurane concentration and corresponding changes in TV in all recruited patients in whom an increased sevoflurane concentration was matched with a decreased TV is shown in Figure 1. Plots of sevoflurane concentration versus TV over time are shown in Figure 2. As the concentration of sevoflurane increased, TV decreased, as expected.

Parameter estimates of the final model and bootstrap validation values are summarized in Table 2. Body weight was a significant covariate for E_0, E_{max}, and adding this covariate resulted in an improvement in OFV (Δ36.89; $P < 0.05$, degrees of freedom = 1) compared with the basic model. Other patient characteristics, such

as sex, height, and body mass index, were not included as covariates.

Diagnostic plots (i.e., goodness-of-fit plots) for the final model are shown in Figure 3; this confirmed that the model had satisfactory performance and no significant bias. Predictive checks of the final model are presented in Figure 4. In total, 5.1% (points below 2.5%, 3.8%; points above 97.5%, 1.5%) of the data were distributed outside of the 95% prediction intervals of the predictive checks.

DISCUSSION

In this study, we developed a PD model for sevoflurane concentration and TV during spontaneous breathing under general anesthesia in a pediatric population. The results demonstrated that changes in TV during spontaneous breathing according to sevoflurane concentration were related to the body weight of the patient. In addition, half reduction of initial TV at 2 vol% of sevoflurane of vaporizer with increasing sevoflurane concentration was related to age. This finding was consistent with clinical expectations.

Nowadays, spontaneous breathing during general anesthesia is popular in the pediatric population due to the absence of residual risks from neuromuscular blockers and some beneficial effects on respiratory function, in relatively short surgeries or procedures. [13] Therefore, if the attending anesthesiologist has information supporting an expected reduction in TV according to the concentration of volatile anesthetic, it would be very helpful in controlling the concentration of volatile anesthetics. We anticipate that this study may lead clinicians to ensure that patients maintain adequate minute ventilation using predicted tidal volume and observed respiratory rate under certain sevoflurane concentration. In addition, it may be a reference to determine if patients who are susceptible to elevated PaCO2, for example, a patient who has intracranial hypertension or a patient who has an intracardiac shunt, need ventilatory support or not. From this perspective, the results of this study are clinically valuable.

According to the result of this study, the value of gamma was relatively high and this means that the concentration-response relation curve was steep. This result is thought to be due to the study protocol that changed the sevoflurane concentration abruptly rather than gradually. This curve may be seen as linear.

However, to maintain general anesthesia in this age group, more than 4 vol% of sevoflurane rarely use clinically. Therefore sevoflurane concentration is not increasing indefinitely and the tidal volume is not decreasing indefinitely as well. This clinically saturable model made us use the sigmoid curve to model fitting.

Traditionally, TV has been set on the basis of patient body weight for mechanical ventilation and, recently, protective mechanical ventilation was recommended at a relatively low TV of 6–8 $m\ell \cdot kg^{-1}$.[14] In this study, the initial TV of the patients was related to body weight. For example, in a patient with a body weight of 30 kg and an initial TV calculated by the PD model to be 135 ml (initial tidal volume = $82.3 \times [\frac{30}{15.4}]^{0.749}$), the estimated TV per body weight would be 4.5 mℓ. Moreover, the maximal reduction in TV was calculated to be 64 mℓ (maximal reduction tidal volume = $36.7 \times [\frac{30}{15.4}]^{0.833}$), which, converted into kilogram units, is 3.2 $m\ell \cdot kg^{-1}$. Although this may be a profound reduction in TV in this patient, usually, it is not common practice to maintain a sevoflurane concentration this high (4 vol%) and it is important to expect that a reduction in TV may be this extensive. In addition, these estimations may be less than the protective mechanical ventilation strategic setting of TV of 180 mℓ (target TV = 30 kg × 6 mℓ) during mechanical ventilation in this patient. Basically, the minute ventilation in children was estimated as 150–200 $m\ell \cdot kg^{-1} \cdot min^{-1}$,[15] and the average minute ventilation was 145 $m\ell \cdot kg^{-1} \cdot min^{-1}$ in our study. This revealed that minute ventilation was slightly lower in spontaneous breathing than mechanical ventilation during sevoflurane anesthesia in children.

A previous study reported that pressure-support ventilation (PSV) and pressure-controlled ventilation result in more appropriate E_TCO_2 compared with spontaneous ventilation, although these 3

ventilation modalities have been safely used with the ProSeal (Teleflex, Westmeath, Ireland) laryngeal mask airway.[2] In that study, the measured TV was not reported; however, there was a significantly smaller TV in spontaneous ventilation (approximately 3.2 mℓ·kg^{-1}) than with PSV. Compared with the results of our study, the expected TV of PSV would be 7.7 (4.5±3.2) mℓ·kg^{-1}. This value would be sufficient for patients during general anesthesia with spontaneous breathing using PSV, although this value should be validated in a properly designed clinical trial. This may confirm that the PD model was well developed and the resultant data fit.

A previous study reported that ventilation with larger TV with isocapnea maintained with added dead-space volume increased the tension of sevoflurane in the arterial blood of adults.[7] This finding may be explained by increases in inspired gas concentration, functional residual capacity and/or alveolar ventilation. The present study demonstrated that the smaller TV considered body weight with hypercapnea and, as a result, the tension of sevoflurane in arterial blood may be less than expected.

Other research has shown that E_TCO_2 monitoring in children, whose lungs were mechanically ventilated, may paradoxically lead to overestimation of E_TCO_2 (E_TCO_2 > $PaCO_2$), with a subsequent risk for unrecognized hypocarbia.[16] Although that study involved mechanical ventilation, which was different from our study, the information could provide a clue that hypercapnia on capnography would be overestimated in children. In the present study, the mean E_TCO_2 during the study period was 44 mmHg. The highest E_TCO_2 was 66 mmHg (range, 54-66 mmHg) in a 6-year-old boy. A previous study reported that the mean E_TCO_2 during spontaneous breathing was 55.2 mmHg and the highest

value was 75 mmHg in a similar age group.[2] Although several studies have investigated the effects of hypercarbia,[17,18] there are still controversies regarding the limits of acceptable or permissive hypercarbia in daily clinical practice. The highest E_TCO_2 was 66 mmHg in one patient and the average E_TCO_2 was 44 mmHg; however, this value would be acceptable during general anesthesia in patients without significant underlying diseases.

To develop the PD model, we first created the basic model and then added covariates, such as age, sex, height, body weight or body mass index, to the final model. After modelling, TV was found to be related to body weight as expected. Because the present study was designed similar to real-world daily clinical practice, we adjusted the sevoflurane concentration to between 2vol% and 4vol%: these values are clinically common sevoflurane concentrations during the maintenance of general anesthesia. Therefore, our results are valuable in estimating the reduction in TV as the sevoflurane concentration changes.

In this study, we did not apply PSV, which may have reduced E_TCO_2 during the study period. In a previous study, PSV with spontaneous breathing during anesthesia reduced E_TCO_2, although spontaneous breathing without pressure support was safe for children. Therefore, further studies should be performed using the design of the present study during PSV.

In conclusion, initial TV and the smallest TV corresponding to 2-4 vol% of inspiratory sevoflurane was affected by body weight during spontaneous breathing under general anesthesia in a pediatric population.

References

1. Ukere A, Marz A, Wodack KH, Trepte CJ, Haese A, Waldmann AD, Bohm SH, Reuter DA (2016) Perioperative assessment of regional ventilation during changing body positions and ventilation conditions by electrical impedance tomography. Br J anesth 117 (2):228-235. doi:10.1093/bja/aew188

2. Templeton TW, Hoke LK, Yaung J, Aschenbrenner CA, Rose DM, Templeton LB, Bryan YF (2016) Comparing 3 ventilation modalities by measuring several respiratory parameters using the ProSeal laryngeal mask airway in children. J Clin Anesth 34:272-278. doi:10.1016/j.jclinane.2016.04.031

3. Lim B, Pawar D, Ng O (2012) Pressure support ventilation vs spontaneous ventilation via ProSeal laryngeal mask airway in pediatric patients undergoing ambulatory surgery: a randomized controlled trial. pediatr anesth 22 (4):360-364. doi:10.1111/j.1460-9592.2012.03819.x

4. McKay RE (2018) Inhaled Anesthetics In: Manuel C. Pardo J, Ronald D. Miller (ed) Basics of anesthesia Elsevier, Philadelphia, PA pp 83-103

5. Dinesh Kumar KK, Bhardwaj N, Yaddanapudi S (2017) Comparison of trapezius squeeze test and jaw thrust as clinical indicators for laryngeal mask airway insertion in spontaneously breathing children. J anesthesiol Clin Pharmacol 33 (1):71-75. doi:10.4103/0970-9185.202204

6. Lee JH, Kang PY, Jang YE, Kim EH, Kim JT, Kim HS (2018) A pharmacodynamic model of respiratory rate and end-tidal carbon dioxide values during anesthesia in children. Acta Pharmacol Sin. doi:10.1038/s41401-018-0156-x

7. Enekvist B, Bodelsson M, Sturesson LW, Johansson A (2010) Larger tidal volume increases sevoflurane uptake in blood: a randomized clinical study. Acta anesthesiol Scand 54

(9):1111-1116. doi:10.1111/j.1399-6576.2010.02291.x
8. Schnider TW, Minto CF, Shafer SL, Gambus PL, Andresen C, Goodale DB, Youngs EJ (1999) The influence of age on propofol pharmacodynamics. Anesthesiology 90 (6):1502-1516
9. Ki SH, Rhim JH, Park JH, Han YJ, Cho YP, Kwon TW, Choi BM, Noh GJ (2018) Quantitative analysis of the effect of end-tidal carbon dioxide on regional cerebral oxygen saturation in patients undergoing carotid endarterectomy under general anesthesia. Br J Clin Pharmacol 84 (2):292-300. doi:10.1111/bcp.13441
10. Neil E. Farber EAES, Astrid G. Stucke and Paul S. Pagel (2015) Inhaled Anesthetics: Pulmonary Pharmacology. In: Miller RD (ed) Miller's anesthesia. Elsevier Saunders, Philadelphia, Pennsylvania, pp 670-705
11. Brown KA, Reich O, Bates JH (1995) Ventilatory depression by halothane in infants and children. Can J anesth 42 (7):588-596. doi:10.1007/BF03011875
12. Miller RD, Cohen NH, Eriksson LI, Fleisher LA, Wiener-Kronish JP, Young WL (2015) Miller's anesthesia. Elsevier/Saunders, Philadelphia, PA
13. Liu YJ, Hung MH, Hsu HH, Chen JS, Cheng YJ (2015) Effects on respiration of nonintubated anesthesia in thoracoscopic surgery under spontaneous ventilation. Ann Transl Med 3 (8):107. doi:10.3978/j.issn.2305-5839.2015.04.15
14. Serpa Neto A, Schultz MJ, Slutsky AS (2015) Current concepts of protective ventilation during general anesthesia. Swiss Med Wkly 145:w14211. doi:10.4414/smw.2015.14211
15. Mason KP (2011) Pediatric Sedation Outside of the Operating Room: A Multispecialty International Collaboration. In. Springer New York, p 114
16. Onodi C, Buhler PK, Thomas J, Schmitz A, Weiss M (2017) Arterial to end-tidal carbon dioxide difference in children

undergoing mechanical ventilation of the lungs during general anesthesia. anesthesia 72 (11):1357-1364. doi:10.1111/anae.13969
17. Sakata K, Kito K, Fukuoka N, Nagase K, Tanabe K, Iida H (2018) Cerebrovascular reactivity to hypercapnia during sevoflurane or desflurane anesthesia in rats. Korean J Anesthesiol. doi:10.4097/kja.d.18.00244
18. Kanaya A, Kuratani N, Kaiho Y, Yamauchi M (2016) Intraoperative hypercapnia and anesthesia emergence after pediatric ambulatory surgery. pediatr anesth 26 (11):1116-1117. doi:10.1111/pan.12984
19. Katoh T, Ikeda K (1992) Minimum alveolar concentration of sevoflurane in children. Br J anesth 68 (2):139-141
20. Eger EI, 2nd, Bahlman SH (1971) Is the end-tidal anesthetic partial pressure an accurate measure of the arterial anesthetic partial pressure? Anesthesiology 35 (3):301-303

Table1. Patients' characteristic

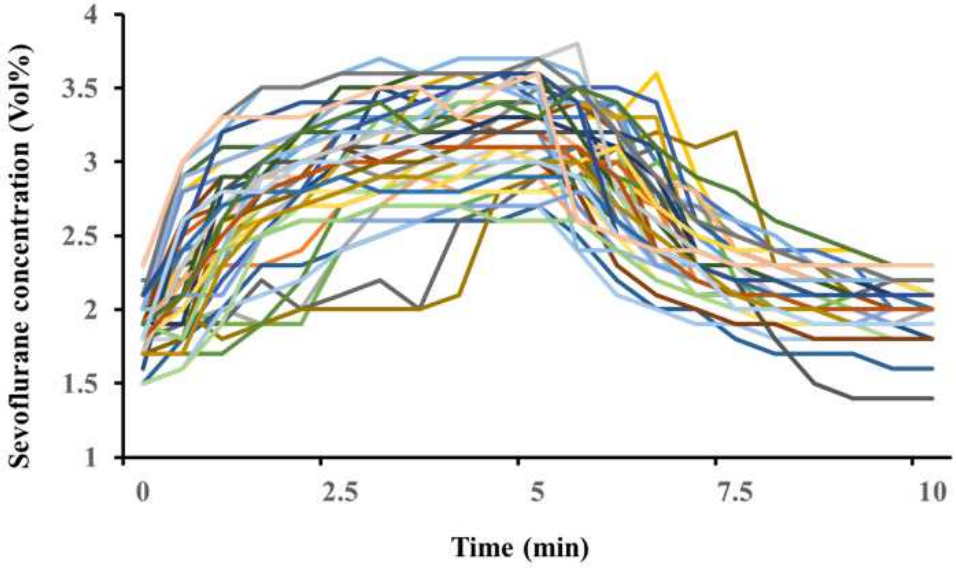
Age (years)	3.42	± 1.7
Sex (Male/Female)	27/21	
Body weight (㎏)	16.5	±5.7
Height (cm)	97.6	± 14.9

Table 2. Pharmacodynamic model parameters estimates from NONMEM and the bootstrap proccedure (with standard errors and confidence intervals). CI, 2.5-97.5% confidence interval; RSE, relative standard error. See text for details regarding parameter definitions.

Parameters	Estimate (RSE, %)				Median [CI]
	Base model	Final model			
E_0, ml	82.9 (5.82)	E_0 (ml) = θ_1 x(WT/15.4)$^{\theta 2}$	θ_1	83.0 (4.40)	78.19-86.15
			θ_2	0.754(25.1)	0.56-0.98
E_{max}, ml	27.6 (20.9)	E_{max} (ml) = θ_3 x(WT/15.4)$^{\theta 4}$	θ_3	29.7 (29.22)	17.37-35.46
			θ_4	0.676(43.7)	0.37-1.49
C_{e50}, vol%	2.79 (2.69)			2.78 (4.59)	2.68-2.97
γ	8.63 (6.81)			8.78 (19.13)	6.96-10.75
k_{e0}, min^{-1}	2.27 (13.79)			2.27 (14.14)	1.78-2.73
OFV	5586.756		5549.866 (Δ36.89)		

Figure 1. Time courses of inspiratory sevoflurane concentration (A) and tidal volume (B) during spontaneous ventilation under general anesthesia in all recruited patients.

(A)



(B)

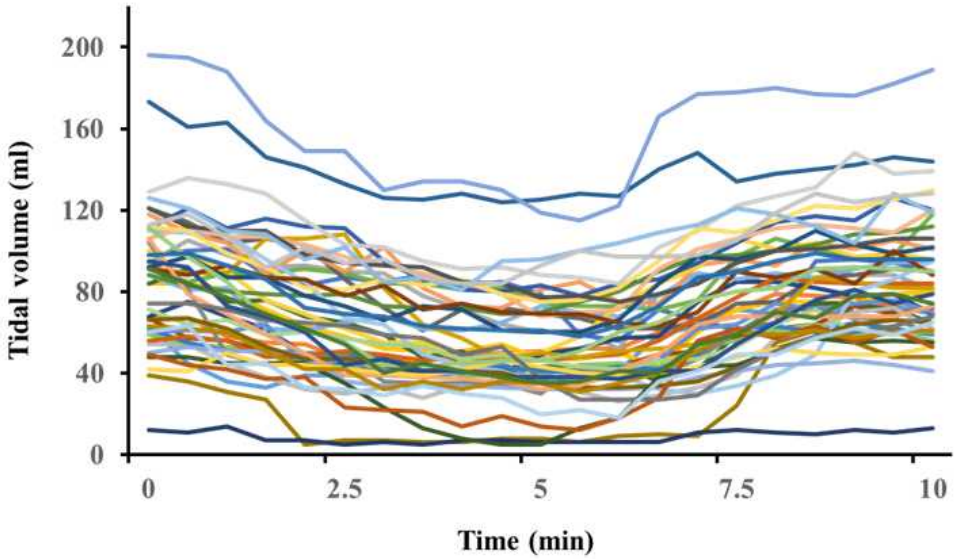


Figure 2. The relationship between inspiratory sevoflurane concentration and tidal volume during study period under general anesthesia in all recruited patients.

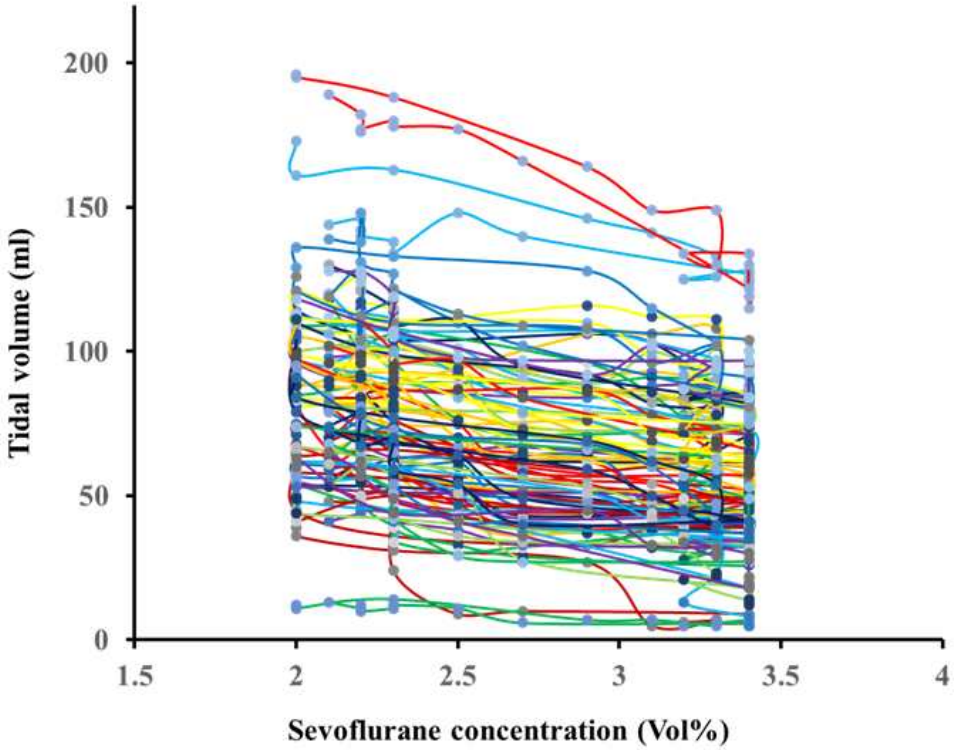


Figure 3. Goodness-of-fit of population (A) and individual prediction (B) of tidal volume of final model. Dotted line represents the line of identify.

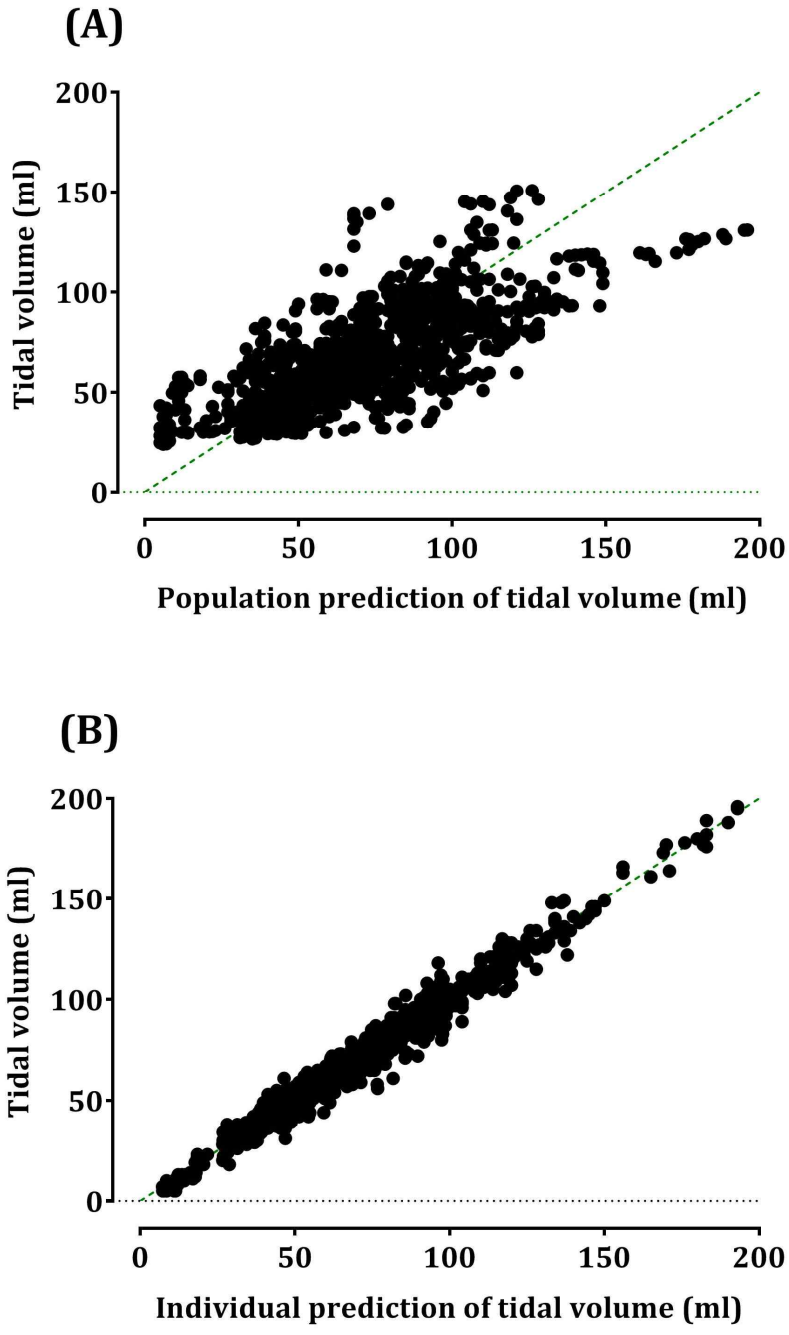
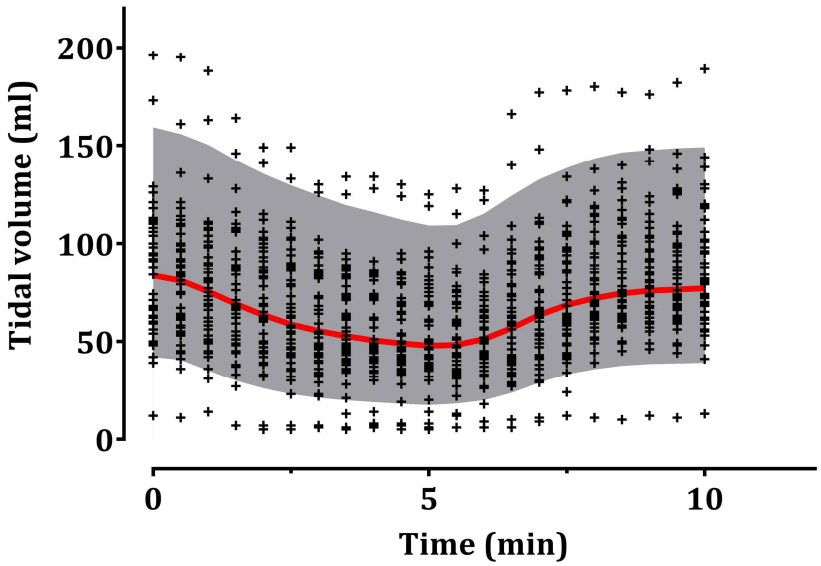


Figure 4. Predictive checks of the final pharmacodynamics model. A black + indicates the observed tidal volume. The solid red line and shaded areas indicate the 50% prediction line and 95% prediction intervals, respectively. In total, 5.6% of the data were distributed outside of the 95% prediction intervals of the predictive checks.



국 문 초 록

목적 : 고농도의 세보플루란은 자발 호흡 시 일회 호흡량을 감소시킨다. 이 연구의 목적은 일회호흡량과 세보플루란 농도 사이의 관계에 영향을 주는 임상적인 요인들을 밝혀내고, 소아 환자들에서 일회호흡량과 세보플루란 농도의 집단 약력한 모델을 구축하는 데에 있다.

방법 : 후두마스크를 이용한 전신마취가 예정되어있었던 48명의 6세 이하 소아 환자들을 대상으로 전향적 관찰연구가 진행되었다. 흡입 세보플루란의 농도가 2 볼륨 퍼센트에 도달하였을 때, 기화기를 4 볼륨 퍼센트로 설정하고 5분을 기다린 후 다시 2 볼륨 퍼센트로 바꾸어 5분을 유지하였다. 연구 기간 동안 일회 호흡량, 호기말 이산화탄소 분압, 세보플루란 농도가 30초 마다 기록되었다. 일회호흡량과 세보플루란 농도 사이의 관계를 알아보기 위하여 S자모양 최대효과 모형을 이용한 약력학적인 분석을 시행하였다.

결과 : 일회호흡량은 흡입 세보플루란 농도가 증가함에 따라 감소하였다. 일회호흡량과 세보플루란 농도 사이에 이력현상이 관찰되었으며 이는 모형 구축 시에 고려되었다. 처음의 일회 호흡량과 일회호흡량의 최대 감소치는 체중과 관련이 있었다. Hill 계수(Hill's coefficient, γ)와 효과처 평형 속도 상수(k_{e0})는 각각 8.78과 2.27이었다.

결론 : 세보플루란을 이용하여 전신마취를 시행하는 중, 자발호흡 시에 세보플루란 농도는 일회호흡량의 변화와 연관이 있다. 소아 환자에서 처음의 일회호흡량과 일회호흡량의 최고 감소 정도는 체중과 관련이 있었다.

주요어 : 소아, 세보플루란, 자발호흡, 일회호흡량

학 번 : 2017-26753