J Anesth (2009) 23:209–214
DOI 10.1007/s00540-008-0730-3

Journal of
Anesthesia

Desflurane requirements for laryngeal mask airway insertion during inhalation induction

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Abstract

Purpose. We hypothesized that the simultaneous use of low concentrations (<6%) of desflurane, nitrous oxide (N_2O), and fentanyl would allow a laryngeal mask airway (LMA) to be inserted safely with inhalation induction of desflurane, even in nonparalyzed patients. This prospective, observational study was performed to determine the 50% effective concentration (EC_{50}) of desflurane for LMA insertion in such patients.

Methods. Twenty-two adult patients undergoing ambulatory surgical procedures under general anesthesia using an LMA were included in the study. Fentanyl was administered intravenously at 1.5 $\mu g \cdot kg^{-1}$, and anesthesia was induced with desflurane in 50% N_2O and oxygen, using a normal tidal volume breathing technique. Subsequently, a preselected steady-state end-tidal desflurane concentration was maintained for 10 min before insertion of the LMA. Successful LMA insertion was defined as the absence of adverse airway responses until cuff inflation. Target concentrations of desflurane for LMA insertion were determined using a modified Dixon's up-and-down method (starting dose, 5%; step size, 0.5%).

Results. All 22 patients completed the study without adverse events related to airway irritation. The EC_{50} of desflurane for insertion of the LMA was determined to be 3.61 ± 0.31%, and the 95% confidence interval (CI) of the EC_{50} obtained using probit analysis was 3.13–3.90.

Conclusion. We demonstrated that N_2O-desflurane inhalation induction with a normal tidal breathing technique after premedication with fentanyl can be used safely without any adverse airway events in nonparalyzed patients. In such patients, the EC_{50} of desflurane for successful LMA insertion was 3.61 ± 0.31% (95% CI, 3.13–3.90).

Key words Desflurane · Inhalation induction · Laryngeal mask airway

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Received: September 17, 2008 / Accepted: December 7, 2008

Introduction

Despite the frequent use of propofol for the induction and maintenance of anesthesia for brief surgical procedures, volatile induction and maintenance of anesthesia (VIMA) remains appealing due to the theoretical advantages of enhanced safety and recovery as a result of monopharmacy [1]. As the least soluble agent (blood gas partition coefficient of 0.42), desflurane is eligible as an ideal inhaled anesthetic in such cases. However, many anesthesiologists feel that its pungent odor and tendency to irritate the upper airway make it unsuitable for maintenance, and more specifically, for induction of anesthesia. However, several studies [2–4] have demonstrated that desflurane can be used in inhalation induction, which may be useful as an alternative to intravenous propofol/neuromuscular blocking drug induction if the maintenance of spontaneous ventilation is preferred or if anesthesia is required for brief procedures in patients with hemodynamic instability or hypovolemia. In such clinical situations, the use of a laryngeal mask airway (LMA) may also be beneficial because it is easy to place and does not require muscle relaxation.

Inhalation induction with desflurane alone causes adverse airway events, such as coughing, bronchospasm, laryngospasm, and copious secretion of varying severity [4,5]. However, these adverse airway responses seem to be related to acute administration at high concentrations [6] and inadequate doses or drugs as adjunctive medication [4,7]. Therefore, we postulated that desflurane inhalation induction in combination with nitrous oxide (N_2O) and a moderate dose (1.5 $\mu g \cdot kg^{-1}$) of fentanyl would be sufficient to optimize insertion conditions for an LMA and prevent the side effects caused by desflurane alone, when administered using a normal tidal volume breathing technique with a low initial inspired concentration followed by gradual increases. However, the optimal depth of desflurane anesthesia for LMA insertion has not been quantified in previous

studies. Therefore, the present study was performed to determine the 50% effective concentration (EC_{50}) of desflurane for successful LMA insertion in such cases.

Patients, materials, and methods

The hospital ethics committee approved the study protocol and written informed consent was obtained from all participants. The participants were 22 adult patients (American Society of Anesthesiologists [ASA] physical status I-II, age 20–60 years) who were scheduled to undergo elective ambulatory surgical procedures under general anesthesia using an LMA. Patients with a history of gastroesophageal reflux, reactive airway diseases, or upper respiratory infection within the previous 2 weeks were excluded, as well as those using medications that may have interfered with the study (e.g., anxiolytics or hypnotics).

No premedication was given to any of the patients in this study. After an intravenous cannula had been inserted, the patients were monitored via electrocardiography, pulse oximetry, and a noninvasive arterial blood pressure monitor. Baseline blood pressure and heart rate were measured before induction of anesthesia, and both values were also measured every 1 min from immediately before the LMA insertion attempt to 3 min after the LMA insertion attempt. The end-tidal concentrations of CO_2 ($P_{ET_{CO_2}}$) and desflurane were measured continuously at the elbow of the breathing circuit with a precalibrated gas monitor (Datex-Ohmeda airway module for Aestiva/5 M-CAiOVX-S5; Datex-Ohmeda, Helsinki, Finland) at a sampling rate of 200 ± 20 ml·min^{-1}. Its accuracy for desflurane was ±0.2% at 0–5% and ±0.5% at 5%–10%.

All patients were given fentanyl (1.5 μg·kg^{-1}) and denitrogenated with 100% oxygen for 3 min. The patients were then asked to maintain normal tidal breathing while induction was carried out with the desflurane setting at 3% in oxygen at 3 l·min^{-1} and N_2O at 3 l·min^{-1} for 2 min. Desflurane was increased by 1% every 1 min, to a maximum of 6%. When 90% or more of the preselected end-tidal desflurane concentration had been achieved, the inspired concentration of desflurane was adjusted to maintain the measured end-tidal concentration at a constant preselected value. Subsequently, a steady-state end-tidal desflurane concentration was maintained for 10 min before insertion of the LMA, to allow equilibrium between the alveolar and brain concentrations [8,9]. To ensure a leak-proof fit and prevent potential entrainment of room air during the study period, a face mask was firmly applied to the patient's face. We used a semiclosed breathing system, keeping the adjustable pressure-limiting valve open until no response occurred in the eyelid test. The consciousness of each patient was checked using the eyelid reflex every 10 s during induction. If the $P_{ET_{CO_2}}$ exceeded 45 mmHg during induction, ventilation was assisted to maintain the $P_{ET_{CO_2}}$ at 30–40 mmHg. The following complications were noted during induction: cough, gag, excitatory movement, breath-holding, and laryngospasm. If such events occurred, the patient was withdrawn from the study.

Three anesthesiologists participated in anesthetic induction. All LMA (LMA-Classic; Intavent Orthofix, Maidenhead, UK) insertions were performed in a blind manner by a single anesthesiologist with experience in more than 100 previous LMA insertions. The LMA was inserted upon instruction from a second anesthesiologist controlling the inspired desflurane concentration. Size 4 and 5 LMAs were used for female and male patients, respectively. The patients' responses to LMA insertion were classified as either "failure" or "success" by a third anesthesiologist, who was also blind to the desflurane concentration. Failure was defined as coughing, bucking, inability to keep the mouth open, resistive tongue movement against LMA placement, or gross purposeful muscular movement. Success was defined as the absence of the above responses until cuff inflation. If the first insertion attempt failed, or if the airway was ineffective, the LMA was reinserted after an intravenous bolus injection of 1 mg·kg^{-1} propofol, and the subject was withdrawn from the study. After LMA insertion, anesthesia was maintained with desflurane in 50% N_2O and oxygen titrated in response to surgical stimulation. Ventilation was assisted or controlled to maintain the $P_{ET_{CO_2}}$ between 30 and 40 mmHg. One hour after anesthesia, all patients were interviewed by an anesthetic nurse, who was blinded to the protocol, to ascertain the patient's level of satisfaction with the anesthetic induction experience. An 11-point numerical rating scale was used, in which 0 was defined as "unpleasant" and 10 as "extremely pleasant."

The target end-tidal concentration for each patient was chosen using a modification of Dixon's up-and-down method [10]. We estimated the EC_{50} and its SD at 5% and 0.5%, respectively, based on our previous experience, and these values were used as the starting dose and step size, respectively. The first patient was tested at a 5% end-tidal desflurane concentration and subsequent patients were tested at a concentration defined by the previous patient's response to LMA insertion. If LMA insertion failed, the desflurane end-tidal concentration was increased by 0.5%. If LMA insertion was successful, the concentration was decreased by 0.5%. Testing of different concentrations of desflurane continued for consecutive patients until an a-priori sample size of 22 patients was reached. Simulation studies for the up-and-down method have established that the estimator of EC_{50} usually converges on a stable

value after 20 subjects [11,12]. The EC_{50} was determined using a turning point indicator of EC_{50}, as proposed and delineated by Choi [12]; briefly, the EC_{50} was determined by calculating the mean of the midpoint concentrations of all crossover pairs (from "failure" to "success" and from "success" to "failure"). Probit regression analysis was performed, using SPSS 12.0 for Windows (SPSS, Chicago, IL, USA) to obtain the dose-response curve and 95% confidence interval (CI) of the EC_{50}. Repeated measures analysis of variance (ANOVA) with Scheffe's post-hoc test was used to analyze hemodynamic changes over time in patients with a successful LMA placement, and $P < 0.05$ was considered significant.

Results

All 22 patients completed the study without adverse events related to airway irritation during mask induction before the LMA insertion attempt. The demographic data are given in Table 1. LMA insertions were successful in 13 patients. Among the 9 patients in whom LMA insertion was unsuccessful, the causes of failure included an insufficiently relaxed jaw that made mouth-opening impossible in 2 patients, coughing, gross purposeful muscular movement, or resistive tongue movements in 6 patients, and coughing or bucking at cuff inflation in 1 patient. The mean patient acceptability score of the overall anesthetic induction experience, which was graded using an 11-point numerical rating scale, was 5.4 ± 2.0 for all 22 patients (Table 1).

Table 1. Patient characteristics and acceptability scores

Sex (M/F)	9/13
Age (years)	37.0 ± 12.8
ASA physical status (I/II)	18/4
Weight (kg)	60.2 ± 9.6
Height (cm)	161.8 ± 9.8
Body mass index ($kg \cdot m^{-2}$)	22.9 ± 2.6
Smoking habit (nonsmoker/smoker)	15/7
Patient acceptability score for the induction experience (0–10)	5.4 ± 2.0

Values are expressed as means ± SD or number of patients

The responses for LMA insertion for each consecutive patient, using a modified Dixon's up-and-down sequence, are shown in Fig. 1. The results of the calculations for the 14 crossover pairs indicated that the EC_{50} of desflurane for successful LMA insertion with fentanyl ($1.5\ \mu g \cdot kg^{-1}$) and 50% nitrous oxide was 3.61 ± 0.31%. The dose–response curve constructed using a probit regression analysis of the data obtained from the up-and-down sequences revealed that the 95% CI was 3.13–3.90 (Fig. 2). In 11 patients with a successful LMA placement, mean blood pressure and heart rate did not increase during the initial 1 min after the LMA insertion trial, but both these values increased significantly over the following 1 min and then stabilized by 3 min after the LMA insertion attempt (Table 2).

Discussion

Using probit regression analysis in combination with a modified Dixon's up-and-down method, we determined that the EC_{50} of desflurane for successful LMA insertion in nonparalyzed patients co-induced with 50% N_2O and fentanyl ($1.5\ \mu g \cdot kg^{-1}$) was 3.61 ± 0.31% (95% CI, 3.13–3.90).

The present study was performed to determine the best method of anesthetic induction for a brief surgical procedure in patients with a reduced cardiovascular reserve or hypovolemia. First, an ideal anesthetic tech-

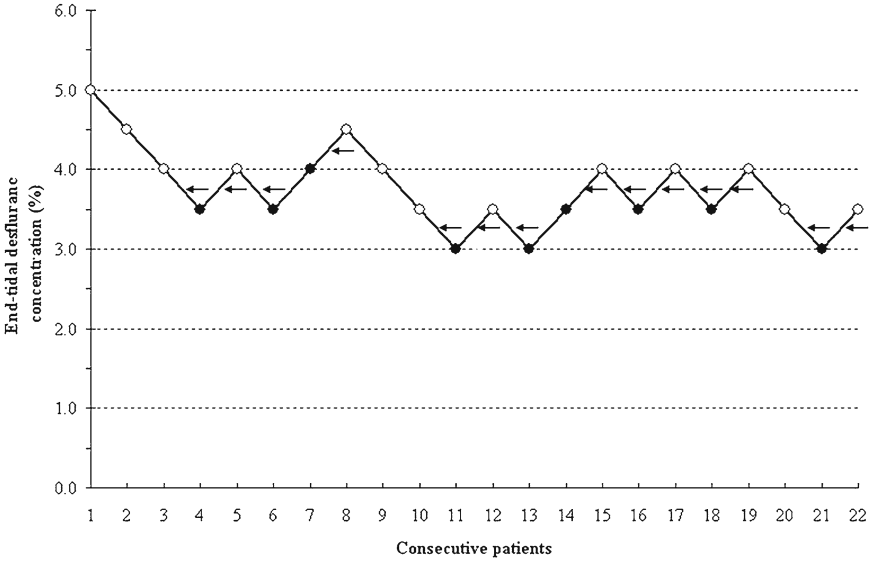

Fig. 1. Responses of 22 consecutive nonparalyzed patients in whom the insertion of a laryngeal mask airway (LMA) was attempted at different end-tidal concentrations of desflurane in 50% N_2O and oxygen. Individual patient data are represented by *circles*. The *arrows* indicate the midpoint concentrations of all crossover pairs (from "failure" [*closed circles*] to "success" [*open circles*] and from "success" to "failure"). The end-tidal concentration of desflurane at which 50% of the patients had a successful LMA insertion (EC_{50}) was calculated as the average of the 14 midpoint concentrations (3.61 ± 0.31%)

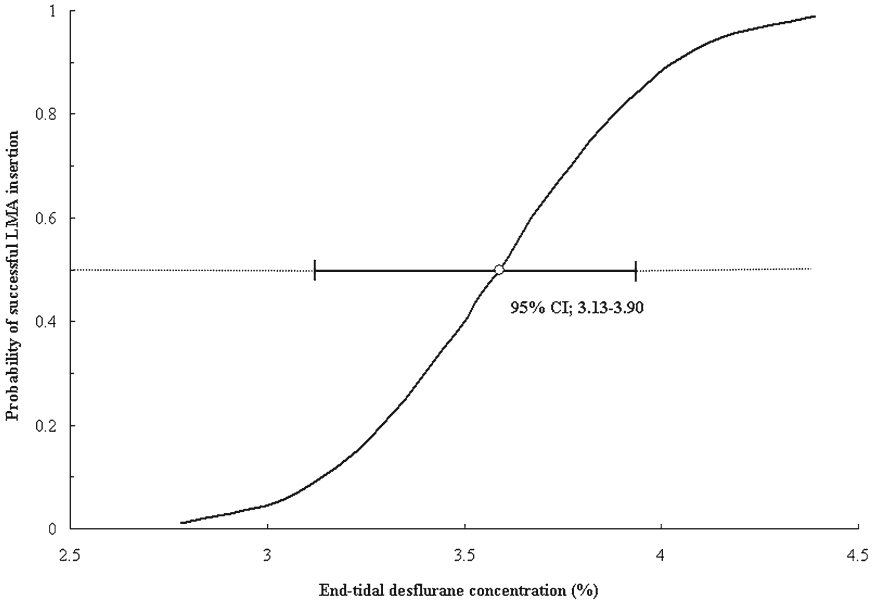

Fig. 2. Dose-response curve for desflurane plotted from the probit regression analysis of the individual end-tidal concentrations and the respective probabilities of successful LMA insertion. The 95% confidence interval (*CI*) of the EC_{50} for desflurane for successful LMA insertion in nonparalyzed patients co-induced with 50% nitrous oxide and fentanyl (1.5 $\mu g \cdot kg^{-1}$) was determined as 3.13–3.90

Table 2. Hemodynamic data during anesthetic induction in patients with a successful LMA placement ($n = 11$)

	Mean blood pressure (mmHg)	Heart rate (beats·min^{-1})
Baseline	95.5 ± 10.1	69.5 ± 12.4
Just before LMA insertion attempt	94.6 ± 8.9	70.8 ± 15.5
1 min after LMA insertion attempt	92.5 ± 10.4	69.3 ± 17.1
2 min after LMA insertion attempt	87.5 ± 10.0*	65.9 ± 14.4*
3 min after LMA insertion attempt	86.3 ± 10.7	63.7 ± 13.1

* $P < 0.05$ compared with mean blood pressure and heart rate at 1 min after LMA insertion attempt
Values are expressed as means ± SD or number of patients

nique for a brief procedure should provide not only rapid awakening, but emergence with a high degree of cognitive ability. Consequently, the low solubility of inhaled anesthetics, such as sevoflurane and desflurane, may be a much more favorable pharmacokinetic characteristic for such cases. Although the difference in solubility between sevoflurane and desflurane is small (0.69 vs 0.46, respectively), the clinical impact on emergence from anesthesia and discharge from the postanesthetic care unit is evident [7,13,14]. Saros et al. [7] proposed desflurane as a viable alternative to sevoflurane for day surgery, even for spontaneously breathing patients with an LMA. They also demonstrated that desflurane provided faster emergence with potential economic savings and no negative impact on recovery. These authors suggested that the rapid onset/offset of desflurane could be utilized advantageously during minor day surgeries with an LMA and spontaneous breathing. Accordingly, we tested a similar anesthetic technique in the present study, which showed several distinct advantages in a brief surgical procedure.

The avoidance of neuromuscular blocking drugs may facilitate recovery. Furthermore, when considering the depressive cardiovascular effects of positive pressure ventilation, the preservation of spontaneous ventilation is especially beneficial in patients with reduced myocardial contractility. Compared to a tracheal tube, an LMA is easy to place and does not require muscle relaxation. Furthermore, an LMA is tolerated at lower anesthetic concentrations than a tracheal tube and therefore allows the patient to breathe spontaneously. Such lower requirements of anesthetics decrease the risk of hypotensive episodes, especially in superficial surgery for patients with cardiovascular instability.

Generally, propofol has been used as the sole induction agent when LMA insertion is required in the absence of neuromuscular blockade. However, it has several disadvantages. Propofol is associated with an increased risk of prolonged apnea. Although apnea can be managed easily in most cases, it can cause serious hypoxemic episodes in patients with a difficult airway. Inhalation induction, however, maintains spontaneous

ventilation, and allows immediate and automatic reduction or cessation of delivery on poor ventilation or apnea, thereby reducing the risk of hypoxemic episodes during airway intervention [15]. In addition, propofol induces significant decreases in mean arterial pressure in patients with little cardiovascular reserve. However, in such patients, desflurane-mediated sympathetic activation can be advantageous [16]. In the present study, both the mean blood pressure and heart rate in the patients with successful LMA placement remained relatively stable over the induction period compared with the preinduction values. Clearly, VIMA with desflurane is associated with slower induction than traditional intravenous induction, but this characteristic may not adversely affect patients with cardiovascular instability.

In the present study, we chose a normal tidal breathing technique because the airway irritant effect of desflurane prevented the use of high initial inspired concentrations or a rapid increase in the inspired concentration. In fact, upper airway irritation is one of the major drawbacks when desflurane is used as the sole induction agent. Various methods have been used to reduce adverse airway responses (coughing, breath-holding, or laryngospasm), including increasing airway humidity using an artificial nose [17], applying a low [2,6] or gradual increase of inspired concentration [2], or premedication with fentanyl [3,18]. Therefore, we incorporated an appropriate dose of fentanyl as part of the inhalation induction with desflurane to prevent adverse airway events. Our pilot study and other research [2,3] demonstrated that a dose of 1.5 $\mu g \cdot kg^{-1}$ was required for complete prevention of the adverse airway events. In addition, such a dose of fentanyl may reduce the requirement of desflurane for successful LMA insertion to less than 6%, at which point airway irritation occurs.

We also chose 50% N_2O as the carrier gas for the inhaled desflurane to accelerate the rate of onset of anesthesia and to further reduce the requirement for desflurane. Kihara et al. [19] reported that 33% and 67% N_2O reduced the EC_{50} of sevoflurane for LMA insertion in children by 22% and 49%, respectively, and that the interaction between N_2O and sevoflurane was additive. Assuming that the same would hold true in adults, we used 50% N_2O to further lower the EC_{50} of desflurane for LMA insertion. The results indicated that the use of 50% N_2O in combination with intravenous fentanyl minimized the EC_{50} of desflurane for LMA insertion, which in turn hastened the induction of anesthesia.

As described by Leong and Ong [2], many clinicians determine the optimal timing of LMA insertion based on subjective jaw relaxation during inhalation induction. In addition to the degree of jaw relaxation, blocking stimulation of the upper airway reflexes is also required to insert an LMA effectively in nonparalyzed patients. Failure to block these upper airway reflexes through insufficient anesthesia results in gagging, coughing, excessive head and limb movement, and even lethal bronchospasm in extreme cases. Although we cannot conclude that desflurane-based inhalation induction is the best possible technique, it may be beneficial in specific clinical situations. Therefore, it is important for clinicians to know the EC_{50} to select the optimal timing of LMA insertion. Of course, further studies are needed to clarify the advantages of VIMA using desflurane and LMA over that using sevoflurane or propofol in a variety of clinical situations. However, our observations will provide a basis for future comparative studies.

Our study design had certain limitations. First, the adjunctive use of fentanyl may have influenced the all-or-none response to LMA insertion. A computer-simulated total brain concentration curve for fentanyl indicated that the maximum brain concentration was reached approximately 10 min after a single bolus injection [20]. However, after the additional 10 min required to equilibrate the cerebral and arterial blood gas pressures of desflurane, the effective site concentration of fentanyl had already reached a peak and was in the slow decline phase at the moment of LMA insertion [21]. Therefore, fentanyl premedication should have little (if any) different effect on the desflurane requirements, due to the interval between bolus injection and LMA insertion. Second, the patients' subjective evaluation of the overall anesthetic induction experience was somewhat low, which appears to have been related to the unpleasant odor of desflurane. Third, we excluded patients with definitely irritable airways (i.e., those with known reactive airway diseases, such as asthma or recent upper respiratory infection). To recruit such patients would be unethical, because no data are currently available regarding the safety of inhalation induction with desflurane in such cases. However, we did not exclude smokers. Previous studies [22,23] have demonstrated that inhalation induction with sevoflurane can be used safely in smokers and that smoking does not augment airway responses to the nominally more pungent anesthetic, desflurane, more than to the nominally nonpungent sevoflurane. Finally, inhalation induction with desflurane requires opioid premedication, and this is not available in nebulized form. Therefore, our method requires intravenous cannulation for the delivery of opioid, which may present a major drawback for needle-phobic patients.

In conclusion, we demonstrated that N_2O-desflurane inhalation induction using a normal tidal breathing technique after premedication with fentanyl (1.5 $\mu g \cdot kg^{-1}$) can be used safely with no adverse airway events in nonparalyzed patients. In such patients, the

EC_{50} of desflurane for successful LMA insertion was 3.61 ± 0.31% (95% CI, 3.13–3.90).

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