Journal of Clinical Monitoring and Computing (2019) 33:115–121
https://doi.org/10.1007/s10877-018-0135-2

ORIGINAL RESEARCH

Low-flow anaesthesia with a fixed fresh gas flow rate

Seyma Bahar[1] · Mahmut Arslan[1] · Aykut Urfalioglu[1] · Gokce Gisi[1] · Gozen Oksuz[1] · Bora Bilal[1] · Hafize Oksuz[1] · Adem Doganer[2]

Received: 17 September 2017 / Accepted: 21 March 2018 / Published online: 23 March 2018

Abstract
During the wash-in period in low flow anaesthesia (LFA), high fresh gas flow is used to achieve the desired agent concentration. In this study, we aimed to evaluate the safety of fixed 1 L/min fresh gas flow desflurane anaesthesia in both the wash-in and maintenance periods in patients including the obese ones. 104 patients undergoing surgery under general anaesthesia were included. After endotracheal intubation, fresh gas flow was reduced to 1 L/min and the desflurane vaporizer was set at 18%. The time from opening the vaporizer to end-tidal desflurane concentration reaching 0.7 MAC was recorded (MAC 0.7 time). Throughout the surgery, hemodynamic variables, FIO2, MAC and BIS values were observed. MAC 0.7 time, BIS and MAC values at the start of surgery, number of adjustments in vaporizer settings, desflurane consumption were recorded. The average MAC 0.7 time was 2.9 ± 0.5 min. MAC and BIS values at the start of the surgery were 0.7 (0.6–0.8) and 39 ± 8.5 respectively. No individual patient had a BIS value above 60 throughout the surgery. Hemodynamic variables were stable and FIO2 did not fall below 30% in any patient. The number of adjustments in vaporizer settings was 56. Average desflurane consumption was 0.33 ± 0.05 mL/min. We demonstrated that LFA without use of initial high fresh gas flow during the wash-in period is an effective, safe and economic method which is easy to perform.

Keywords Low flow anaesthesia · Desflurane · Obese · Wash-in · BIS · Fixed fresh gas flow rate

1 Introduction

There are several advantages of low-flow anaesthesia (LFA) with a fresh gas flow (FGF) of ≤ 1 L/min: consumption of the inhalation agent is reduced, the heat and humidity of the respiratory tract are preserved, and the cost of anaesthesia and atmospheric pollution created by waste gases are reduced [1]. In addition, respiratory function and mucociliary clearance are better maintained because temperature and humidity in the tracheobronchial tree are preserved [2].

Due to the low tissue and blood solubility of desflurane, it is highly suitable as an anaesthetic agent for LFA. As the anaesthetic gases are diluted with re-breathing in LFA, there is a discrepancy between the inspired (F_I) and dialed (F_D) anaesthetic agent concentrations, and therefore, some anaesthetists prefer higher FGF. The time taken to reach an end-tidal anaesthetic agent concentration (EtAA) that will provide sufficient anaesthetic depth is known as the 'wash-in' time. This wash-in period should not last too long, as the effect of the intravenous induction agents will diminish over time. Different methods have been proposed for performing LFA without prolonging the wash-in time [3–5]. Often, an initial high FGF is used during the wash-in period to achieve the desired EtAA in the anaesthesia circuit and alveoli. Some of the methods proposed include multiple steps, some require a very high FGF, some exclude patients with a BMI > 30 kg/m^2 and most of them do not include the whole period of anaesthesia. Although there is a scheme that can achieve every alveolar anaesthetic agent concentration by combining FGF and F_D, it is inconvenient because complex mathematical calculations are required [6].

The aim of this study was to evaluate the efficacy and practicability of low-flow desflurane anaesthesia with a fixed FGF of 1 L/min during both the wash-in and maintenance periods in patients, including obese patients.

✉ Mahmut Arslan
mahmutarslan177@gmail.com

[1] Department of Anesthesiology and Reanimation, School of Medicine, Kahramanmaras Sutcu Imam University, Kahramanmaras, Turkey

[2] Department of Biostatistics and Medical Informatics, School of Medicine, Kahramanmaras Sutcu Imam University, Kahramanmaras, Turkey

2 Methods

Approval for the study was granted by the Ethics Committee of the Healthcare Application and Research Hospital of Kahramanmaras Sutcu Imam University (Approval no. 154, dated 4 May 2016). The study included a total of 104 patients with ASA grade I–III, aged 18 years and above, who underwent surgery under general anaesthesia at the General Surgery and Plastic Surgery Clinics. Patients were excluded from the study if they had a life-threatening pulmonary or cardiac condition or unstable haemodynamics, carried a risk of malignant hyperthermia, were scheduled for surgical procedures with an expected duration of < 30 min or refused to participate in the study.

Verbal and written informed consent was obtained from all the study participants before the study was started. We used the Dräger Primus (Dräger AG, Lübeck, Germany) anaesthesia machine and the standard circle breathing circuit with a soda lime absorbent. Before the procedure was performed in each patient, the soda lime was changed and the leakage test for the ventilator and breathing circuit was repeated. In addition, the vaporizer was checked before each procedure to ensure that it was completely full. Standard monitoring procedures, including pulse oximetry, electrocardiography, temperature measurement and non-invasive arterial pressure measurement were performed, and a bispectral index (BIS, BIS-XP, A-2000; Aspect Medical Systems, Newton, MA, USA) electrode was attached to the patient's forehead and baseline values were recorded prior to induction of anaesthesia.

After premedication with intravenous administration of midazolam (0.03 mg/kg), the patients were pre-oxygenated with 100% O_2 at an FGF of 8 L/min for 2 min via an anaesthesia face mask. Then, anaesthesia was induced with intravenous fentanyl (2 mcg/kg) and propofol (1.5 mg/kg) administration. Rocuronium (0.6 mg/kg) was administered for muscle relaxation. Throughout the procedure, remifentanil infusion (0.01–0.3 mcg/kg/min) was administered. After tracheal intubation, ventilation was achieved with a Drager Primus anaesthesia machine in the volume autoflow mode. Tidal volume was initially set at 6–8 mL/kg at a respiratory rate of 12 breaths/min and then adjusted to maintain an end tidal CO_2 of 35–45 mm Hg.

After intubation, FGF was reduced to 1 L/min (0.5 L/min O_2, 0.5 L/min air) and the desflurane vaporizer was set at 18%. The time from opening the vaporizer until the EtAA concentration reached 0.7 MAC (minimum alveolar concentration) was recorded (MAC 0.7 time). The MAC values were age adjusted according to the algorithm of the Drager anaesthesia machine. Then, the desflurane vaporizer was set at a 2% higher value than the EtAA concentration required to achieve 0.7 MAC. Throughout the surgery, MAC was maintained within 0.6–0.8 by adjusting the F_D. Within these limits, if the BIS value exceeded 60, the F_D was increased by 1%. Following intubation desflurane administration was started (= time zero). The EtCO2, MAC and EtAA, inspired O_2 concentration (F_IO_2), BIS value and patient's oropharyngeal temperature were manually recorded at the following study times: 0, 2, 4, 6, 8, 10, 15, 20, 25, 30, 45, 60 min, and every 30 min thereafter until the end of surgery. The MAC and BIS values at the start of surgery were recorded. Remifentanil infusion was terminated 10 min before the estimated end of the surgery. When the last skin suture was placed, the inhalation agent was discontinued and FGF was increased to 8 L/min.

The Drager Primus calculates volatile agent consumption on a case-by-case basis. When the anaesthesia machine is on the 'standby' mode, the logbook presents the consumption of volatile agent in millilitres, which was charted for each patient at the end of the case. This parameter is calculated by built-in undisclosed proprietary method. Total duration of anaesthesia defined as the time from induction to switching off the vaporizer.

The primary study end points were the time required to reach 0.7 MAC, the BIS and MAC values at the start of surgery and the number of adjustments made to the vaporizer settings. The secondary end points were desflurane consumption (mL/min) and the EtAA required to achieve a MAC of 0.7 (MAC 0.7 EtDES).

Data analysis was performed using the SPSS 22 (IBM) software. For evaluation of the data, variables were identified using descriptive statistics and assessed for conformity to normal distribution with the Shapiro–Wilks test. For comparison of two groups, the independent samples *t*-test was used, and for comparison of more than two groups, one-way analysis of variance was used. For data with a skewed distribution, the Mann Whitney *U*-test was used to compare two groups and the Kruskal Wallis *H*-test was used to compare more than two groups. For examining the relationships between variables, Pearson correlation analysis and Spearman correlation analysis were used. Parametric data were expressed as the mean and standard deviation values, and non-parametric data were expressed as median, minimum and maximum values. A p value of < 0.05 was considered to indicate statistical significance.

3 Results

A total of 104 patients were recruited, of whom 4 were later excluded as a result of intentional or unintentional disconnection of the breathing circuit. The demographic data for the 100 patients are presented in Table 1.

The mean MAC 0.7 time was 2.9 ± 0.5 min (minimum, 2 min; maximum, 4.3 min) (Table 2; Fig. 1). There was

Table 1 Demographic data for the 100 patients

Parameter	Value
Age (years)	47 ± 15
Weight (kg)	74 ± 16
Height (cm)	163 ± 10
Body mass index	27 (15–48)
Sex (male/female)	43/57
ASA classification (I–II–III)	36–31–33

Data for age, weight and height are presented as the mean ± standard deviation. Sex and ASA classification are presented as number of patients. Body mass index is presented as median (minimum–maximum)

ASA American Society of Anesthesiologists

Table 2 Duration of anesthesia, MAC 0.7 EtDES, MAC 0.7 time, desflurane consumption, MAC and BIS values at the start of surgery

Parameter	Value
Duration of anesthesia (min)	106 ± 5.5
MAC 0.7 EtDES (%)	4.7 ± 0.4
MAC 0.7 time (min)	2.9 ± 0.5
Desflurane consumption (mL/min)	0.33 ± 0.05
MAC surgery[a]	0.7 (0.6–0.8)
BIS surgery[b]	39 ± 8.5

[a]MAC surgery: MAC value at the start of surgery

[b]BIS surgery: BIS value at the start of surgery

a negative correlation between MAC 0.7 time and age ($r = -0.588$, Pearson correlation analysis). We found no other significant correlation between the MAC 0.7 and weight, height, BMI and gender. When patients were grouped according to BMI, there were 32 obese, 35 overweight, 30 normal and 3 underweight patients. MAC 0.7 time and desflurane consumption did not differ between the BMI groups. The mean MAC 0.7 times in the obese and overweight patients were 2.9 ± 0.6 and 2.9 ± 0.5 min, respectively.

MAC at the start of the surgery ranged between 0.6 and 0.8, and the median value was 0.7. BIS values at the start of surgery varied between 21 and 59, and the mean (±SD) value was 39 ± 8.5. Individual MAC values throughout the surgeries ranged between 0.6 and 0.9 (Fig. 2). No individual patient had a BIS value above 60 at the start of surgery (min, 21; max, 59) and till the end of surgery (Fig. 3).

Mean desflurane consumption was 0.33 ± 0.05 mL/min. Duration of anaesthesia and total desflurane consumption for each patient are presented in Fig. 4.

Heart rate and blood pressure did not change by > 20% during the wash-in and maintenance periods in any patient. We did not observe any signs of sympathetic stimulation related to desflurane wash-in. Further, the F_IO_2 value did not fall below 30% in any of the patients (Fig. 5).

The number of adjustments required in the vaporizer settings was three in 2 patients, two in 7 patients and one in 24 patients. In 67 patients, no vaporizer adjustments were necessary.

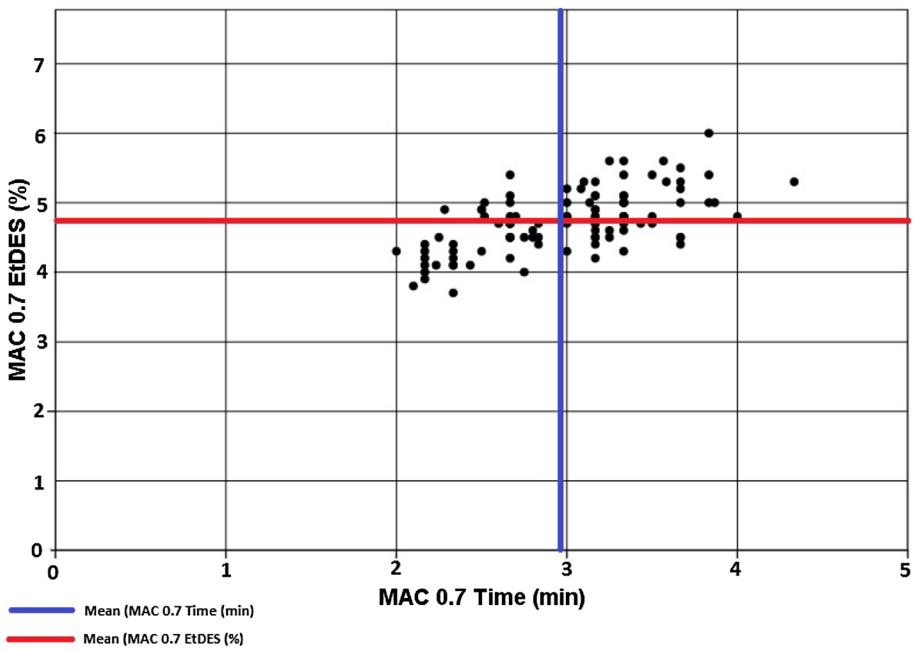

Fig. 1 The MAC 0.7 times and MAC 0.7 EtDES concentrations of the individual patients. Time zero is the start of administration of desflurane

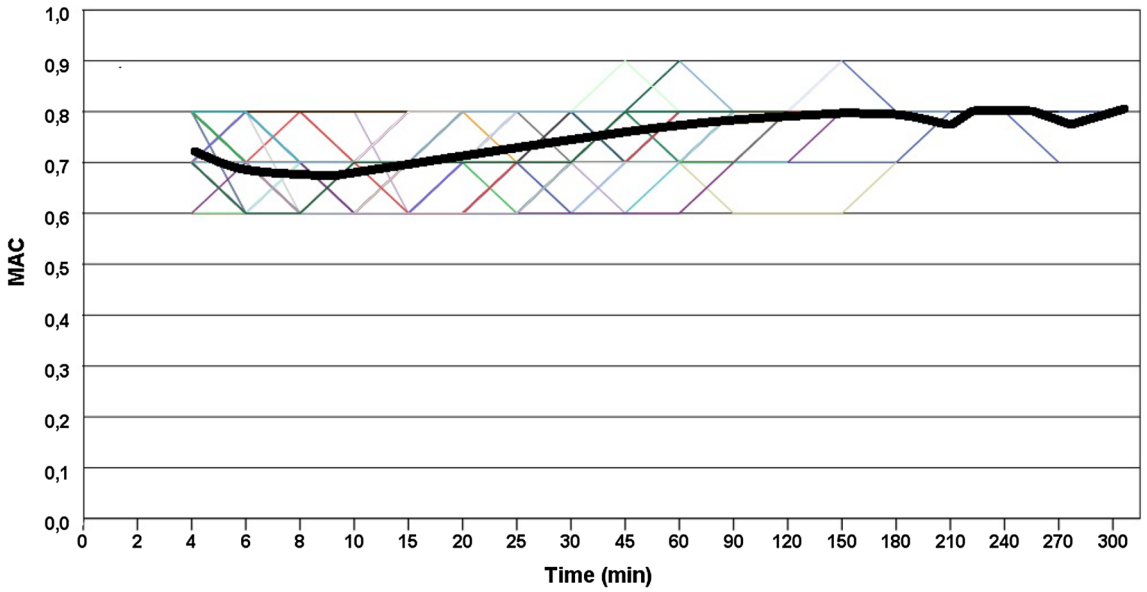

Fig. 2 MAC values of the individual patients (thin lines) and mean MAC value of all patients combined (thick line). Time zero is the start of administration of desflurane. The X-axis is not a linear scale

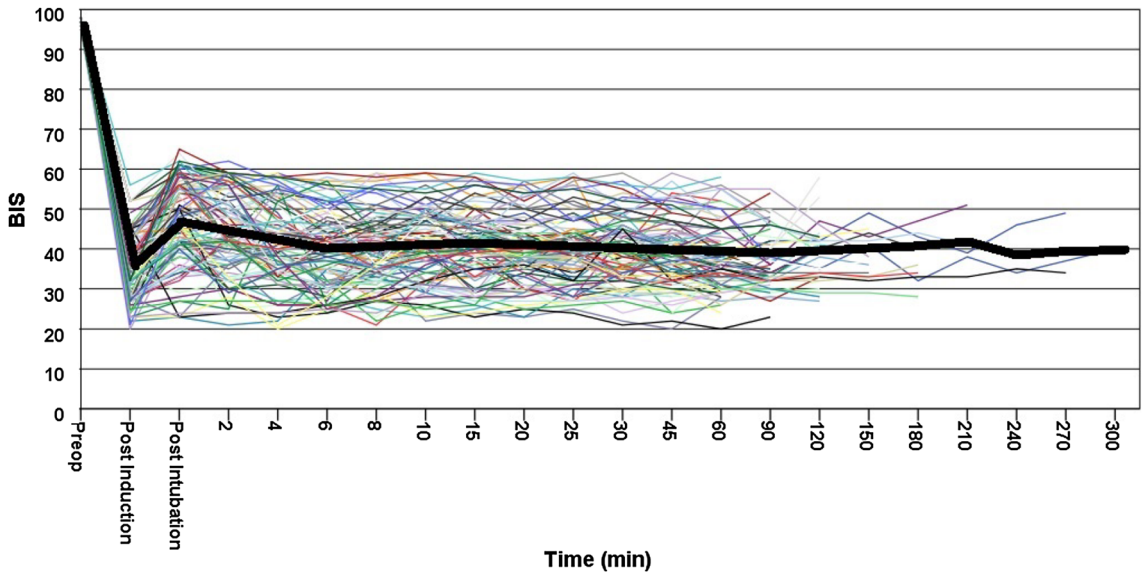

Fig. 3 BIS values of the individual patients (thin lines) and mean BIS value of all patients combined (thick line). Time zero is the start of administration of desflurane immediately after endotracheal intubation. The X-axis is not a linear scale

4 Discussion

Temporary loss of consciousness is essential when providing general anaesthesia. General anaesthesia is clinically composed of three stages: the induction, maintenance and recovery stages. While intravenous agents are generally preferred in the induction stage, inhalation agents are usually used in the maintenance stage. To prevent patient awareness throughout the procedure a volatile agent concentration of 0.5–0.7 MAC must be maintained [7, 8]. Unlike LFA studies that target a 1–1.5 MAC EtAA [3, 9, 10], in the current study, we aimed to achieve a MAC of 0.7. During the wash-in, anesthesia is maintained by the combined effects of IV induction agents (that are decreasing) and inhaled agents (that are increasing). To ensure sufficient depth of anaesthesia, BIS monitoring was used. It has been reported that BIS values should be kept in the

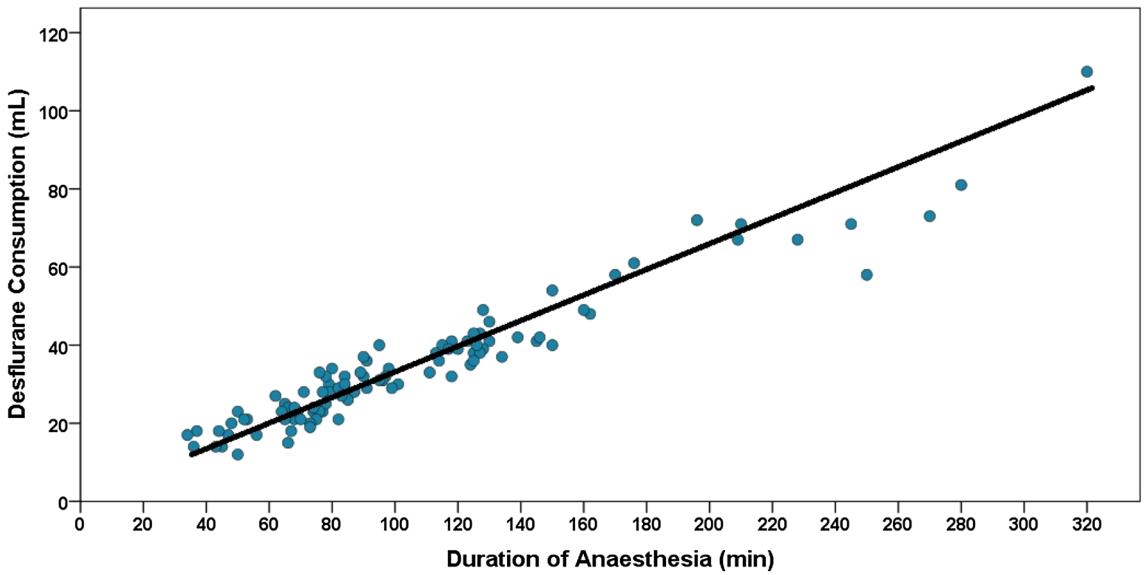

Fig. 4 Desflurane consumption. Each plot represents a single patient; straight line represents mean desflurane consumption: time × 0.33 mL/min. Time zero is the start of administration of desflurane. The X-axis is not a linear scale

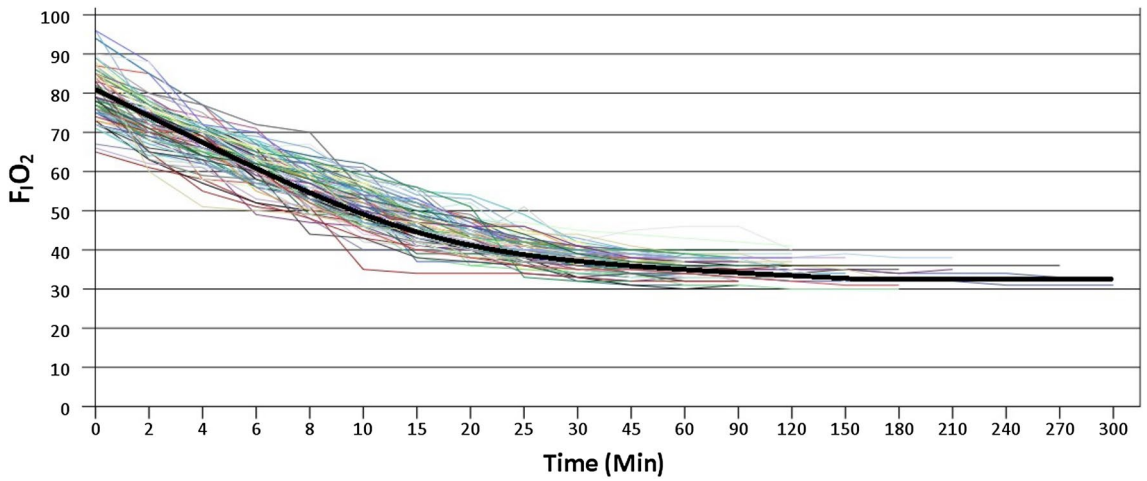

Fig. 5 F_IO_2 values of the individual patients (thin lines) and mean F_IO_2 value of all patients combined (thick line). Time zero is the start of administration of desflurane. The X-axis is not a linear scale

range of 40–60 to ensure that there is no memory or awareness [11–13]. In the present study, the EtAA reached 0.7 MAC within a mean time of 2.9 ± 0.5 min (max, 4.3 min), and within this period, the BIS value did not exceed 60 in any of the patients. Throughout the procedures, the BIS values were below 60 and the MAC values were between 0.6 and 0.9. Therefore, the method applied in this study can be considered to be convenient and likely to ensure a state of unconsciousness by maintaining a MAC of at least 0.6, in the presence of a plasma opioid concentration equivalent to about 2 ng/mL fentanyl.

In a study by Mapleson [3], it was shown that an EtAA of 1 MAC could be reached within 1 min with 3.5 L/min FGF for desflurane, if the vaporizer was set at 3 MAC. Yam et al. [9] applied this theoretical model to 90 cases of elective tonsillectomy performed under general anaesthesia. The aim was to increase the EtAA concentration to 1 MAC as soon as possible and then to keep it stable. In the desflurane group, FGF was 3.5 L/min and F_D was 18%, and an EtAA of 1 MAC was achieved within 1 min. Then, FGF was decreased to 1 L/min, and F_D was set at 9.9% (1.5 MAC) and then decreased to 7.9% (1.2 MAC) after 10 min. The EtAA of 1

MAC was reached within 1 min and maintained for 20 min at slightly above 1 MAC. The current study differed from the abovementioned previous studies in that they used a high FGF in the wash-in period and made frequent adjustments to the vaporizer. In contrast, in the current study, a stable anaesthesia depth was maintained not just for 20 min but also for procedures that were longer than 5 h and very few adjustments were required.

In a study by Horwitz and Jakobsson [10] which was similar to the current study, patients were divided into four groups, and desflurane and sevoflurane were used at an FGF of 1 or 0.5 L/min from the beginning. The vaporizer was set at 6% for sevoflurane and 18% for desflurane in the wash-in period. The time required to reach 1 and 1.5 MAC was determined. Throughout the surgical procedure, the EtAA was maintained at 0.8 MAC. Sevoflurane reached a concentration of 1 MAC within 15.2 ± 2.4 min at a flow rate of 0.5 L/min and within 6.2 ± 1.3 min at a flow rate of 1 L/min, while desflurane reached a concentration of 1 MAC within 8.5 ± 1.7 min at a flow rate of 0.5 L/min and within 3.7 ± 0.7 min at a flow rate of 1 L/min. In the current study, a concentration of 0.7 MAC was reached within 2.9 ± 0.5 min. When the targeted values are considered (1 vs 0.7 MAC), the times are highly consistent. In the Horwitz and Jakobsson study, the depth of anaesthesia in the period taken to reach a sufficient MAC value was not examined by BIS or any another monitor. Especially in the 0.5 L/min FGF group, the effect site concentrations of intravenously administered induction agents may become too low to continue to ensure hypnosis before a sufficiently high end-expired partial pressure of the inhaled agents has been attained—additional intravenous drug boluses may be required to maintain an adequate depth of anaesthesia. Besides the slow rise of the end-expired concentration caused by the low fresh gas flows, it also has to be appreciated that the end-tidal partial pressure of inhaled anesthetics lags behind the partial pressure in the brain (hysteresis). Complete equilibration is achieved in three brain time constants, which for 3 times 2 min. Therefore, there is about a 6-min delay before which the end-tidal desflurane partial pressure is reflected in the brain [14]. In the current study, a sufficient MAC level was reached in the expired gas at 2.9 ± 0.5 min, and during this time, the depth of anaesthesia was monitored with BIS, suggesting sufficient, appropriate effect site partial pressure were present.

A very rapid increase in the desflurane concentration may lead to sympathetic stimulation, and therefore, the use of high F_D such as 18% should be combined with low FGF and appropriate opioids. Ebert and Muzi [15] reported that while a 1 MAC desflurane concentration did not affect heart rate, a concentration of 1.5 MAC can lead to sympathetic stimulation, resulting in tachycardia and hypertension. Weiskopf et al. [16] examined the haemodynamic effects of desflurane concentrations of 0.83, 1.24 and 1.66 MAC with high FGF. They reported that the 0.83 MAC desflurane concentration did not affect the heart rate, but that tachycardia became evident at desflurane concentrations above 1 MAC when there was a rapid increase in the desflurane concentration. We used 1 L/min FGF during the wash-in period, 2 mcg/kg fentanyl during induction and remifentanil infusion after intubation. No sympathetic stimulation findings associated with desflurane were encountered and haemodynamic data were stable.

In the case of most LFA protocols, anaesthetists have to spend time adjusting the F_IO_2 and vaporizer settings to ensure patient safety and adequacy of anaesthesia. Lucangelo et al. [17] compared end-tidal controlled anaesthesia and manually controlled anaesthesia (MCA) under 1 L/min FGF. In the 40 patients in the MCA group, 137 manual adjustments were required to stabilize EtAA. In the current study, the vaporizer settings were adjusted only 44 times: three times in 2 patients, twice in 7 patients, once in 24 patients. Moreover, no adjustments were required in the remaining 67 patients. In the case of the 2 patients who required three adjustments, the duration of anaesthesia was 280 and 320 min. Given that the total duration of anaesthesia was 10,615 min, it can be deduced that it was necessary to change the vaporizer setting only once in 241 min on average, and this is a very practical number. Therefore, the anaesthetist was not distracted and he/she could focus on the patient and the surgery.

One of the most important concerns regarding LFA is the possibility of formation of hypoxic gas mixtures in the course of anaesthesia. When FGF is reduced, it must be taken into consideration that there will be a difference between the set and inspired oxygen concentration [18]. Therefore, to ensure absolute patient safety in LFA, it is mandatory to continuously monitor the inspired oxygen concentration. In this study, F_IO_2 did not fall below 30% in any patient.

5 Conclusion

When LFA is performed with a FGF of 1 L/min (0.5 L/min O_2, 0.5 L/min air) and 18% F_D desflurane, 0.7 MAC can be achieved within 2–4.3 min (absolute range). Thereafter, a minimum number of vaporizer setting changes are needed to maintain the appropriate desflurane concentration.

Compliance with ethical standards

Conflict of interest The authors declare no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

The study was approved by the Ethics Committee of the Healthcare Application and Research Hospital of Kahramanmaras Sutcu Imam University (no.154 dated 04.05.2016).

References

1. Brattwall M, Warrén-Stomberg M, Hesselvik F, Jakobsson J. Brief review: theory and practice of minimal fresh gas flow anesthesia. Can J Anaesth. 2012;59(8):785–97.
2. Bilgi M, Goksu S, Mizrak A, Cevik C, Gul R, Koruk S, et al. Comparison of the effects of low-flow and high flow inhalational anaesthesia with nitrous oxide and desflurane on mucociliary activity and pulmonary function tests. Eur J Anaesthesiol. 2011;28(4):279–83.
3. Mapleson WW. The theoretical ideal fresh-gas flow sequence at the start of low-flow anaesthesia. Anaesthesia 1998;53(3):264–72.
4. Hendrickx JF, Dewulf BB, De Mey N, Carette R, et al. Development and performance of a two-step desflurane-O_2/N_2O fresh gas flow sequence. J Clin Anesth. 2008;20(7):501–7.
5. Sathitkarnmanee T, Tribuddharat S, Suttinarakorn C, et al. 1-1-12 one-step wash-in scheme for desflurane-nitrous oxide low-flow anesthesia: rapid and predictable induction. Biomed Res Int. 2014. https://doi.org/10.1155/2014/867504.
6. Hendrickx JF, Lemmens H, De Cooman S, et al. Mathematical method to build an empirical model for inhaled anesthetic agent wash-in. BMC Anesthesiol. 2011;11:13.
7. Mashour GA, Shanks A, Tremper KK, et al. Prevention of intraoperative awareness with explicit recall in an unselected surgical population: a randomized comparative effectiveness trial. Anesthesiology 2012;117(4):717–25.
8. Avidan MS, Jacobsohn E, Glick D, Burnside BA, Zhang L, Villafranca A, Karl L, Kamal S, Torres B, O'Connor M, Evers AS, Gradwohl S, Lin N, Palanca BJ, Mashour GA. BAG-RECALL Research Group: prevention of intraoperative awareness in a high-risk surgical population. N Engl J Med. 2011;365(7):591–600.
9. Ip-Yam PC, Goh MH, Chan YH, Kong CF. Clinical evaluation of the Mapleson theoretical ideal fresh gas flow sequence at the start of low-flow anaesthesia with isoflurane, sevoflurane and desflurane. Anaesthesia 2001;56:160–4.
10. Horwitz M, Jakobsson JG. Desflurane and sevoflurane use during low- and minimal-flow anesthesia at fixed vaporizer settings. Minerva Anestesiol. 2016;82:180–5.
11. Gan TJ, Glass PS, Windsor A, et al. Bispectral index monitoring allows faster emergence and improved recovery from propofol, alfentanil, and nitrous oxide anesthesia. BIS Utility Study Group. Anesthesiology 1997;87(4):808–15.
12. Ekman A, Lindholm ML, Lennmarken C, Sandin R. Reduction in the incidence of awareness using BIS monitoring. Acta Anaesthesiol Scand. 2004;48(1):20–6.
13. Myles PS, Leslie K, McNeil J, Forbes A, Chan MT. Bispectral index monitoring to prevent awareness during anaesthesia: the B-Aware randomised controlled trial. Lancet. 2004;363(9423):1757–63.
14. McKay RE. Inhaled anesthetics. In: Strales LM, Miller RD. Miller's anesthesia review. 2nd ed. Philadelphia: Saunders; 2013. p. 45.
15. Ebert TJ, Muzi M. Sympathetic hyperactivity during desflurane anesthesia in healthy volunteers: a comparison with isoflurane. Anesthesiology 1993;79(3):444–53.
16. Weiskopf RB, Cahalan MK, Eger El 2nd, Yasuda N, et al. Cardiovascular actions of desflurane in normocarbic volunteers. Anesth Analg. 1991;73(2):143–56.
17. Lucangelo U, Garufi G, Marras E, Ferluga M, Turchet F, Bernabè F, Comuzzi L, Berlot G, Zin WA. End-tidal versus manually-controlled low flow anaesthesia. J Clin Monit Comput. 2014;28(2):117–21. https://doi.org/10.1007/s10877-013-9516-8.
18. Baum JA. Low-flow anesthesia: theory, practice, technical preconditions, advantages, and foreign gas accumulation. J Anesth. 1999;13:166–74.