Comparison of the Hemodynamic Effects of Sevoflurane and Desflurane during Induction of Anesthesia: a Prospective Randomized Controlled Trial

<Original Article>

Comparison of the Hemodynamic Effects of Sevoflurane and Desflurane during Induction of Anesthesia: a Prospective Randomized Controlled Trial

Kentaro IMAGAWA[1,2], Nobuyasu KOMASAWA[2],
Kaori OKAMOTO[1,2], and Toshiaki MINAMI[2]

[1]Department of Anesthesiology, Takatsuki Red Cross Hospital, Takatsuki, Osaka 569-1045, Japan
[2]Department of Anesthesiology, Division of Vital Care and Reconstruction Medicine, Faculty of Medicine, Osaka Medical College, Takatsuki, Osaka 569-8686, Japan

Key words: desflurane, sevoflurane, hemodynamic change, randomized controlled trial

ABSTRACT

Background: Anesthesiologists frequently confront hypotension during the induction of anesthesia, which can lead to various complications such as cardiac or cerebral ischemia. In this study, we investigated the hemodynamic effects of sevoflurane and desflurane during the induction of anesthesia.

Methods: Anesthesia was induced with 1.5 mg/kg propofol and 2 μg/kg fentanyl, and rocuronium 0.9 mg/kg was administered as a muscle relaxant. A total of 150 adult patients were assigned to three groups (S group: inhalation anesthesia was induced with 2% sevoflurane, D1 group: with 6% desflurane, D2 group: with 9% desflurane). Hemodynamics changes before and after (i.e., 2.5 minutes after) induction of anesthesia were compared between the three groups.

Results: The rate of change (Post-anesthesia/Pre-anesthesia) in SBP was significantly higher in the D2 group compared to the S group ($P<0.001$), but not compared to the D1 group ($P=0.051$). Rate of changes of MBP, DBP, and heart rate were significantly higher in the D2 group compared to the S and D1 groups ($P<0.001$).

Conclusion: Our results suggest that inhalation of 9% desflurane prevents hypotension relative to sevoflurane or 6% desflurane during the induction of anesthesia. However, tachycardia is a consideration when using high-dose desflurane.

Address correspondence to:
Nobuyasu Komasawa, MD, PhD., Department of Anesthesiology, Division of Vital Care and Reconstruction Medicine, Faculty of Medicine, Osaka Medical College, 2-7 Daigakumachi, Takatsuki, Osaka 569-8686, Japan
Phone: +81-72-683-2368 Fax: +81-72-684-6552 E-mail: ane078@poh.osaka-med.ac.jp

INTRODUCTION

Hemodynamic changes during the induction of anesthesia can result in vascular dilation or sympathetic nerve suppression [1]. The two goals during anesthesia induction are to maintain a sufficient depth of anesthesia and to prevent hemodynamic collapse [2]. Excessively deep anesthesia can cause severe hypotension, which is associated with organ ischemia. Cardiac or cerebral ischemia, for example, can lead to severe outcomes. Conversely, an insufficient depth of anesthesia can result in patient movement, awakening, and bucking, as well as tachycardia, which is associated with right and left heart strain [3].

Inhalational anesthetics are chemical compounds that possess general anesthetic properties and can be delivered via inhalation. Agents of significant clinical interest include volatile anesthetic agents such as isoflurane, sevoflurane, and desflurane, as well as certain anesthetic gases such as nitrous oxide [4]. Sevoflurane and desflurane are the most commonly used inhalational anesthetics for inducing and maintaining general anesthesia [5,6]. However, hemodynamics changes that occur during their use have not been fully evaluated.

We hypothesized that sevoflurane and desflurane would minimize hemodynamics changes during the induction of anesthesia and different desflurane concentration would affect the vital sign changes. To this end, we conducted a prospective randomized controlled study to compare hemodynamic changes that occur during the induction of anesthesia with sevoflurane and desflurane.

METHODS

The research ethics committee of Takatsuki Red Cross Hospital approved this study (NO.25-15, approved on December 9, 2013, Chief Wataru Chiba). From December 2013 to April 2014, 194 patients aged 20 to 80 years who were scheduled to undergo general anesthesia in the supine position were assessed for eligibility to participate. Thirty eight patients were excluded and six patients refused to participate. After obtaining oral informed consent, 150 patients were assigned randomly using an envelope method to the 2% sevoflurane group (S group; 50 patients), 6% desflurane group (D1 group; 50 patients), and 9% desflurane group (D2 group; 50 patients) (**Figure 1**). Doses of these anesthetics were determined by 1.0 (2% sevoflurane, 6% desflurane) or 1.5 (9% desflurane) minimum alveolar concentrations for adults, which are indicators of anesthesia depth. Exclusion criteria included patients with arrhythmia, hypotension with a systolic blood pressure under 80 mmHg, emergency operations, and relatively high risk patients (American Society of Anesthesiologists Classification 3 or 4).

Blood pressure, heart rate, electrocardiography, percutaneous oxygen saturation, and end-tidal carbon dioxide tension were routinely monitored [7]. Without any premedication, anesthesia was induced with 1.5 mg/kg propofol, 2.0 μg/kg fentanyl, and 0.9 mg/kg rocuronium. After loss of consciousness, mask ventilation was performed according to group assignment.

Hemodynamics changes or arrhythmia occurrence were monitored. Blood pressure (systolic blood pressure, SBP; diastolic blood pressure, DBP; mean blood pressure, MBP) and heart rate were monitored both pre- and post-anesthesia induction. Post-anesthesia vital sign measurements were made 2.5 minutes (measured by timer) after induction of anesthesia. Rate of change in vital signs were calculated from Post-anesthesia/Pre-anesthesia.

Statistical analyses were performed with JMP® 11 (SAS Institute Inc., Cary, NC, USA) [8]. The Turkey-Kramer test was used to analyze SBP, DBP, MBP, and heart rate. Data are presented as mean±SD or median±IQR, unless otherwise indicated. $P<0.05$ was considered statistically significant.

Table 1 Patient characteristics.

	S (n=50)	D1 (n=50)	D2 (n=50)
Height (cm)	160.2±10.2	159.6±6.9	162.2±8.7
Weight (kg)	59.2±11	57.5±9.8	61.4±13.1
Age (year)	60.2±16.7	60.6±15.9	59.6±15.2
Male/Female	24/26	21/29	30/20
Antihypertensive medication	13	14	15
ASA 1/2	33/17	32/18	32/18

Data are presented as mean±SD or number of patients.

ASA: American Society of Anesthesiologists, S group: inhalation anesthesia was induced with 1.5% sevoflurane, D1 group: inhalation anesthesia was induced with 6% desflurane, D2 group: inhalation anesthesia was induced with 9% desflurane.

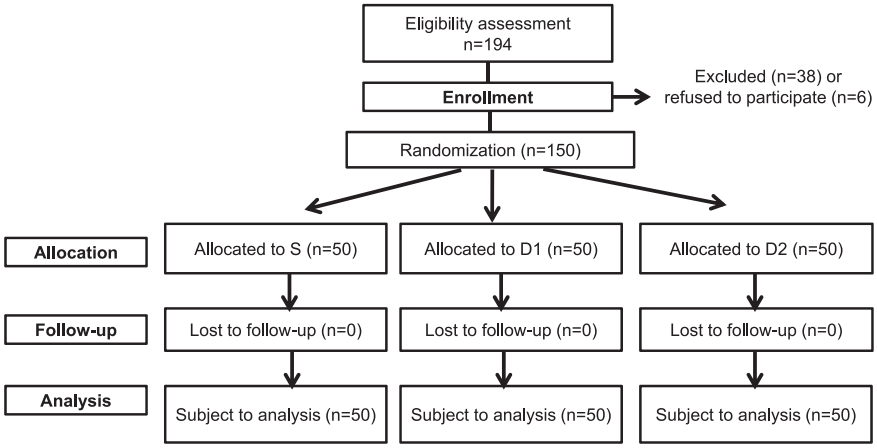

Figure 1 Flowchart of patient recruitment. S group: Inhalation anesthesia was induced with 2% sevoflurane, D1 group: inhalation anesthesia was induced with 6% desflurane, D2 group: inhalation anesthesia was induced with 9% desflurane.

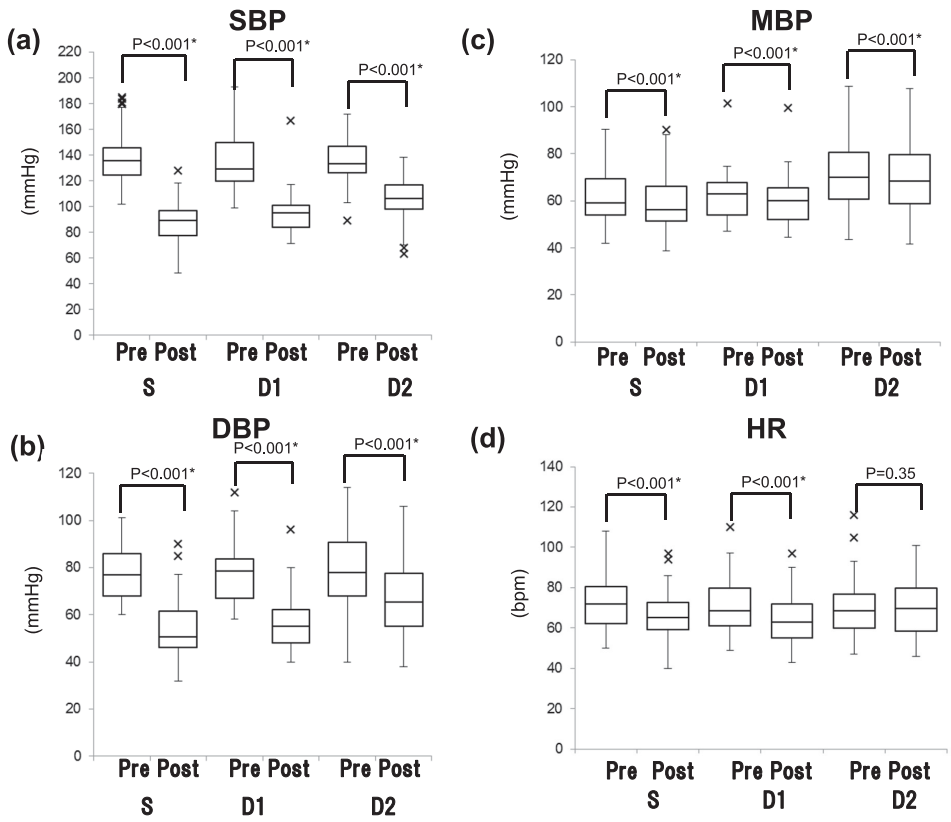

Figure 2 Box-and-whisker plot (median, IQR, and range) of sealing pressure after successful insertion among the three groups. S group: inhalation anesthesia was induced with 2% sevoflurane, D1 group: inhalation anesthesia was induced with 6% desflurane, D2 group: inhalation anesthesia was induced with 9% desflurane. × is outlier in the box-and-whisker plot.

RESULTS

Patient characteristics are summarized in Table 1. No case was abandoned or lost to follow-up during this trial (Figure 1).

Blood pressure and heart rate changes before and after inhalation

Changes in blood pressure and heart rate before and after induction of anesthesia among the three groups are shown in Figure 2. SBP, DBP, and heart rate significantly decreased post-induction in all groups

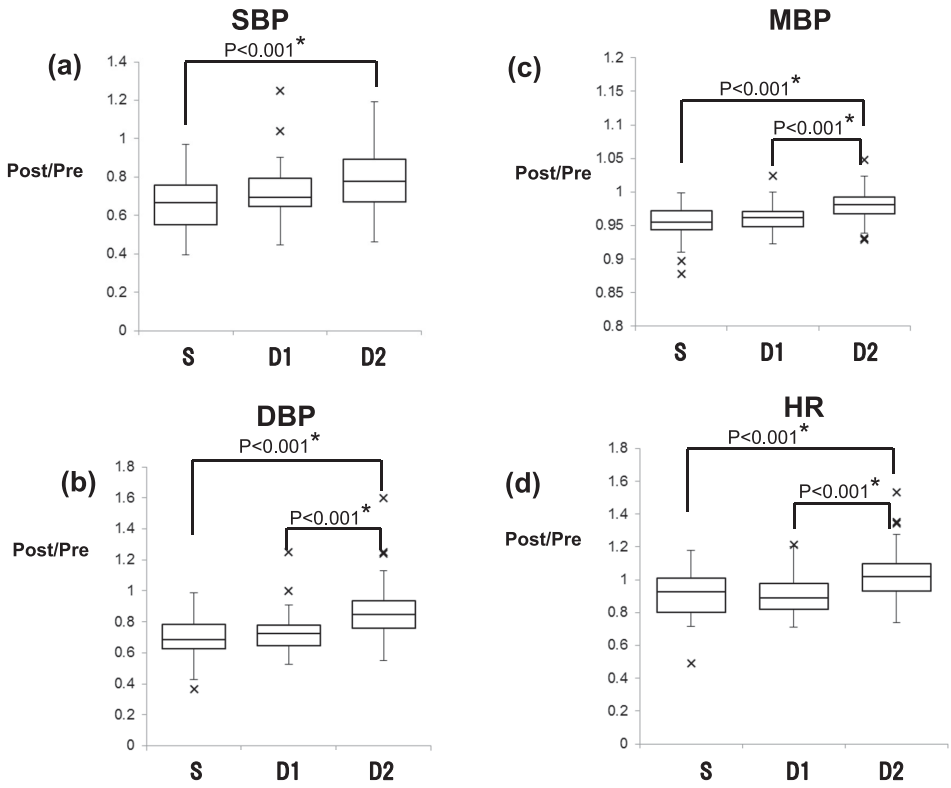

Figure 3 Box-and-whisker plot (median, IQR, and range) of rate of change in vital signs (Post-anesthesia/Pre-aneshtesia) among the three groups. S group: inhalation anesthesia was induced with 2% sevoflurane, D1 group: inhalation anesthesia was induced with 6% desflurane, D2 group: inhalation anesthesia was induced with 9% desflurane. × is outlier in the box-and-whisker plot.

(P<0.001). Heart rate also significantly decreased in S and D1 groups (P<0.001), but not in the D2 group (P=0.35).

Rates of change in vital signs (Post-anesthesia/Pre-anesthesia) among the three groups are shown in Figure 3. The rate of change in SBP was significantly higher in the D2 group compared to the S group (P< 0.001), but not compared to the D1 group (P=0.051). The rate of changes in MBP, DBP, and heart rate were significantly higher in the D2 group compared to S and D1 groups (P<0.001). MBP, DBP, and heart rate did not significantly differ between S and D1 groups.

Incidence of arrhythmia during induction of anesthesia

None of the patients in the three groups exhibited arrhythmias such as premature ventricular contraction or atrial fibrillation during the 2.5-minute observational period after induction of anesthesia.

DISCUSSION

Sevoflurane (1,1,1,3,3,3-hexafluoro-2-(fluoromethoxy) propane, also known as fluoromethyl hexafluoroisopropyl ether), is a sweet-smelling, nonflammable, highly fluorinated methyl isopropyl ether used as an inhalational anesthetic for the induction and maintenance of general anesthesia [9]. The name sevoflurane derives from the seven fluorine atoms in its substituents, alongside a standard suffix for such agents. This anesthetic is also known for its bronchial dilation effects and preconditioning effects [10,11], suggesting its efficacy in cardiac and lung protection [12-14]. It is one of the most commonly used volatile anesthetic agents, particularly for outpatient anesthesia. It is also commonly used for inducing anesthesia in children and infants, as well as in the veterinary medicine setting. In Japan, sevoflurane has replaced isoflurane and halothane. Although sevoflurane exerts various organ protective effects [15], its major drawback relates to hypotension, which may be caused by sympathetic nerve down-regulation or peripheral vascular dilation.

Desflurane (1,2,2,2-tetrafluoroethyl difluoromethyl ether) is a highly fluorinated methyl ethyl ether used to maintain general anesthesia [16]. Like halothane, enflurane, isoflurane, and sevoflurane, it exists as a racemic mixture of (R) and (S) optical isomers (enanti-

omers). Together with sevoflurane, it is gradually replacing classic inhalational anesthetics for human use. It has the most rapid onset and offset among volatile anesthetic drugs used for general anesthesia due to its low solubility in blood [17]. Some of its drawbacks include low potency, pungency, and high cost. It may also cause airway irritability when administered at higher concentrations. This has led to its infrequent use for inducing anesthesia via inhalation techniques. Desflurane administration has also been reported to occasionally trigger tachycardia, which can lead to cardiac ischemia [18].

In this study, we demonstrated that rate of change in the blood pressure was significantly higher in the D2 group compared to the S group. Furthermore, the rate of change in MBP, DBP and HR was significantly higher in D2 group than in D1 group. Thus, higher desflurane concentrations may alleviate the cardiovascular suppression during induction of anesthesia. Interestingly, blood pressure and heart rate were paradoxically maintained in the D2 group, while depth of anesthesia was considered deeper in the D2 group than in D1 group. One possible reason is that serum noradrenaline and vasopressin increase in response to elevation in desflurane concentration [18]. It is also notable that no arrhythmia was observed in the D1 or D2 group. These results suggest that desflurane may help prevent circulatory collapse during the induction of anesthesia.

Our study has several limitations. First, we did not measure the depth of anesthesia by brain waves. Such data could clarify the circulatory and anesthetic effects of sevoflurane and desflurane. Second, we measured changes in blood pressure with a non-invasive cuff method. An arterial line may provide a more accurate picture of vital sign changes. Third, this study was conducted at a single institute. A large-scale multicenter study or meta-analysis will be needed to confirm the utility of desflurane during the induction of anesthesia. Moreover, the evaluation of serum catecholamines during inhalation of desflurane would help clarify the role of desflurane's effect on circulation.

In conclusion, we found that induction of anesthesia with 9% desflurane prevents hypotension relative to induction with sevoflurane or 6% desflurane.

Author contributions

K.I: designed the study, conducted the study, analyzed data, and wrote the manuscript; K.O., N.K.: analyzed data and wrote the manuscript; and T.M.: designed the study and prepared the manuscript. All authors discussed the results and approved the final version of the manuscript.

Declaration of interest

The authors have no affiliation with any manufacturer of any device described in the manuscript and declare no financial interest in relation to the material described herein.

Funding

Financial support for the study was provided by our institution.

REFERENCES

1. Nakayama M, Kanaya N, Edanaga M, Namiki A. Hemodynamic and bispectral index responses to tracheal intubation during isoflurane or sevoflurane anesthesia. J Anesth 2003;17:223-6.
2. Aranake A, Mashour GA, Avidan MS. Minimum alveolar concentration: ongoing relevance and clinical utility. Anaesthesia 2013;68:512-22.
3. Robins K, Lyons G. Intraoperative awareness during general anesthesia for cesarean delivery. Anesth Analg 2009;109:886-90.
4. Ciofolo MJ, Reiz S. Circulatory effects of volatile anesthetic agents. Minerva Anestesiol 1999;65: 232-8.
5. Ebert TJ, Harkin CP, Muzi M. Cardiovascular responses to sevoflurane: a review. Anesth Analg 1995;81:S11-22.
6. Weiskopf RB. Cardiovascular effects of desflurane in experimental animals and volunteers. Anaesthesia 1995;50:14-7.
7. Fujiwara A, Komasawa N, Nishihara I, Miyazaki S, Tatsumi S, Nishimura W, Minami T. Muscle relaxant effects on insertion efficacy of the laryngeal mask ProSeal® in anesthetized patients: A prospective randomized controlled trial. J Anesth Feb 10 [Epub ahead of print].
8. Miyazaki Y, Komasawa N, Matsunami S, Kusaka Y, Minami T. Laryngoscope facilitates successful i-gel insertion by novice doctors: A prospective randomized controlled trial. J Anesth 2015 Apr 25. [Epub ahead of print].
9. Yasuda N, Lockhart SH, Eger EI II, Eger EI 2nd, Weiskopf RB, Johnson BH, Freire BA, Fassoulaki A. Comparison of kinetics of sevoflurane and isoflurane in humans. Anesth Analg 1991;72:316-24.
10. Shiomi M, Miyamae M, Takemura G, Kaneda K, Inamura Y, Onishi A, Koshinuma S, Momota Y, Minami T, Figueredo VM. Sevoflurane induces cardioprotection through reactive oxygen species-mediated upregulation of autophagy in isolated guinea pig hearts. J Anesth. 2014;28:593-600.

11. Shiomi M, Miyamae M, Takemura G, Kaneda K, Inamura Y, Onishi A, Koshinuma S, Momota Y, Minami T, Figueredo VM. Induction of autophagy restores the loss of sevoflurane cardiac preconditioning seen with prolonged ischemic insult. Eur J Pharmacol. 2014;724:58-66.
12. Landoni G, Fochi O, Torri G. Cardiac protection by volatile anaesthetics : A review. Curr Vasc Pharmacol 2008;6:108-11.
13. Swyers T, Redford D, Larson DF. Volatile anesthetic-induced preconditioning. Perfusion 2014;29:10-5.
14. Park KW, Dai HB, Lowenstein E, Sellke FW. Epithelial dependence of the bronchodilatory effect of sevoflurane and desflurane in rat distal bronchi. Anesth Analg 1998;86:646-51.
15. Guarracino F, Landoni G, Tritapepe L, Pompei F, Crivellari M, Maselli D, De Luca M, Fochi O, D'Avolio S, Bignami E, Calabrò MG, Zangrillo A. Myocardial damage prevented by volatile anesthetics: A multicenter randomized controlled study. J Cardiothorac Vasc Anesth 2006;20:477-83.
16. Yasuda N, Lockhart SH, Eger EI II, et al. Kinetics of desflurane, isoflurane, and halothane in humans. Anesthesiology 1991;74:489-98.
17. Strum EM, Szenohradszki J, Kaufman WA, Anthone GJ, Manz IL, Lumb PD. Emergence and recovery characteristics of desflurane versus sevoflurane in morbidly obese adult surgical patients: a prospective, randomized study. Anesth Analg 2004;99: 1848-53.
18. Weiskopf RB, Moore MA, Eger EI II. Rapid increase in desflurane concentration is associated with greater transient cardiovascular stimulation than with rapid increase in isoflurane concentration in humans. Anesthesiology 1994;80:1035-45.

Received May 18, 2015
Accepted June 16, 2015