apm ANESTHESIA & PAIN MEDICINE

Anesth Pain Med 2020;15:434-440
https://doi.org/10.17085/apm.20055
pISSN 1975-5171 • eISSN 2383-7977

Clinical Research

Change of inspired oxygen concentration in low flow anesthesia

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Received June 24, 2020
Revised August 25, 2020
Accepted September 4, 2020

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Background: There are several advantages of low flow anesthesia including safety, economics, and eco-friendliness. However, oxygen concentration of fresh gas flow and inspired gas are large different in low flow anesthesia. This is a hurdle to access to low flow anesthesia. In this study, we aimed to investigate the change in inhaled oxygen concentration in low flow anesthesia using oxygen and medical air.

Methods: A total of 60 patients scheduled for elective surgery with an American Society of Anesthesiologist physical status I or II were enrolled and randomly allocated into two groups. Group H: Fresh gas flow rate (FGF) 4 L/min (FiO_2 0.5). Group L: FGF 1 L/min (FiO_2 0.5). FGF was applied 4 L/min in initial phase (10 min) after intubation. After initial phase FGF was adjusted according to groups. FGF continued at the end of surgery. Oxygen and inhalation anesthetic gas concentration were recorded for 180 min at 15 min interval.

Results: The inspired oxygen concentration decreased by 5.5% during the first 15 min in the group L. Inspired oxygen decreased by 1.5% during next 15 min. Inspired oxygen decreased by 1.4% for 30 to 60 min. The inspired oxygen of group L is 35.4 ± 4.0% in 180 min. The group H had little difference in inspired oxygen concentration over time and decreased by 1.8% for 180 min.

Conclusions: The inspired oxygen concentration is maintained at 30% or more for 180 min in patients under 90 kg. Despite some technical difficulties, low flow anesthesia may be considered.

Keywords: Balanced anesthesia; General anesthesia; Inspired oxygen; Low flow.

INTRODUCTION

Low-flow anesthesia is economical and environmentally-friendly, as it reduces the consumption of O_2 and anesthetics during inhalation anesthesia. Clinically, the method is advantageous for raising the temperature and humidity of the inspired gas in patients. Low-flow anesthesia was first introduced by Foldes et al. [1] in 1952, and it was established when minimum-flow anesthesia (0.5 L/min) was introduced by Virtue [2] in 1974. At the same time, the technologically advanced anesthetic machine facilitated safe and accurate rebreathing as well as monitoring, and the currently promoted advantage of the machine is the support for low-flow anesthesia. With the wide use of sevoflurane and desflurane in anesthesia instead of halothane with a high absorption rate, the complicated calculation of

the anesthetic gas concentration within the anesthetic circuit during low-flow anesthesia became relatively simple [3,4]. Despite the advanced machines and the development and use of anesthetics with low absorption rates, low-flow anesthesia is still a novelty to several anesthesiologists who, due to concerns of safety, tend to resort to the use of fresh gas at a high flow of ≥ 3 L/min for anesthesia in clinical practice [5].

In this study, the latest anesthetic device and various monitoring devices were used. The fraction of inspired oxygen (FiO_2) supplied to the fresh gas was constant, while low-flow anesthesia was applied using O_2, medical air, sevoflurane, and desflurane. This study aimed to examine the changes in inspired oxygen concentration within the anesthetic circuit and their stability.

MATERIALS AND METHODS

Subjects

This study was conducted after the approval of the Institutional Review Board (no. KUGH-2019-04-14). The goals and methods of the study were explained to the patients and informed consent was obtained from each patient before the study. As a prospective intervention study based on the physical statuses I and II of the American Society of Anesthesiologists, the study recruited 60 patients aged 20–65 years scheduled to receive thyroid surgery under general anesthesia. The cases with predicted surgery duration of less than 1 h were excluded, as the duration is insufficient for monitoring the changes in oxygen saturation. Patients with preoperative pulmonary dysfunction, acute or chronic lung disease, asthma, systemic diseases, such as hypertension and diabetic kidney disease or liver disease, a history of surgery within the previous month, and a history of smoking were excluded. The cases requiring inotropic or antihypertensive injection or blood transfusion were also excluded.

Methods

The Dräger Primus anesthetic machine (Dräger AG, Germany) and the standard circular respiratory circuit with a heated breathing tube (VentStar Helix heated, Dräger AG) were used. The Vapor® 2000 vaporizer (Dräger AG) was used for sevoflurane and D-Vapor® (Dräger AG) was used for desflurane. For each patient, leak tests of the ventilator and respiratory circuit were performed before anesthesia. Drägersorb Free (Dräger AG) was used for the CO_2 absorbent, and the substance was replaced with a new one every morning before the daily tasks.

During the surgery, non-invasive techniques were used to assess arterial pressure, electrocardiogram, pulse oxygen saturation, end-tidal CO_2 fraction, and body temperature. The standard monitoring procedures, including the Bispectral index score (BIS, Vista™, USA), were also performed. The measurements were taken from before the induction of anesthesia; arterial pressure was measured at 5-min intervals, and other recordings were made in real-time.

For the induction of anesthesia, 8 L/min of 100% O_2 was used for 2-min spontaneous breathing for denitrification, after which 0.2 mg glycopyrrolate was injected. At the onset of denitrification, remifentanil was initially injected at 0.2 μg/kg/min. To induce the loss of consciousness, 0.05 mg/kg midazolam and 1 mg/kg propofol were injected. As a neuromuscular agent, 0.9 mg/kg rocuronium was injected, and endotracheal intubation was performed after 90 s. An esophageal thermometer was inserted through the oral cavity.

For the continuation of anesthesia, controlled ventilation was performed while maintaining 6–8 ml/kg tidal volume, 10–15 times/min respiratory rate, and 30–40 mmHg of end-tidal CO_2 fraction. In both groups during the experiment, a minimum alveolar concentration (MAC) of ≥ 0.8 was maintained, and the bispectral index score was maintained within 40–60. Based on the blood pressure before anesthetic induction, the remifentanil injection was adjusted within a rate of 1–10 μg/min. If necessary, 5–10 mg rocuronium was intermittently used for muscular relaxation.

Following intubation, the rate of fresh gas flow was 4 L/min, whereas the inhaled anesthetics were maintained at 2.2 vol% sevoflurane and 6.0 vol% desflurane for 10 min. After 10 min, the fresh gas flow was lowered to 1 L/min in the low-flow anesthesia group (group L), for which the sevoflurane and desflurane injections were increased to 2.5 and 7.0 vol%, respectively. In the high-flow anesthesia group (group H), the fresh gas flow and anesthetic gas concentration were maintained at identical levels even after 10 min. It was planned that the patients whose inspired oxygen concentration reduced to ≤ 25% during surgery would be excluded while increasing the fresh gas flow to 4 L/min. For the cases with ≥ 20% intraoperative blood pressure in-

creases or decreases, the plan was to increase or decrease the inhaled anesthetics by 10%. The inspired oxygen, expired oxygen, inspired anesthetic, and expired anesthetic concentrations were recorded at 15-min intervals based on the elapsed time after 10 min from intubation.

SPSS 20.0 (IBM Co., USA) was used for the statistical analyses. The measured data were expressed as mean ± SD. The demographic data, such as sex, the types of anesthetic, and the American Society of Anesthesiologists classes were compared using the chi-squared test. The age, height, and weight were compared using the independent *t*-test. The Mann–Whitney *U* test was used to compare surgery duration and mean arterial pressure. The linear mixed model was used to compare the inspired oxygen concentration, inspired anesthetic concentration, end-tidal CO_2, pulse oxygen saturation, and body temperature. $P < 0.05$ represented statistical significance.

RESULTS

For the analyses, each experimental group contained 30 patients. The demographic statistics for group L and group H were not significantly different (Table 1). The heart rate, arterial pressure, minute ventilation, and bi-spectral index score of group L and group H were not statistically different (Table 2). The end-tidal CO_2 was maintained at 32–36 mmHg in both groups, and the bispectral index score was regulated within 40–60 range.

From the baseline of 10 min after endotracheal intubation, the inspired oxygen concentrations in group H and group L were 46.3 ± 1.0% and 45.7 ± 1.6%, respectively; they were not significantly different ($P = 0.107$). In group H, the difference in the time-dependent inspired oxygen concentration was small, with a 1.8% reduction within 180 min. In group L, the inspired oxygen concentration during the first 15 min was 40.2 ± 2.0%, corresponding to a 5.5% reduction ($P < 0.001$). After 1 h, the inspired oxygen concentration was 37.3 ± 2.6%, corresponding to a further decrease by 1.4% ($P < 0.001$). The concentration within 120 min after the first 60 min was reduced by only 1.9%, with a recorded value of 35.4 ± 4.0%. The change in the expired oxygen concentration was similar to that of the inspired oxygen concentration. Between the baseline of 10 min after intubation and the end-point of anesthesia, the difference between the inspired and expired oxygen concentrations were maintained at approximately 4.8–5.5% in group H and 4.9–5.7% in group L (Fig. 1).

For individual patients, the lowest inspired oxygen concentration during 180 min was 44% in group H and 26% in group L. One of the 30 patients in group L showed a reduction in the inspired oxygen concentration to < 30%, and the lowest inspired oxygen concentration for the remaining

Table 1. Demographic Data

Variable	Group H (n = 30)	Group L (n = 30)	P value
Sex (M/F)	9/21	10/20	0.781
Age (yr)	47.0 ± 9.8	49.8 ± 12.8	0.346
Height (cm)	163.4 ± 8.8	163.5 ± 10.3	0.968
Weight (kg)	64.8 ± 14.0	69.7 ± 12.5	0.158
ASA (I/II)	13/17	12/18	0.793
Operative time	151.5 ± 37.6	145.5 ± 32.6	0.534
Inhalation agent (Sevo/Des)	13/17	13/17	1.000

Values are presented as number or mean ± SD. Group H: fresh gas flow 4 L/min, FiO_2 0.5, O_2 1.5 L /min, Air 2.5 L/min; Group L: fresh gas flow 1 L/min, FiO_2 0.5, O_2 0.37 L/min, Air 0.63 L/min. ASA: American Society of Anesthesiologist, Sevo: Sevoflurane, Des: Desflurane. P values for differences were determined by using the chi-squares, *t*-test.

Table 2. Hemodynamic Parameters at Baseline

Variable	Group H (n = 30)	Group L (n = 30)	P value
SBP (mmHg)	114.5 ± 22.4	110.8 ± 13.5	0.450
DBP (mmHg)	73 ± 14.8	71.2 ± 9.1	0.503
HR (beats/min)	85.4 ± 18.5	87.0 ± 14.5	0.716
MV (L/min)	5.8 ± 1.0	5.6 ± 1.0	0.387
BIS	43.8 ± 8.7	40.3 ± 6.9	0.187

Values are presented as mean ± SD. Group H: fresh gas flow 4 L/min, FiO_2 0.5, O_2 1.5 L/min, Air 2.5 L/min; Group L: fresh gas flow 1 L/min, FiO_2 0.5, O_2 0.37 L/min, Air 0.63 L/min. SBP: systolic blood pressure, DBP: diastolic blood pressure, HR: heart rate, MV: minute ventilation, BIS: bispectral index score. P values for differences were determined by using the *t*-test.

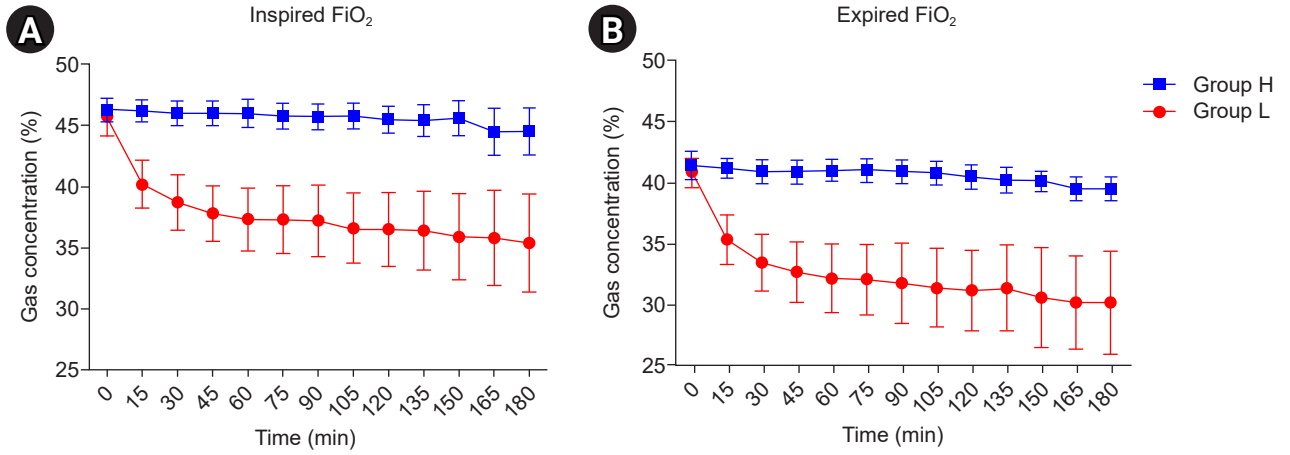

Fig. 1. Changes in inspired (A) and expired (B) oxygen concentration over time in both group. Data represents mean ± SD. Group H = fresh gas flow 4 L/min, FiO_2 0.5, O_2 1.5 L/min, Air 2.5 L/min; Group L = fresh gas flow 1 L/min, FiO_2 0.5, O_2 0.37 L/min, Air 0.63 L/min.

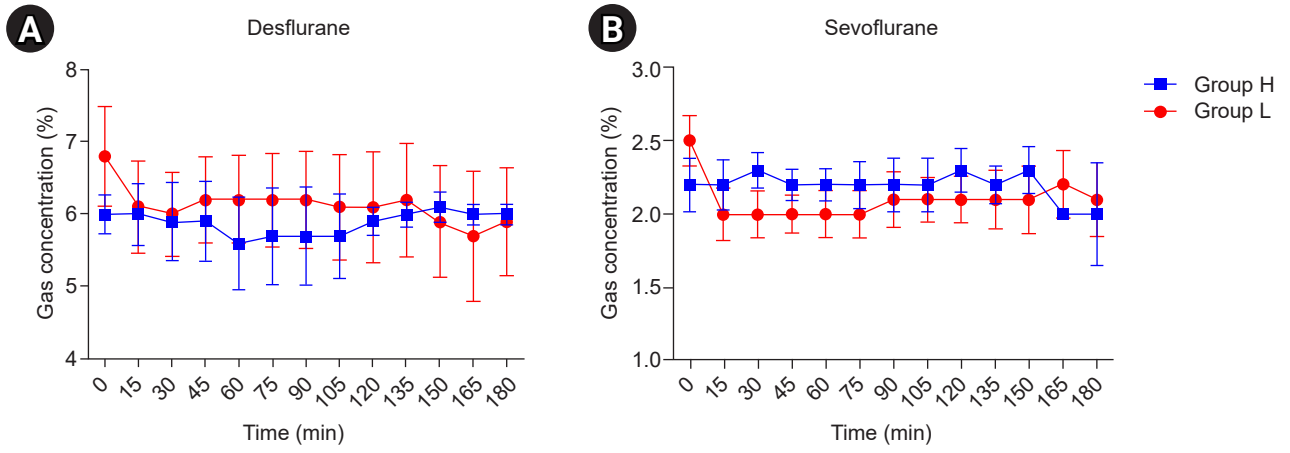

Fig. 2. Changes in inspired desflurane (A) and sevoflurane (B) concentration over time in both group. Data represents mean ± SD. Group L = fresh gas flow 1 L/min, FiO_2 0.5, O_2 0.37 L/min, Air 0.63 L/min; Group H = fresh gas flow 4 L/min, FiO_2 0.5, O_2 1.5 L/min, Air 2.5 L/min.

29 patients was 32%. In both groups L and H, there was no drop-out due to a reduction in the inspired oxygen concentration to < 25%.

For the inspired concentration of inhaled anesthetics recorded at the onset of anesthesia, no significant difference was found between group H (6.0 ± 0.3 vol% desflurane and 2.2 ± 0.2 vol% sevoflurane) and group L (6.9 ± 0.7 vol% desflurane and 2.5 ± 0.2 vol% sevoflurane) (P = 0.201). The inspired concentrations of inhaled anesthetics after one hour were as follows: 5.7 ± 0.6 vol% desflurane and 2.2 ± 0.1 vol% sevoflurane in group H; 6.3 ± 0.6 vol% desflurane and 2.0 ± 0.2 vol% sevoflurane in group L (Fig. 2).

For the body temperatures, no significant difference was found between group H and group L (P = 0.248), but group L showed slightly higher temperatures with time (Fig. 3). The intraoperative temperature was 36.2 ± 0.3°C in group

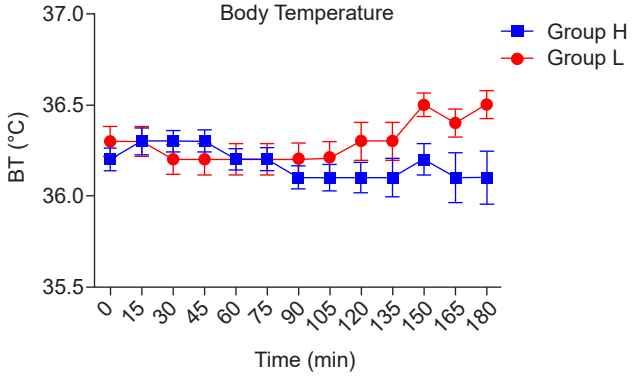

Fig. 3. Changes in esophageal body temperature (BT) over time in both group. Data represents mean ± SD. Group L = fresh gas flow 1 L/min, FiO_2 0.5, O_2 0.37 L/min, Air 0.63 L/min; Group H = fresh gas flow 4 L/min, FiO_2 0.5, O_2 1.5 L/min, Air 2.5 L/min.

H and 36.3 ± 0.4°C in group L during the early hours and 36.1 ± 0.3°C in group H and 36.3 ± 0.5°C in group L after

120 min.

In both groups, the pulse oxygen saturation was maintained at 99–100%, with no significant difference (P = 0.215). No case of delayed postoperative recovery, difficulty breathing, or pulmonary complication until discharge was reported.

DISCUSSION

The benefits of low-flow anesthesia, including the reduced cost based on the reduced use of anesthetic gas, the safety of medical staff working in operation rooms, and environmental protection, are generally accepted [5]. Kim [6] claimed that the continuous monitoring of inspired oxygen concentration and oxygen saturation in low-flow anesthesia enabled the anesthesiologist to focus more on the patient and better understand the pharmacokinetics of the inhaled anesthetics; however, due to the difference between the oxygen concentration in the fresh gas injected to the anesthetic circuit and the inspired oxygen concentration measured by the monitoring device for gas concentration, the anesthesiologists could not readily apply low-flow anesthesia in clinical practice due to safety concerns [7]. The well-known previous studies on low-flow anesthesia mostly focused on the delivery of inhaled anesthetics or used N_2O and O_2. A recent study by Venkatachalapathy et al. [8] also focused on the comparison between the use of medical air and the conventional use of N2O [1,2]. Concerns about the expansion of body cavity or nausea have reduced the use of N2O while increasing the use of medical air [9]. No study has demonstrated the difference between low-flow anesthesia and the currently popular anesthetic methods using medical air, and this motivated the present study.

Raymond [10] reported that the relationship between FiO_2 and inspired oxygen concentration in 1 L/min fresh gas flow is linear, and the difference was maintained at approximately 20%. The study also showed that the supply of O_2 should be ≥ 0.5 L/min to maintain an inspired oxygen concentration of ≥ 30%. Virtue et al. [2] reported that when anesthesia was continued with 0.5 L/min fresh gas flow, the inspired oxygen concentration was not reduced to ≤ 30% until 60 min of anesthesia in patients weighing < 80 kg; in several patients weighing ≥ 80 kg, the inspired oxygen concentration was reduced to ≤ 20% to increase the proportion of oxygen in fresh gas [11]. Based on the previous studies, the present study determined that 1 L/min fresh gas flow was ideal for accessibility and stability in low-flow anesthesia. The study found that the inspired oxygen concentration was not reduced to ≤ 30% until 60 min of anesthesia in group L, which contained 6 patients weighing ≥ 80 kg. One patient in group L, on the other hand, showed a considerably greater reduction in inspired oxygen concentration in fresh gas flow than was predicted; the patient was 180 cm in height and 95 kg in weight, and the inspired oxygen concentration began reducing below 30% after 60 min of anesthesia, which continued to 26% until the end of surgery. The simple regression analysis based on bodyweight and inspired oxygen concentration showed that in group L, the inspired oxygen concentration decreased as body weight increased, and the negative correlation was stronger at 120 min (r = –0.16, R2 = 0.41) than at 60 min (r = –0.14, R2 = 0.49); in group H, the correlation was considerably weak regardless of time (60 min, r = –0.01, R2 = 0.01; 120 min, r = –0.03, R2 = 0.15) (Fig. 4). Considering the report of Okada et al. [12,13] on the relationship between body weight and oxygen consumption during low-flow anesthesia at 0.6 L/min (O_2, 0.3 L/min; N_2O, 0.3 L/min) and the correlation between body weight and inspired oxygen concentration found in this study, careful monitoring is required in applying 1 L/min fresh gas flow in patients weighing ≥ 90 kg (Fig. 4).

This study was not designed to analyze the inherent properties of inhaled anesthetics; however, a remark may be made on the related findings. Bailey [14] proposed that to achieve an adequate MAC concentration during low-flow anesthesia, anesthetics should be supplied with sufficient flow for ≥ 10 min after the onset of anesthesia. Due to the difference between the concentrations of the inhaled anesthetics dial and the anesthesia circuit of the vaporizer, the dial should be adjusted to a level slightly higher than the target during low-flow anesthesia [15]. Based on the findings of Bailey [14] a high flow of 4 L/min was applied for 10 min in the two groups in this study, while the concentration of inhaled anesthetics was slightly increased upon reducing the flow in group L. As the amount of inhaled anesthetics was adjusted based on the BIS and MAC levels in both groups, it is difficult to quantitatively analyze the changes in the concentration of the two inhaled anesthetics. However, it was found that the concentration was maintained at approximately 1 MAC with stability in both groups. Despite the delivery of high-flow inhaled anesthetics for 10 min, a rapid reduction in the concentration of inhaled anesthetics was observed during the first 15 min in

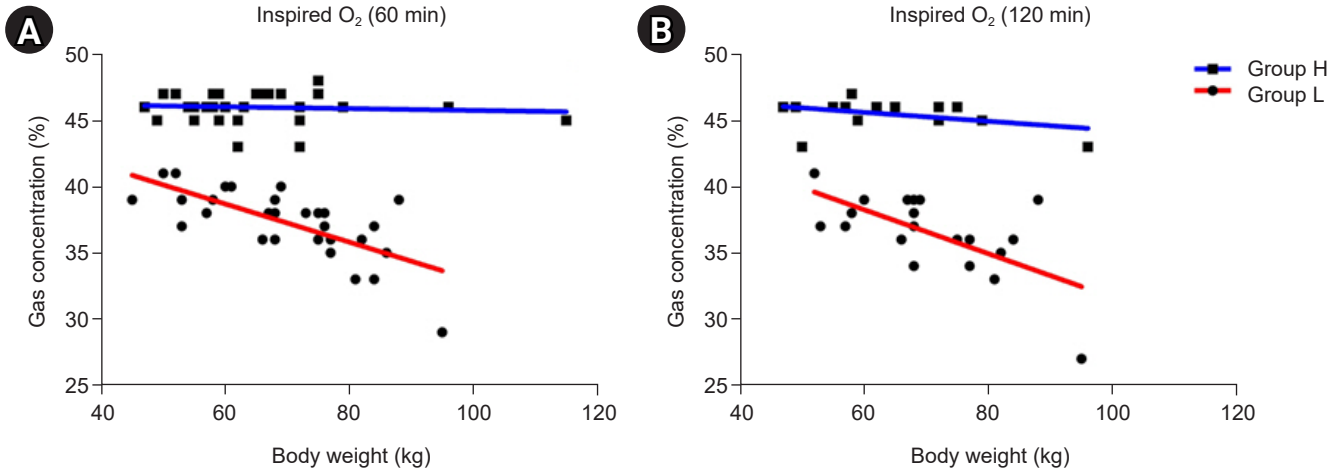

Fig. 4. Correlation between inspired oxygen concentration and body weight in 60 min (A), 120 min (B). Group H = fresh gas flow 4 L/min, FiO_2 0.5, O_2 1.5 L/min, Air 2.5 L/min; Group L = fresh gas flow 1 L/min, FiO_2 0.5, O_2 0.37 L/min, Air 0.63 L/min.

group L, followed by relatively steady values. Further studies should obtain the concentration of inhaled anesthetics at 1-min intervals during the first 15 min of anesthesia, which is predicted to lead to a V-shaped concentration curve for inhaled anesthetics as observed by Bailey [14].

With the advancement and establishment of balanced anesthesia, the continuous injection of narcotic analgesics in addition to inhaled anesthetics and the intermittent or continuous injection of neuromuscular blocking agents have been commonly used, which consequently reduce the proportion of inhaled anesthetics for the maintenance of anesthetic depth [16–18]. During low-flow anesthesia, the relatively slow change in MAC has been pointed out as a significant drawback that inhibits adequate response to surgical stimulation; however, this may complement by the balanced anesthesia method. In this study, narcotic analgesics and neuromuscular blocking agents were used in combination, and the sudden change in the concentration of inhaled anesthetics in group L may not have been necessary.

The body temperatures of groups L and H measured in this study were not significantly different, but this may have been due to the use of a heated breathing circuit (VentStar Helix heated, Dräger AG) for maintaining the body temperature. A trend of rise in temperature by approximately 0.2°C was observed in group L 120 min after the onset of anesthesia. This was consistent with the result of Kleemann [19], and as the current emphasis is on maintaining the perioperative body temperature of the patient, the benefits of low-flow anesthesia-related to body temperature maintenance deserves careful attention.

This study has several limitations. First, the study was designed as a pilot study to investigate the relationship between low-flow anesthesia and various patient factors. A simple regression analysis was performed to investigate the correlation between body weight and inspired oxygen saturation, and multiple regression analysis was not performed for height, age, sex, and other variables. Further studies should carry out additional correlation analyses with adequate sample sizes. Second, for the gas analyzer and the vaporizer for sevoflurane and desflurane in the anesthetic machine, deviations may have arisen despite the annual quality control, as a single device was not used for individual measurements. This is expected to be resolved by conducting a prospective randomized controlled study with appropriate sample size.

In conclusion, low-flow anesthesia with 1 L/min fresh gas flow was used to maintain the inspired oxygen concentration at ≥ 25% for up to 3 h. Considering the known advantages related to air pollution and economic issues, low-flow anesthesia should be considered in clinical practice despite one or two technological challenges, compared to the high flow anesthesia with 4 L/min fresh gas flow. Further studies should, however, investigate the possibility that 1 L/min fresh gas flow may not be sufficient for some patients when the duration of anesthesia exceeds 180 min.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

AUTHOR CONTRIBUTIONS

Conceptualization: Jiwook Kim, Doosik Kim. Data curation: Hochul Lee, Sungwon Ryu. Formal analysis: Hochul Lee. Methodology: Siejeong Ryu. Project administration: Jiwook Kim. Visualization: Donghee Kang. Writing - original draft: Jiwook Kim. Writing - review & editing: Jiwook Kim, Siejeong Ryu, Doosik Kim. Supervision: Doosik Kim. Validation: Siejeong Ryu, Doosik Kim.

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