The optimal effect-site concentration of sufentanil for laryngeal mask insertion during induction with target-controlled propofol infusion at 4.0 μg/mL

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ABSTRACT

Objective: The objective of this study is to determine the optimal effect-site concentration (Ce) of sufentanil for satisfactory insertion of laryngeal mask airway (LMA) when administered with a target-controlled infusion (TCI) of propofol at 4.0 μg/mL. **Materials and Methods:** A total of 25 adult patients scheduled for minor elective surgery were enrolled in this study. All patients received induction with a combination of propofol and sufentanil TCI. The TCI of sufentanil was started at a target Ce of 0.1 ng/mL. After equilibrium with the plasma concentration, the TCI of propofol was initiated, targeting a preset Ce of 4.0 μg/mL. After the loss of consciousness, LMA was inserted and assessed by an experienced Anesthesiologist. The Ce of sufentanil for the next patient was guided by modified Dixon's up-and-down method using 0.05 ng/mL as a step size. The Ce of sufentanil required for successful LMA insertion in 50% of adults (EC50) was determined by calculating the midpoint concentration of all independent pairs of patients after at least seven crossover points. **Results:** The optimal Ce (EC50) of sufentanil for LMA insertion during propofol induction using target Ce of 4 μg/mL was 0.16 ng/mL (95% confidence interval [CI] = 0.12-0.20). There was a significant reduction in propofol induced pain score P = 0.0275 and insignificant hemodynamic changes. **Conclusion:** Ce of sufentanil required for successful LMA insertion in 50% of patients (EC50) using propofol target Ce of 4.0 μg/mL was 0.16 ng/mL (95% CI = 0.12-0.20) with a significant reduction in the propofol induced pain and hemodynamic stability.

Key words: *Laryngeal mask airway, propofol, sufentanil*

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INTRODUCTION

Laryngeal mask airway (LMA) is one of the most popular airway devices in anesthetic practice. Rapid and easy placement, hemodynamic stability at induction, smooth emergence from anesthesia as well as, lower incidence of sore throat are the main advantages of LMA over the tracheal tube.[1] Satisfactory insertion of the LMA necessitates adequate mouth opening and sufficient depth of anesthesia to prevent untoward events of coughing, gagging and laryngospasm.[2] It has been shown that propofol is the induction agent of choice for LMA insertion because it better relaxes the jaw and has a greater depressant effect on airway reflexes.[3,4] Smooth LMA insertion with propofol alone requires a dose often exceed the recommended induction dose[5] that frequently associated with unacceptable cardiorespiratory depression especially in elderly and unfit patients.[6-8] Consequently, a potent and short-acting opioid is often added to facilitate laryngeal mask insertion in adults with minimal hemodynamic changes.[9] Target-controlled infusion (TCI) is a significant step forward in the administration of drugs by intravenous infusion and has been successfully implemented in the clinical practice.[10,11] Sufentanil is a short synthetic μ-opioid analgesic characterized by good potency and negligible cardiovascular effects.[12,13] Furthermore; sufentanil TCI provides stable analgesia, better hemodynamic control and anticipated recovery from anesthesia.[14,15] The present study was designed to determine the optimal effect-site concentration (Ce) of sufentanil in providing successful LMA insertion when given with a TCI of propofol at 4.0

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μg/mL as the primary outcome and to assess the incidence and severity of injection pain of propofol as a secondary outcome.

MATERIALS AND METHODS

Following approval of Research and Ethics Committee of Dammam University and written informed consent, American Society of Anesthesiologists physical Status I and II patients, aged 18-65 years, scheduled for minor elective surgery were prospectively enrolled in this study. Patients were excluded from the study if they were at risk of aspiration, unable to lie supine, taking analgesic medication or if they had a body mass index >30 kg/m^2, cervical spine disease, an expected difficult airway (Mallampati Grade III or IV), a mouth opening less than 2.5 cm, symptoms of upper respiratory tract disease, a history of cardiovascular, hypertensive and renal diseases or allergies to any anesthetic agent.

All patients were fasted for over 6 h and were not premedicated. In the operating room, after intravenous access was established and a slow infusion of crystalloid commenced, routine monitors (electrocardiography, non-invasive blood pressure, pulse oximetry) and a bispectral index sensor (BIS; Aspect Medical Systems, Norwood, MA, USA) were attached and baseline values were recorded. Two pre-filled TCI pumps (Alaris Medical Systems, UK) one for propofol (10 mg/mL) and the other for sufentanil (1 μg/mL) were connected to the IV cannula using a three-way tap.

After pre-oxygenation, all patients received induction with a combination of propofol and sufentanil TCI using the pharmacokinetic models reported by Schnider *et al*.[16] and Gepts *et al*.[17] respectively. First, the TCI of sufentanil was started with a target Ce of 0.1 ng/mL. After the target Ce of sufentanil was equilibrated with its plasma concentration (Cp), the TCI of propofol was initiated, targeting a preset Ce of 4 μg/mL. After the loss of consciousness (LOC) [loss of verbal contact, loss of eyelash reflex and a BIS value <60] the LMA was inserted by an experienced anesthesiologist according to manufacturer's recommendations.[18] The same anesthesiologist performed LMA insertion in all patients, using size 3 LMA for all the females and size 4 for all the males.

The response of patients to the insertion of the laryngeal mask was classified as either "movement" or "no movement." Movement was defined as difficult mouth opening, gross purposeful muscular movement, coughing, gagging or any evidence of upper airway obstruction occurring before or after inflation of laryngeal mask cuff. No movement was defined as the absence of the above reactions after insertion or inflation of LMA. Patients who did not lose verbal contact or their eyelash reflex or showed BIS >60, before airway insertion were classified as "movement." The physician who performed and assessed the conditions of laryngeal mask insertion was unaware of the dose of sufentanil.

The dose of sufentanil given to each patient was determined by the response of the previously tested patient using a modified Dixon's up-and-down method (using 0.05 ng/mL as a step size).[19] The first patient was tested at a target Ce of 0.1 ng/mL of sufentanil if patient responded with "movement," then the next patient received an increment of 0.05 ng/mL sufentanil if patient responded with "no movement," then the next patient received a decrement of 0.05 ng/mL sufentanil. The research continued until we obtained seven crossover midpoints. Mean arterial pressure (MAP), heart rate (HR), oxygen saturation (SpO_2) and BIS value were recorded during induction, immediately before and 1 min after laryngeal mask insertion. The incidence and severity of injection pain of propofol were assessed using a four point scale 0 = no pain; 1 = mild pain; 2 = moderate pain and 3 = severe pain.

RESULTS

In this study, 25 patients were enrolled; demographic data are shown in Table 1. Dose-response data for each patient obtained by the up-and-down method are shown in Figure 1. The optimal Ce of sufentanil for LMA insertion

Table 1: Demographic data

Variables	Values
Age (year)	35.6±12.6
Height (cm)	169.5±9.5
Weight (kg)	76.0±8.0
BMI (kg/m²)	25.1±4.1
Gender (male/female)	10/13

The values are means (SD) or ratio. SD: Standard deviation; BMI: Body mass index

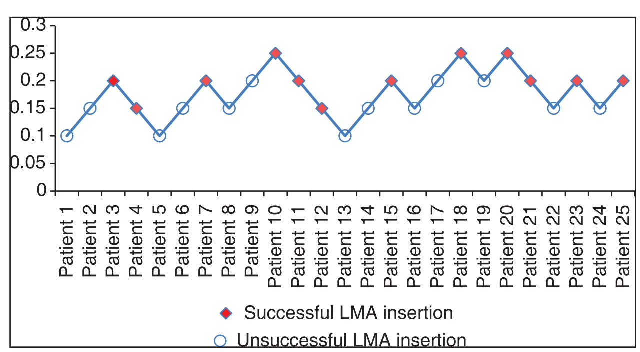

Figure 1: Responses to laryngeal mask airway insertion with a modified Dixon's up-and-down method

in 50% (ED50) of patients during propofol induction using 2% propofol target Ce to 4 μg/mL was = 0.16 ng/mL (95% confidence interval [CI] = 0.12-0.20 ng/mL).

The data characteristics of both successful and unsuccessful LMA insertion patients showed a rate of successful LMA insertion of 56.5%. It also showed a significant low total dose of propofol (P = 0.016), high BIS value (P = 0.02) and low pain score to propofol injection (P = 0.01), in successful compared with unsuccessful LMA insertion patients [Table 2].

There were no significant differences in either MAP or heart values at baseline, at LMA insertion or 1 min after insertion in both successful and unsuccessful LMA insertion patients [Table 3].

DISCUSSION

In our study, the optimal Ce of sufentanil for successful LMA insertion in 50% (ED50) of patients was 0.16 (95% CI = 0.12-0.20) ng/mL during induction using a TCI of 4.0 μg/mL of 2% propofol, with hemodynamic stability and significant reduction in the propofol induced pain.

Sufentanil is the most potent opioid analgesic available at present.[20-22] It is so potent that it continues to exert its effects when the concentrations in the plasma are at very low levels. TCI has been recently developed and successfully implemented to rapidly achieve and maintain particular target Cp or Ce of drugs.[10,11] Sufentanil TCI provides more stable analgesia, better hemodynamic control and improves the quality of anesthesia during the perioperative period.[14,15]

Table 2: Characteristic of successful and unsuccessful LMA insertion

Variables	Successful	Unsuccessful	*P*-value
Number	12/25	13/25	
Dose of propofol (mg)	124.9±17.5	146.4±19.7	*P*=0.0162*
Dose of sufentanil (μg)	12.6±2.7	9.76±2.7	*P*=0.0279*
BIS value	55.6±2.8	52.4±3.0	*P*=0.0211*
Pain score	1.0 (0.0-1.0)	2.0 (0.17-2.0)	*P*=0.0193*

*Significant difference. LMA: Laryngeal mask airway; BIS: Bispectral index sensor

Table 3: MAP and HR during LMA insertion

Hemodynamics	Baseline	Before insertion	1 min after insertion	*P* value
Successful				
MAP	72.6±7.7	69.8±7.2	72.4±7.4	0.620
HR	74.5±8.7	72.0±7.0	73.6±7.1	0.752
Unsuccessful				
MAP	82.5±7.9	79.6±8.4	81.3±9.2	0.751
HR	77.7±7.7	80.0±9.8	81.3±9.3	0.539

MAP: Mean arterial pressure; HR: Heart rate; LMA: Laryngeal mask airway

Our study was conducted using, the Orchestra Base Primea TCI device, which enabled administration of propofol and sufentanil on the basis of effect-site TCI.[23] This is different from the Cp control as it permits an overshoot in the Cp allowing rapid achievement of the desired Ce. Furthermore, it more accurately produced the desired time course of drug effect.[24] Variability in a TCI device may result from a variety of different possible sources. Both Pandin *et al*.[25] and Slepchenko *et al*.[26] have evaluated the accuracy of a sufentanil TCI system using the pharmacokinetic parameter set developed by Gepts *et al*.[17] and they concluded that sufentanil can be administered by TCI with acceptable bias and inaccuracy.

In our study all patients with either successful or unsuccessful LMA insertion, did not show any significant changes in both HR or MAP pre- or post-LMA insertion. This finding confirm the study of Kay *et al*.[27] and Iannuzzi *et al*.[28] who demonstrated the cardiovascular stability of sufentanil during tracheal intubation healthy patients or even during induction and pre-bypass in patients undergoing cardiac surgery.[29] Moreover, when used as part of anesthesia induction with propofol in children, sufentanil 0.2 μg/kg 2 min before induction was effective in attenuating the cardiovascular intubation response.[30]

In the present study, patients with successful LMA insertion showed LOC at a significant low total dose of propofol and at higher BIS value, compared with patients with unsuccessful LMA insertion. This totally agree with the results of Lysakowski *et al*.[31] and Iselin-Chaves *et al*.[32,33] who showed that, analgesic concentration of different opioids facilitate LOC induced by propofol (occurred at lower propofol concentration), however, the BIS did not show this increased hypnotic effect (i.e., LOC occurred at higher BIS value).

Pain induced during propofol injection is a common problem and can be very distressing to the patient. The incidence of this pain varies between 28% and 90% in adults and may be severe.[34,35] The use of opioids, especially short-acting drugs such as alfentanil, fentanyl and remifentanil, was observed to decrease pain induced by propofol injection.[34-36] To date, there is only one study[37] reported the efficacy of pre-induction bolus dose of sufentanil in reducing the propofol injection pain. Our study is the first study reported that propofol injection pain was greatly reduced during TCI with sufentanil. This could be explained by allowing the Ce of sufentanil to reach a level effective for pain reduction before infusing propofol.

CONCLUSION

Ce of sufentanil required for successful LMA insertion in 50% of patients (EC50) using propofol target Ce of 4 μg/mL was 0.16 ng/mL (95% CI = 0.12-0.20) with a significant reduction in the propofol induced pain and hemodynamic stability.

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