Does Equi–Minimum Alveolar Concentration Value Ensure Equivalent Analgesic or Hypnotic Potency?

A Comparison between Desflurane and Sevoflurane

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ABSTRACT

Background: Minimum alveolar concentration (MAC) has traditionally been used to compare the potency of volatile anesthetics. However, as it reflects the spinal mechanism of immobility rather than the cerebral mechanism of analgesia and hypnosis, it is doubtful that equi-MAC connotes equivalent analgesic or hypnotic potency. The level of analgesia and hypnosis can be assessed using surgical pleth index and bispectral index (BIS) values, respectively. This study was designed to compare the surgical pleth index and BIS values produced by equi-MAC of desflurane and sevoflurane in patients undergoing single-agent volatile anesthesia.

Methods: Eighty-nine patients were randomly allocated to two groups receiving either desflurane (n = 44) or sevoflurane (n = 45). Anesthesia was only maintained with assigned volatile anesthetic of age-corrected 1.0 MAC. Surgical pleth index values as an analgesic estimate and BIS values as a hypnotic estimate were obtained under standard tetanic stimulation.

Results: Post-stimulation surgical pleth index values (mean ± SD), the primary outcome, were significantly lower for the desflurane group than those for the sevoflurane group (49 ± 10 *vs.* 64 ± 14, difference, 15 [95% CI, 10 to 20], $P < 0.001$). The desflurane group showed significantly lower poststimulation BIS values (median [interquartile range]) than the sevoflurane group (36 [31 to 41] *vs.* 41 [38 to 47], difference, 6 [95% CI, 2 to 9], $P = 0.001$).

Conclusions: During a steady-state of 1.0 MAC, desflurane and sevoflurane did not cause similar surgical pleth index and BIS values under the standardized nociceptive stimulus. These findings suggest that equi-MAC of desflurane and sevoflurane may not ensure equivalent analgesic or hypnotic potency.

Visual Abstract: An online visual overview is available for this article at http://links.lww.com/ALN/B726. **(Anesthesiology 2018; 128:1092-8)**

IDEAL general anesthesia is achieved from an appropriate combination of analgesia, hypnosis, and immobility.[1,2] Various anesthetics act on the entire central nervous system, including the subcortical (analgesia) and cortical (hypnosis) brain areas, as well as the spinal cord (immobility), but have different spectra in analgesic, hypnotic, and immobilizing potencies.[3,4] Minimum alveolar concentration (MAC) has traditionally been used as the standard measure to compare the potencies of volatile anesthetics.[5–7] Since MAC reflects the spinal mechanism of immobility rather than the cerebral mechanism of analgesia and hypnosis,[8,9] specific MAC values might not guarantee analgesic or hypnotic levels.

Owing to their rapid pharmacokinetics, the volatile anesthetics desflurane and sevoflurane are widely used in balanced anesthesia in combination with anesthetic adjuvants such as remifentanil. To ensure the safe administration of anesthetic adjuvants and early recovery from anesthesia, it is essential to comprehend the differences in analgesic and hypnotic potencies of various volatile anesthetics.

We hypothesized that different volatile anesthetics at equi-MAC would not have equivalent analgesic and hypnotic potencies. The levels of analgesia and hypnosis were assessed using surgical pleth index and bispectral index (BIS) values, respectively. The aim of this study was to compare the surgical pleth index and BIS values produced by desflurane and sevoflurane at equi-MAC under standardized nociceptive stimuli in patients undergoing single-agent volatile anesthesia.

What We Already Know about This Topic

- The dose of volatile anesthetic agents is measured in minimum alveolar concentration (MAC) multiples. MAC, however, is a reflection of the activity of volatile agents on the spinal cord and it is not clear whether equi-MAC doses of volatile agents result in equivalent analgesia and hypnosis.

What This Article Tells Us That Is New

- In patients anesthetized with 1.0 minimum alveolar concentration of either desflurane or sevoflurane, analgesic and hypnotic potency, as measured by surgical pleth index and bispectral index, were greater with desflurane than with sevoflurane.
- The results suggest that volatile agent equivalence of effect at the spinal cord is not equivalent to the effect at the brain, when evaluated by analgesia and hypnosis.

Materials and Methods

This prospective, randomized trial was approved by the Institutional Ethics Committee (Kangbuk Samsung Hospital Institutional Review Board, Seoul, Republic of Korea; Approval number: KBSMC 2015-12-023) and registered

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at ClinicalTrials.gov (Clinical Trial No. NCT02698514, principal investigator: Kyoung-Ho Ryu, date of registration: February 22, 2016; https://clinicaltrials.gov/ct2/show/NCT02698514) prior to enrollment of the first subject.

Before randomization, all eligible patients scheduled for arthroscopic knee surgery were asked to participate in this study. Written informed consents were obtained from all participating subjects. Inclusion criteria were as follows: aged between 19 and 65 yr and American Society of Anesthesiologists physical status classification I and II. Exclusion criteria were as follows: any neurologic or psychiatric disease (*e.g.,* stroke, dementia, and major depressive disorder), cardiac arrhythmia, diabetes mellitus, alcohol or drug abuse, and use of any medication affecting the central or autonomic nervous system (*e.g.,* hypnotics, anxiolytics, antidepressants, analgesics, beta-blockers, and anticholinergics).

The subjects were randomly allocated to two groups (desflurane and sevoflurane groups) of equal numbers to determine the maintenance anesthetics using a random-permuted block randomization algorithm *via* a web-based response system (www.randomization.com). Allocation concealment was performed using serially numbered opaque envelopes, each containing a folded paper on which the anesthesia protocol (desflurane and sevoflurane) was recorded. The envelopes were stored and opened by an independent researcher in a laboratory distant from the hospital. The subject allocation was not changed after the envelope was opened.

The subjects received no premedication, such as anticholinergics or sedatives. After arrival in the operating room, standard monitoring (S/5 Anesthesia Monitor; GE Healthcare, Finland), including electrocardiography, noninvasive blood pressure, and pulse oximetry for surgical pleth index were applied and a BIS-Quatro sensor (Covidien, USA) was attached to the forehead of the subject. Surgical pleth index and BIS values were used as surrogate measures to assess the analgesic and hypnotic levels of single-agent volatile anesthesia, respectively. The level of muscle relaxation was monitored by train-of-four using a piezoelectric neuromuscular monitor device (M-NMT MechanoSensor, GE Healthcare, Finland). A train-of-four count of 1 to 2 was maintained in both groups during the study period. End-tidal anesthetic concentration was continuously measured using the infrared spectrophotometric analyzer (S/5 Anesthesia Monitor). The esophageal temperature and end-tidal partial pressure of carbon dioxide were monitored to ensure normothermia and normocapnia, respectively.

Photoplethysmographic waveforms were collected from the contralateral index finger of the arm with a noninvasive blood pressure cuff. The surgical pleth index is a dimensionless numerical index obtained by a finger clip sensor used for measuring transcutaneous oxygen saturation to monitor the intraoperative nociception-antinociception balance. It is a measure of the combination of a central sympathetic tone, denoted by heart beat interval, and a peripheral sympathetic tone, denoted by photoplethysmographic pulse wave amplitude. The SPI is calculated based on an algorithm combining normalized heart beat interval (HBI_{norm}) and normalized photoplethysmographic pulse wave amplitude ($PPGA_{norm}$) data using the following equation: surgical pleth index = 100 – (0.33 × HBI_{norm}) + (0.67 × $PPGA_{norm}$).[10] The surgical pleth index values range from 0 (representing minimum surgical stress level) to 100 (representing maximum surgical stress level). A surgical pleth index value of 50 represents a mean surgical stress level during general anesthesia.

All monitoring data including surgical pleth index, BIS, mean arterial pressure (MAP), and heart rate (HR) were collected every 20 s. Before induction of anesthesia, the baseline values of surgical pleth index, BIS, MAP, and HR were recorded as mean values for 1 min. To standardize and minimize bolus dose of propofol (Fresofol MCT 1%; Fresenius Kabi Austria GmbH, Austria), anesthetic induction was performed using target-controlled infusion. Propofol infusion *via* target-controlled infusion device (Orchestra Base Primea; Fresenius Vial, France) was used only for the induction of anesthesia. The maintenance of anesthesia was achieved with randomly assigned volatile anesthetic only. Using the Marsh pharmacokinetic model,[11] the initial target predicted effect-site concentration of propofol was set to 3.0 μg/ml, and propofol infusion was started in the flash mode. Immediately after loss of consciousness, effect-site concentration of propofol in the target-controlled infusion device was adjusted to 0.0 μg/ml, and propofol infusion was stopped. Simultaneously, the assigned volatile anesthetic, either desflurane (Suprane; Baxter Healthcare, Puerto Rico) or sevoflurane (Sevorane; AbbVie Ltd, United Kingdom), was administered through a tight-fitting facemask. After rocuronium 0.6 mg/kg was administered for neuromuscular block, a supraglottic airway (SGA) device (i-gel; Intersurgical Ltd., United Kingdom) was inserted according to the manufacturer's recommendations and mechanical ventilation was initiated.

The anesthetic concentration increase was facilitated by overpressurization using approximately 2.0 MAC, with the aim of reaching 1.0 MAC. The MAC values were corrected based on age-related iso-MAC charts.[12,13] Anesthesia was maintained with the volatile anesthetic at 1.0 MAC as the single anesthetic agent. Other anesthetic adjuvants, such as nitrous oxide and opioid, were not used throughout the study period. To allow the effects of propofol to be cleared and to ensure brain-alveolar equilibration of volatile anesthetics, after an initial 30-min waiting period from the induction of anesthesia had elapsed, the participants were subjected to standardized noxious stimulation. The vaporizer dial was adjusted by an independent coordinator, who was blinded to the study protocol, to maintain the end-tidal anesthetic concentration at 1.0 MAC during the 30-min waiting period. Outcomes measurements were performed after confirming a steady-state (defined as a brain-alveolar equilibration

condition in which constant target end-tidal anesthetic concentration is maintained without vaporizer dial adjustment) of 1.0 MAC for the last 10 min of the waiting period.

The prestimulation measurement window was designated as 1 min before stimulation. Immediately before applying noxious stimulation, the prestimulation values of the surgical pleth index, BIS, MAP, and HR were recorded as mean values for 1 min at a steady-state of 1.0 MAC. The stimulation electrodes of a peripheral nerve stimulator (EZstim II, Model ES400; Life-Tech, USA) were placed over the ulnar nerve on the volar side of the wrist of the opposite arm from the surgical pleth index sensor. The standardized noxious stimulation was generated by long-lasting tetanic stimulation (square-wave, duration of 30 s, amplitude of 50 mA, and frequency of 50 Hz).[14] The poststimulation measurement window was designated as 1 min after stimulation, based on the pilot study in which all study outcomes showed the maximum response within 1 min. The poststimulation values of the surgical pleth index, BIS, MAP, and HR were recorded as the maximum change values from the prestimulation values within 1 min after the start of tetanic stimulation at a steady-state of 1.0 MAC. Change of variables as a response to tetanic stimulation was denoted as reaction value, defined as the maximal difference between the prestimulation and poststimulation values. Consequently, the following four values were obtained at three predefined time points, as shown in figure 1:

(1) Baseline: mean value for 1 min before induction of anesthesia.
(2) Prestimulation: mean value for 1 min before applying tetanic stimulation after induction of anesthesia.
(3) Poststimulation: maximum change value from the prestimulation value within 1 min after the start of tetanic stimulation.
(4) Reaction: difference value between the prestimulation and poststimulation values as a response to tetanic stimulation.

The study outcomes were recorded by an investigator who was blinded to the group allocation. To ensure brain-alveolar equilibration of the anesthetic, all outcomes were recorded only after meeting a steady-state of 1.0 MAC. To minimize the effects of propofol on depth of anesthesia, all the study outcomes were collected after the effect-site concentration of propofol of the target-controlled infusion device was reduced to less than 0.2 μg/ml. The operating room was kept as quiet as possible and all external stimuli other than tetanic stimulation were minimized during the study period. The scheduled operation began after a long enough waiting period (about 20 min of sterile draping) had elapsed since the poststimulation values were obtained. Within 72 h after surgery, anesthesia awareness was assessed using the questionnaire, modified from Brice *et al.*[15] At any time during the study period, if the BIS value was greater than 70, MAP was less than 60 mmHg, HR was fewer than 45 beats/min, or HR was greater than 140 beats/min, then additional sedatives, vasopressors, vagolytics, or beta-blockers were administered, respectively, and the subject was considered a drop out and the data for the subject were excluded from the final analysis.

Statistical Analysis

The primary outcome of this study was the poststimulation surgical pleth index value at a steady-state of age-corrected

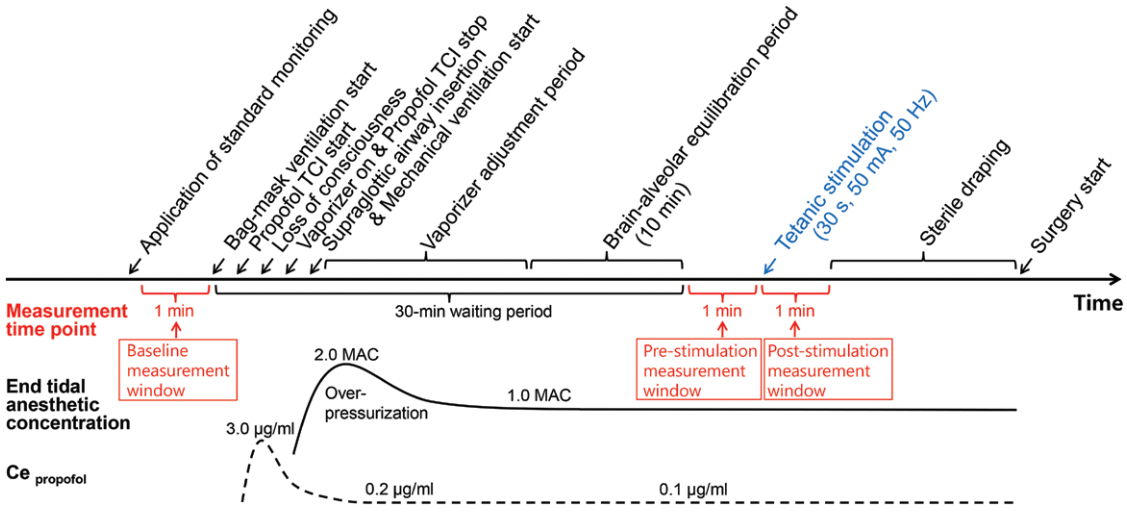

Fig. 1. Study timeline. Four values (baseline, prestimulation, poststimulation, and reaction value) were obtained at three predefined time points (*red arrows*). To ensure brain-alveolar equilibration of volatile anesthetics, a waiting period of 30 min was allowed before tetanic stimulation. The standardized noxious stimulation (*blue arrow*) was generated by long-lasting tetanic stimulation (square-wave, duration of 30 s, amplitude of 50 mA, frequency of 50 Hz). The solid line indicates end-tidal anesthetic concentration; the dashed line indicates the predicted effect-site concentration (Ce) of propofol by target-controlled infusion (TCI) device. MAC = minimum alveolar concentration.

1.0 MAC. The sample size was calculated based on the results of a pilot study of 30 cases (fifteen patients per group). In the pilot study, poststimulation surgical pleth index values (mean ± SD) were 52 ± 14 in desflurane group and 60 ± 12 in sevoflurane group, respectively. A sample size of 42 patients per group was estimated using a two-tailed *t* test, a power of 80%, and a significance level of 5%. To allow for potential dropouts of 5%, 90 patients were recruited.

Statistical analyses were performed using the PASW software (PASW Statistics version 18.0; IBM, USA). All analyses were performed according to the initially allocated group based on the intention-to-treat principle. No interim analysis was planned or performed. Data are presented as frequency for categorical variables, and mean ± SD or median (interquartile range) for continuous variables, as appropriate. The normal distribution of the continuous variables was first evaluated using the Shapiro–Wilk test. The baseline demographic characteristics and study outcomes were compared between the two groups using the chi-square test or Fisher exact test for categorical variables, and the Student's *t* test or the Mann–Whitney U test for continuous variables, as appropriate. The point estimates and corresponding 95% CIs for the differences between groups were presented for all study outcomes, and those for non-normally distributed data were quantified by the Hodges-Lehmann estimates with their 95% CIs.[16] *P* values less than 0.05 were considered statistically significant.

Results

One-hundred twenty-six patients were recruited between February 2016 and July 2016; however, two patients declined participation and 34 were ineligible based on the exclusion criteria. Therefore, 45 subjects were included in each group. One subject was excluded from the desflurane group because of the administration of esmolol. Thus, the final analyses were confined to 89 subjects, with 44 subjects in the desflurane group and 45 subjects in the sevoflurane group (fig. 2). The baseline demographic characteristics, mean propofol dose used for the induction of anesthesia, and type of surgery were not significantly different between the two groups (table 1). Mean end-tidal anesthetic concentrations of desflurane group and sevoflurane group at age-corrected 1.0 MAC were 6.7 ± 0.5 vol% and 1.8 ± 0.1 vol%, respectively. None of the subjects reported explicit awareness with recall.

Table 2 represents the baseline, prestimulation, poststimulation, and reaction values of the study outcomes. The baseline values before the induction of anesthesia were not significantly different between the two groups. At a steady-state of age-corrected 1.0 MAC, the poststimulation surgical pleth index values were significantly lower for the desflurane group than those for the sevoflurane group (49 ± 10 *vs.* 64 ± 14; difference, 15 [95% CI, 10 to 20], $P < 0.001$). The prestimulation surgical pleth index values were also significantly lower for the desflurane group than those for the sevoflurane group (23 [19 to 30] *vs.* 29 [21 to 33]; difference, 4 [95% CI, 1 to 8], $P = 0.024$). The desflurane group showed significantly lower reaction value of surgical pleth index than the sevoflurane group (23 ± 10 *vs.* 34 ± 13; difference, 11 [95% CI, 6 to 15], $P < 0.001$).

At a steady-state of age-corrected 1.0 MAC, the poststimulation BIS values were significantly lower for the desflurane group than those for the sevoflurane group (36 [31 to 41] *vs.* 41 [38 to 47]; difference, 6 [95% CI, 2 to 9],

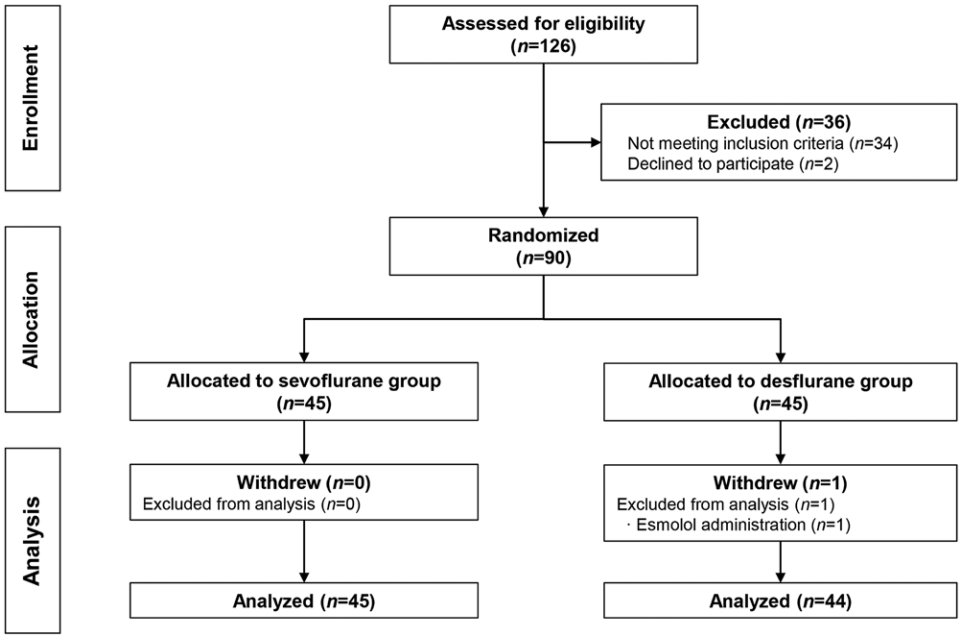

Fig. 2. The Consolidated Standards of Reporting Trials flow diagram. Enrollment, randomization, and allocation of the study subjects.

Table 1. Demographic and Clinical Data

	Desflurane Group (n = 44)	Sevoflurane Group (n = 45)	*P* Value
Age (yr)	38 ± 12	40 ± 12	0.514
Sex (male/female)	27 / 17	24 / 21	0.444
Height (cm)	170 ± 9	167 ± 9	0.163
Weight (kg)	74 ± 11	70 ± 13	0.092
BMI (kg/m^2)	25.5 ± 3.3	24.7 ± 3.5	0.281
ASAPS (I/II)	38 / 6	37 / 8	0.592
Propofol dose (mg/kg)*	1.09 ± 0.08	1.08 ± 0.06	0.288
Type of surgery			0.213
Meniscectomy	29	35	
Ligament Reconstruction	15	10	

Data are expressed as the mean ± SD or number of subjects, as appropriate. No statistically significant differences were observed between the two groups.

*Bolus dose (mg/kg of body weight) infused *via* target-controlled infusion device for the induction of anesthesia.

ASAPS = American Society of Anesthesiologists physical status; BMI = body mass index.

P = 0.001). The prestimulation BIS values were also significantly lower for the desflurane group than those for the sevoflurane group (33 [29 to 38] *vs.* 37 [31 to 42]; difference, 3 [95% CI, 0 to 6], *P* = 0.038). The desflurane group showed significantly lower reaction value of BIS than the sevoflurane group (3 [1 to 6] *vs.* 5 [2 to 9]; difference, 2 [95% CI, 0 to 4], *P* = 0.021).

In hemodynamics, the prestimulation, poststimulation, and reaction values of MAP were significantly lower for the desflurane group than those for the sevoflurane group, while those of HR showed no significant differences between the two groups.

Discussion

The aim of this randomized controlled trial was to compare the surgical pleth index and BIS values for desflurane and sevoflurane of age-corrected 1.0 MAC in response to standard tetanic stimulation during single-agent volatile anesthesia. The two volatile anesthetics at equi-MAC did not produce similar surgical pleth index and BIS values in response to equivalent stimuli.

General anesthesia comprises a combination of three major components: analgesia, hypnosis, and immobility.[1,2] Therefore, ideal general anesthesia can be achieved by a combination of various anesthetic agents with different action mechanisms.[17] Most volatile anesthetics act on the entire central nervous system; however, agent-specific actions at various central nervous system sites, including the cortical (hypnosis) and subcortical (analgesia) brain areas, as well as the spinal cord (immobility) have been reported.[4,8,18] In recent years, balanced anesthesia using volatile anesthetics, such as desflurane and sevoflurane, with rapid pharmacokinetics have been widely conducted in combination with anesthetic adjuvants.[17,19] Therefore, it is mandatory to

Table 2. Variables during Steady-state Anesthesia of Age-corrected 1.0 MAC

Variables	Desflurane Group (n = 44)	Sevoflurane Group (n = 45)	Difference (95% CI)	*P* Value
Baseline*				
SPI	71 (63 to 76)	70 (65 to 77)	–1 (–4 to 4)	0.774
BIS	92 (88 to 97)	93 (88 to 97)	0 (–1 to 2)	0.745
MAP (mmHg)	104 ± 16	102 ± 11	–2 (–7 to 4)	0.608
HR (beat/min)	68 ± 12	68 ± 13	0 (–4 to 6)	0.776
Prestimulation†				
SPI	23 (19 to 30)	29 (21 to 33)	4 (1 to 8)	0.024
BIS	33 (29 to 38)	37 (31 to 42)	3 (0 to 6)	0.038
MAP (mmHg)	78 ± 9	85 ± 9	7 (3 to 11)	< 0.001
HR (beat/min)	75 ± 14	74 ± 12	–1 (–6 to 5)	0.787
Poststimulation‡				
SPI	49 ± 10	64 ± 14	15 (10 to 20)	< 0.001
BIS	36 (31 to 41)	41 (38 to 47)	6 (2 to 9)	0.001
MAP (mmHg)	88 ± 13	99 ± 14	11 (6 to 17)	< 0.001
HR (beat/min)	96 ± 17	96 ± 14	0 (–6 to 7)	0.868
Reaction values§				
SPI	23 ± 10	34 ± 13	11 (6 to 15)	< 0.001
BIS	3 (1 to 6)	5 (2 to 9)	2 (0 to 4)	0.021
MAP (mmHg)	7 (4 to 12)	13 (7 to 20)	4 (1 to 8)	0.018
HR (beat/min)	20 (10 to 30)	22 (12 to 30)	2 (–3 to 6)	0.480

Data are expressed as the mean ± SD or median (interquartile range), as appropriate. The differences between groups for non-normally distributed data were quantified by the Hodges-Lehmann estimates with corresponding 95% CI.

*Preanesthetic baseline value at "awake" status after the attachment of standard monitoring. †Postanesthetic value immediately before standardized tetanic stimulation. ‡Peak value after standardized tetanic stimulation. §Reaction value defined as the maximal difference between the pre- and poststimulation values.

BIS = bispectral index; HR = heart rate; MAC = minimum alveolar concentration; MAP = mean arterial pressure; SPI = surgical pleth index.

understand the differences in the analgesic and hypnotic potencies of various volatile anesthetics for maintenance of an appropriate anesthetic depth and rapid recovery from anesthesia.

Traditionally, MAC has been widely used to compare the potencies of different volatile anesthetics.[5,6] MAC is defined as the concentration of anesthetic vapor at one atmosphere that prevents movement in 50% of subjects in response to surgical incision.[5,6,12] Volatile anesthetic-induced immobility is mediated by spinal α-motor neuron depression.[7–9] Because the MAC reflects the spinal mechanism of immobility rather than the cerebral mechanism of analgesia and hypnosis, it is doubtful that MAC concept connotes analgesic or hypnotic potency.[20] Kim *et al*. suggested that the respective potencies of volatile anesthetics, such as hypnotic, analgesic, and immobilizing potencies, should be distinguished.[21] However, there have been no controlled studies which compare the analgesic and hypnotic potencies between different volatile anesthetics at equi-MAC.

In general anesthesia, the level of hypnosis and muscle relaxation has been evaluated by numerous monitoring tools, such as electroencephalogram (EEG)-derived index and train-of-four. The level of analgesia could be assessed using tools, such as numerical rating scale and visual analog scale; however, these scales are not applicable to patients under general anesthesia. Until recently, there were no objective estimates to the level of analgesia during general anesthesia. Nevertheless, the newly developed surgical pleth index has been indicated to reflect the level of analgesia during general anesthesia.[10,22–25] It has been shown that the surgical pleth index value is low when a nociceptive input is low or the analgesic concentration is high, and the surgical pleth index value is high when a nociceptive input is high or the analgesic concentration is inadequate.[10] Gruenewald *et al*. showed that the surgical pleth index response to standardized nociceptive stimuli was dependent on the analgesic concentration.[23] As such, it may be more useful in analyzing analgesic states by the trend in changes of relative values rather than absolute values. In our study, both poststimulation and reaction values of surgical pleth index in response to equivalent stimuli were significantly lower for desflurane than those for sevoflurane at a steady-state of 1.0 MAC. Based on the results of this study and previous studies, it can be suggested that desflurane may have greater analgesic potency than sevoflurane at equi-MAC.

The BIS is an EEG-derived single dimensionless index, ranging from 99 (awake) to 0 (EEG silence), and it correlates with the hypnotic depth of anesthesia.[26,27] It is dose-dependent on volatile anesthetic concentration in a linear fashion.[28–30] The result of our study that the BIS values for the desflurane group were significantly lower than those for the sevoflurane group is consistent with the result of a previous study.[21] These findings suggest that desflurane at equi-MAC may have a greater hypnotic potency than sevoflurane.

The strengths of this study include the use of age-corrected MAC value, the application of a standardized stimulation, and pure volatile anesthesia with no anesthetic adjuvants such as remifentanil and nitrous oxide. However, the use of muscle relaxants is the major limitation of this study. If the motor response to standard tetanic stimulation had been obtained as an outcome variable, it would have provided important information to compare and confirm 1.0 MAC. Another limitation of this study is the use of propofol for anesthetic induction. The minimum propofol dose required for loss of consciousness was used, a waiting period of more than 30 min was allowed, and all outcomes were obtained after the effect-site concentration of propofol was reduced to less than 0.2 μg/ml.[31] Nevertheless, effect-site concentration of propofol of approximately 0.2 μg/ml may have affected the surgical pleth index and BIS values.[32] This study may also be criticized because data were recorded at 20-s intervals. More frequent data recordings are necessary to yield more accurate results. Further studies using a high-frequency electronic recording system are needed to validate our findings.

For several reasons, the results of the study need to be interpreted with caution. First, although surgical pleth index and BIS are validated monitoring indices, they are still surrogate measures of analgesic and hypnotic levels. In this study, different surgical pleth index profiles at 1.0 MAC of two volatile anesthetics might reflect the difference in direct effects on vascular tone or autonomic nervous system, rather than the difference in analgesic potencies. Therefore, the conclusion about whether different surgical pleth index and BIS profiles of various volatile anesthetics connote different analgesic and hypnotic potencies should be carefully drawn. Second, although long-lasting electrical tetanic stimulation (30 s, 50 mA, 50 Hz) has been used as standard experimental pain model for surgical pain,[14] it is not the same as the stimulus used to obtain the originally MAC values (2-cm surgical incision).[5] Finally, this study is based on the premise that the age-related iso-MAC charts[12,13] were accurate. If the previously reported MAC values were inaccurate, equi-MAC of two volatile anesthetics were not administered, so the above interpretation would be unreasonable.

This randomized controlled trial highlights the limitations of MAC as metrics of volatile anesthetic potency. In conclusion, during a steady-state of 1.0 MAC single-agent volatile anesthesia, desflurane and sevoflurane did not produce similar surgical pleth index and BIS values under a standardized nociceptive stimulus. These findings suggest that the equi-MAC of desflurane and sevoflurane may not ensure equivalent analgesic or hypnotic potency. Further investigations are needed to determine whether these findings will provide clinically beneficial effects in the optimization of anesthetic adjuvant administration and early recovery from anesthesia.

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Support was provided solely from institutional and/or departmental sources.

Competing Interests

The authors declare no competing interests.

Reproducible Science

Full protocol available at: drkhryu@gmail.com. Raw data available at: drkhryu@gmail.com.

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