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Brief communication (Original)

Comparative study of effective-site target controlled infusion with standard bolus induction of propofol for laryngeal mask airway insertion

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Background: The laryngeal mask airway (LMA) is widely used in emergency medicine and surgical anesthesia. Several studies demonstrated induction of anesthesia with different plasma target-controlled infusion (TCI) of propofol for LMA insertion. However, there has been no study to compare the standard bolus propofol induction with the effective site TCI for LMA insertion.

Objective: Compare the efficacy of induction of anesthesia with propofol for LMA insertion between the effective-site TCI, using 6 μg/mL, and the standard bolus propofol dose of 2.5 mg/kg in elective surgical patients.

Methods: A randomized, prospective, single-blinded, clinical study was used for this study. Seventy-eight unpremedicated patients, American Society of Anesthesiologists (ASA) physical status I and II undergoing elective surgical procedure were randomly allocated between two groups. Group 1 received the standard bolus propofol dose of 2.5 mg/kg. Group 2 received effective site TCI (Schnider model) dose of 6 μg/mL for LMA insertion. The hemodynamics and anesthetic depth (Bispectral index score) were monitored and recorded during and immediately after LMA insertion. The number of insertion attempted, insertion quality score, induction time, and propofol doses used were recorded and compared between groups.

Results: The success rate of first insertion attempt was equal in both groups (92.3%). There was no significant hemodynamic response difference between the groups during pre-induction, induction, insertion, and post insertion period. The BIS score was significantly lower during post insertion period in group 1 (51.4±11.0) than group 2 (58.4±3.2) ($p=0.013$). The propofol doses in group 2 were significantly lower than in group 1 (110.6±14.8 *vs.* 153.5±21.5) ($p<0.001$). Patients in group 2 required significantly more induction time than group 1 (146.9±42.3 *vs.* 103.4±33.6 ($p<0.001$).

Conclusion: Propofol induction with TCI provided equal success rate as compared with standard bolus propofol induction for LMA insertion and insertion quality score. TCI significantly lowered the propofol consumption when compared with the standard 2.5 mg/kg propofol dose.

Keywords: Anesthetics, effect-site concentration, laryngeal mask airway, propofol, target-controlled infusion

The laryngeal mask airway (LMA) is an airway device invented by Dr. Brain [1]. It is widely used in emergency medicine and surgical anesthesia. The benefits of LMA are high success rate of insertion (70-90%) in the first attempt [1-3], and better hemodynamic stability than endotracheal tube intubation during induction and emergence [4, 5]. Successful LMA insertion requires adequate depth of anesthesia to provide jaw relaxation and suppression of upper airway reflexes without cardio-respiratory compromise. Propofol 2.5 mg/kg given intravenously is the recommended intravenous induction dose for LMA insertion [6]. This recommended the dose of propofol provide plasma concentration of 8-10 μg/mL, which could be associated with cardiovascular and respiratory depression [7].

Target controlled infusion (TCI) is an intravenous drugs delivery system, which anesthesiologists can set the target plasma or effective site concentration to achieve the desired clinical effect [8, 9]. The

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Schnider pharmacokinetic effective site TCI model [10] was found to have better speed of induction and hemodynamic stability than plasma target model [11, 12]. Several studies demonstrated induction of anesthesia with different plasma target controlled infusion of propofol for LMA insertion [13-15]. However, there is no study to compare the standard bolus propofol induction with the effective site TCI for LMA insertion.

The aim of our study was to compare the success rate of LMA insertion between propofol bolus injections 2.5 mg/kg with the 6 μg/mL effective-site target controlled infusion system.

Materials and methods

This study was approved by the Ethics Committee by the Bangkok Metropolitan Administration, with written informed consent form signed by all candidates. Seventy-nine patients undergoing surgery in which the use of LMA was indicated were enrolled. All patients were of physical status I and II by ASA (American Society of Anesthesiologists), aged 18-62 years, and weighed 40-85 kg. Exclusion criteria included significant central nervous system impairment, risk of pulmonary aspiration, body mass index (BMI) more than 30 kg/m^2, pregnancy, and known allergies to any anesthetic drugs.

All patients were unpremedicated and scheduled for elective gynecological, surgical, plastic or orthopedic surgery. The patients were allocated randomly by computer-generated number into two groups as follows.

Group 1: received continuous infusion of propofol 2.5 mg/kg rate 200 mL/min using the Injectomat TIVA Agilia™ Syringe pump (software version 4.0, Fresenious Kabi AG, Homburg, Germany) in total intravenous anesthesia (TIVA) mode.

Group 2: received an effective site target concentration of 6 μg/mL by propofol TCI with Schnider pharmacokinetic model software. The machine was stopped after the calculated effective site concentration reached 6 μg/mL.

All patients were cannulated using a 20G catheter connected to a syringe pump (Injectomat TIVA Agilia™) via a 1.4 mL extension tube at the contralateral side of blood pressure cuff arm. After baseline measurements by electrocardiogram (EKG), heart rate (HR), systolic (SBP), and diastolic (DBP) arterial blood pressure, oxygen saturation (SpO_2) and bispectral index (BIS) (A2000 BIS™ XP monitor, Aspect Medical Systems, Newton, USA.), each patient was preoxygenated with 100% oxygen for three minutes before induction. All patients initially received morphine sulfate 0.1 mg/kg IV, and anesthesia was induced with propofol by one anesthesiologist, according to allocation randomization. The LMA (Unique™, Laryngeal Mask, Henley-on-Thames, UK) was lubricated with water-based gel (size 3 for female and size 4 for male), and was inserted using a partial cuff inflation method [16] within 20 seconds after the calculated amount of propofol already infused in *Group 1* or the predicted target effective-site concentration reached 6 μg/mL in *Group 2*.

Arterial blood pressure (SBP, DBP), HR, and SpO_2 were monitored every minute, and the BIS value was recorded every 30 seconds until the end of LMA insertion. The investigator recorded the frequency of attempted LMA insertion and the insertion quality score [17]. This was assessed as follows.

Score 1 = full mouth opening and no movement,
Score 2 = partially mouth opening, slight gagging, and fingers movement,
Score 3 = difficult mouth opening, coughing and gross limbs movement.

The induction time was defined by the time from start of propofol infusion to the end of LMA insertion. When the first attempt at LMA insertion was failure, additional propofol 50 mg was administered. An LMA insertion was repeated within 30 seconds. The administered total dose of propofol was recorded in each group.

Statistical analysis

Data were expressed as mean±SD. Independent unpaired "t"-test was used for comparison of age, weight, height, body mass index (BMI), total propofol dose, induction time, hemodynamic variables, and BIS value. The Pearson's Chi-Square test was used for comparison of gender, LMA insertion attempt, and insertion quality between groups. A p-value less than 0.05 was considered as significant.

Sample size was estimated based on the study by Brodrick et al. [2] as follows.

$$N = \frac{(Z_\alpha + Z_\beta)^2 \times 2P(1-P)}{(P_1 - P_2)^2} \quad (1)$$

$$P = \tfrac{1}{2}(P_1 + P_2),$$

Where N is sample size of each group, Z_α and Z_β are Z-value of type I and type II errors, P_1 and P_2 are success rate of LMA insertion with bolus and TCI technique. According to Brodrick et al. [2], 90% success rate in the first attempt of LMA insertion can be obtained with propofol 2.5 mg/kg intravenously ($P_1 = 0.9$). In the present study, we expected that the success rate of LMA insertion with the TCI technique should be within 30% of standard technique ($P_2 = 0.63$). When we considered $\alpha = 0.05$ and $\beta = 0.20$ (then, $Z_\alpha = 1.96$, $Z_\beta = 0.84$), we obtained P = 0.765, and N = 39. Accordingly, the sample size of each group required 39 patients.

Results

Table 1 and **Table 2** show demographic data and baseline values of patients. There was no significant difference between the two groups in age, gender, weight, height, body mass index and type of surgery. The arterial blood pressure (MAP), heart rate, SpO2, and BIS did not differ significantly between the two groups.

Table 1. Demographic data. Value are expressed as mean±SD or number (%).

	Bolus injection (n=39)	Target-controlled injection (n=39)
Age (year)	38.4±10.4	39±14.2
Gender (male/female)	24/15	20/19
Weight (kg)	61.6±8.6	58.5±9.2
Height (cm)	163.4±8.6	161.7±8.3
Body mass index (BMI)	23.9±5.6	22.4±3.5
Type of surgery (number, %)		
General surgery	17 (43.6)	13 (33.3)
Plastic surgery	6 (15.4)	8 (20.5)
Orthopedic surgery	7 (17.9)	5 (12.8)
Gynecologic	9 (23.1)	13 (33.3)

Table 2. Hemodynamic response, oxygen saturation and depth of anesthesia during LMA insertion. Values are expressed as mean±SD.

	Bolus injection (n=39)	Target-conrolled injection (n=39)	P-value
Preinduction			
MAP (mmHg)	94.5±12.4	92.7±14.5	0.555
HR (1/min)	79.1±16.5	80.6±17.0	0.680
SpO2 (%)	99.3±0.83	99.5±1.14	0.431
BIS score	92.7±5.50	90.9±5.73	0.156
One minute after induction			
MAP (mmHg)	86.8±16.17	85.5±14.23	0.706
HR (/min)	82.7±12.49	77.9±14.95	0.129
SpO2 (%)	99.8±0.53	99.8±0.63	1.000
BIS score	81.2±15.27	79.8±17.21	0.713
During LMA insertion			
MAP (mmHg)	78.4±14.24	74.2±12.99	0.177
HR (1/min)	76.5±13.21	70.9±12.55	0.059
SpO2 (%)	99.9±0.31	99.9±0.39	0.727
BIS score	51.8±13.34	55.5±13.63	0.238
Post LMA insertion			
MAP (mmHg)	72.0±10.63	72.9±12.10	0.721
HR (/min)	72.2±15.48	70.6±13.53	0.620
SpO2 (%)	99.9±0.31	99.9±0.31	1.000
BIS score	51.4±11.0	58.4±13.15	0.013

Figure 1 shows hemodynamic responses before and after bolus injection and target-controlled infusion (TCI).

The hemodynamic response to propofol at the first minute of induction and during insertion of LMA showed no statistically significant difference between bolus group and TCI group. The depth of anesthesia showed no significant difference during induction of anesthesia in the first minute and during LMA insertion in both groups. BIS scores were significantly lower in the bolus group than the TCI group during post LMA insertion period. No patients had incidence of hypotension (decrease blood pressure to more than 30% from baseline) or hypoxemia (SpO_2 <90%) in the present study.

There were statistically significant differences in the propofol doses and induction time in this study (**Table 3**). The bolus group showed significantly higher propofol doses for induction than the TCI group. The TCI group took significantly longer induction time than the bolus group. The success rate of LMA insertion in the first attempt was equal in both groups. The insertion quality scores were not significantly different between the two groups. In 28 patients of the bolus group and 30 patients of the TCI group, LMA were inserted with the insertion quality score of 1.

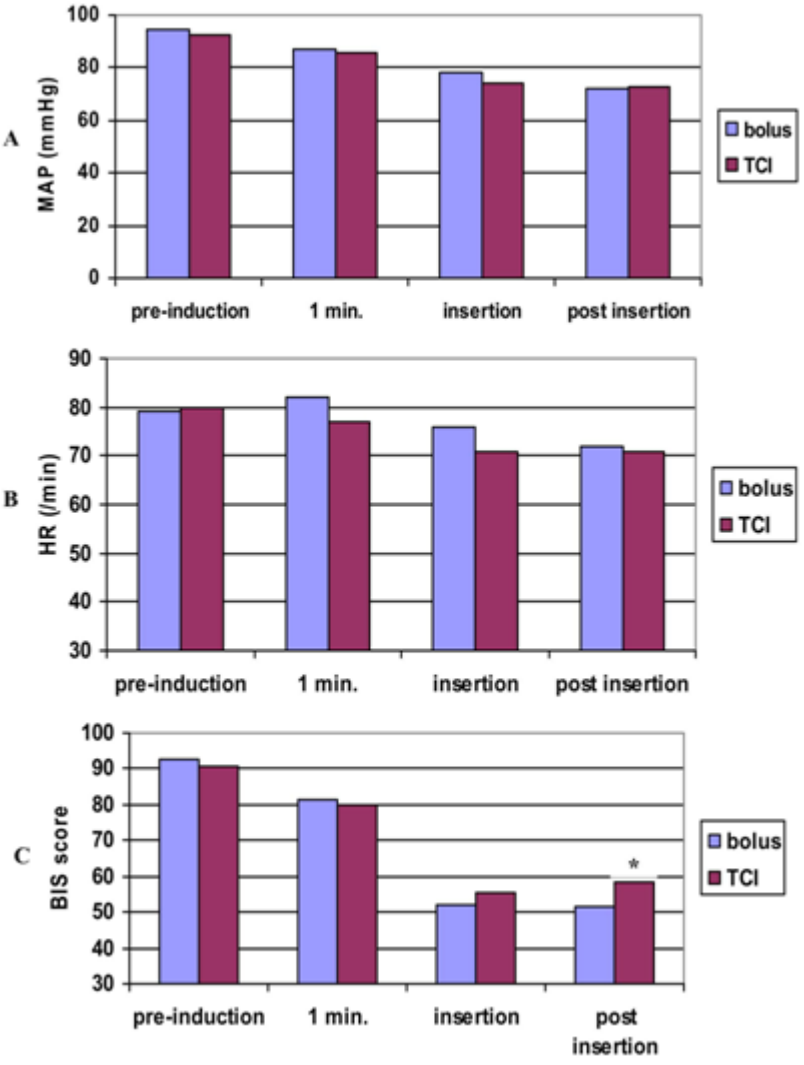

Fig. 1 Hemodynamic responses during pre-induction period, one minute after induction, during LMA insertion and immediate post insertion period in (**A**) mean arterial blood pressure (MAP), (**B**) heart rate (HR), and (**C**) bispectral index score (BIS). *BIS in bolus group was significantly lower than TCI group in post insertion period (51.4 $\pm$11.0 *vs.* 58.4 $\pm$13.2, p-value= 0.013).

Table 3. Propofol doses for LMA insertion and insertion characteristics. Values are expressed as mean±SD or number (%).

	Bolus group	TCI group	P-value
Propofol doses (mg)	153.5±21.51	110.6±14.79	<0.001
Induction time (sec.)	103.4±33.61	146.9±42.32	<0.001
Number of attempt			
1 attempt	36 (92.3)	36 (92.3)	1.000
2 attempt	3 (7.7)	3 (7.7)	
Insertion quality score			
Score 1 (easy)	28 (71.8)	30 (76.9)	0.604
Score 2 (moderate)	11 (28.2)	9 (23.1)	
Score 3 (difficult)	-	-	

Discussion

Target controlled infusion (TCI) been described by Schwilden et al. [18]. It is a method of delivering specific intravenous anesthetic drugs in the concept of converting a dose-effect drug administration to a concentration-effect relationship. The mathematical calculations of pharmacokinetic compartment models converted a dose into plasma or effective site (cerebral) concentration and interface between anesthesia provider and the computer-controlled syringe pump. The first commercially available TCI pump was "Diprifusor" developed by Zeneca pharmaceuticals using a pharmacokinetic model by March to calculate the propofol level of plasma concentration [19]. Several studies determined the target plasma concentration for LMA insertion. Higuchi et al. [20] studied LMA insertion with the TCI system, and found that the EC50 (effective concentration that 50% of patients responded) plasma concentration for LMA insertion was 8.7 μg/mL. Casati et al. [21] revealed that LMA insertion with the Diprifusor TCI system at target plasma concentration of 6 μg/mL with 95% success rate. Kodaka et al. [22] studied the target concentration of propofol required to prevent movement in 50% (Cp50) of propofol for LMA insertion, and calculated that the Cp50 for LMA insertion was 4.07 μg/mL. When the plasma concentration is targeted, the TCI machine will rapidly infuse propofol to increase the plasma concentration of propofol to the selected level. The effective site will gradually increase in propofol concentration to equilibrate with the plasma level depending on the plasma/effective site equilibration rate constant. When the effective site is targeted, the plasma site must be overdosed initially to drive the drug into the effective site. Struys et al. [11] found that targeting the effective site concentration shorted the time to loss of consciousness compared with the targeting the plasma site. Our study demonstrated the success of LMA insertion in 92.3% with mean induction time for 147 seconds, compared with previous plasma-targeted studies that needed 10-15 minutes for plasma/effective site equilibration before LMA insertion.

Brimacombe [23] suggested that insertion of LMA should take place when the anesthesia depths are maximum following bolus injection of propofol. Ludbrook et al. [24] found the maximum depth of anesthesia occurred about two minutes following completion of propofol injection. In our study, we also found significant reduction of the BIS value compared to the TCI group in the post induction period (mean induction time of bolus group = 1.43 minutes). The effective site TCI system was found to have a better control of the level of anesthetic depth in some studies [11, 12]. When we considered the same successful LMA insertion in the first attempt between both groups, our study showed the significantly lower dose of propofol used in TCI group than the bolus group. It could be concluded that the TCI system, at the effect-site target 6 μg/mL, provided comparable success rate of LMA insertion to the standard bolus technique with a significantly lower propofol doses administered.

We found no significant cardiovascular depression during and after LMA insertion between both groups. Wakeling and Struys [11, 12] found no adverse cardiovascular consequences during peak drug effect and the peak cardiovascular depression occurred later than the peak EEG suppression. Baik et al. [15] also found significant decreased blood pressure at the target concentration of propofol higher than 6 μg/mL.

Careful attention of the hemodynamic response is needed when performing TCI with the target higher than 6 μg/mL.

In conclusion, the TCI of propofol induction with effective-site target concentration of 6 μg/mL provided an equal success rate of LMA insertion (92.3%) compared to the standard bolus injection of 2.5 mg/kg of propofol. Dosage of propofol used in TCI group was significantly lower than in the bolus group. No significant difference in hemodynamic response and depth of anesthesia during induction period was seen. However, the BIS value was significantly lower in the bolus group than in the TCI group in post LMA insertion period.

The authors have no conflict of interest to report.

References

1. Brain AIJ. The laryngeal mask—a new concept in airway management. Br J Anesth. 1983; 55: 801-5.
2. Brodrick PM, Webster NR, Nunn JF. The laryngeal mask airway. A study of 100 patients during spontaneous breathing. Anaesthesia. 1989; 44:238-41.
3. Smith I, White PF. Use of the laryngeal mask airway as an alternative to a face mask during outpatient arthroscopy. Anesthesiology. 1992; 77: 850-5.
4. Braude N, Clements EAF, Hodges UM, Andrews BP. The pressor response and laryngeal mask insertion. A comparison with tracheal intubation. Anaesthesia. 1989; 44:551-4.
5. Brimacombe J.The advantage of the LMA over the tracheal tube or facemask: a meta-analysis. Can J Anesth. 1995; 42:1017-23.
6. Brain AIJ. The Laryngeal Mask Airway (LMA) Instruction Manual. Henley:Intavent Research, 1995.
7. Coates DP, Monk CR, Prys Roberts C, Turtle M. Hemodynamic effects of infusions of the emulsion formulation of propofol during nitrous oxide anesthesia in humans. Anesth Analg. 1987; 66: 64-70.
8. Schwilden H. A general method for calculating the dosage scheme in linear pharmacokinetics. Eur J Clin Pharmacol. 1981; 20:379-86.
9. Shafer SL, Gregg KM. Algorhithms to rapidly achieve and maintain stable drug concentrations at the site of drug effect with a computer-controlled infusion pump. J Pharmacokinet Biopharm. 1992; 20:147-69.
10. Schnider T, Minto C, Shafer SL, Gambus PL, Andresen C, Goodale DB, Youngs EJ. The influence of age on propofol pharmacodynamics. Anesthesiology.1999; 90:1502-16.
11. Struys MMRF, De Smet T, Depoorter B, Versichelen LFM, Mortier EP, Dumortier FJE, et al. Comparison of plasma compartment versus two methods for effect compartment-controlled target comtrolled infusion for propofol. Anesthesiology. 2000; 92:399-406.
12. Wakeling HG, Zimmerman JB, Howell S, Glass PSA. Targeting effect compartment or central compartment concentration for propofol. Anesthesiology. 1999; 90: 92-7.
13. Taylor N, Kenny GNC. Requirements for target-controlled infusion of propofol to insert the laryngeal mask airway. Anaesthesia. 1998; 53:222-6.
14. Kodaka M, Handa F, Kawasaki J, Miyao H. Cp50 of propofol for laryngeal mask airway insertion using predicted concentrations with and without nitrous oxide. Anaesthesia. 2002; 57:956-9.
15. Baik HJ, Kim JH, Lee CH. Laryngeal mask insertion during target-controlled infusion of propofol. J Clin Anesth. 2001; 13:175-81.
16. Matta BF, Marsh DS, Nevin M. Laryngeal mask airway-a more successful method of insertion. J Clin Anesth. 1995; 7:132-5.
17. Somboonvibul W, Lelanukrom R, Sriprachittichai P. The laryngeal mask airway in pediatric anesthesia. Thai J Anesthesiol. 1995; 21: 64-9.
18. Schwilden H. A general method for calculating the dosage scheme in linear pharmacokinetics, Eur J Clin Pharmacol. 1981; 20: 379.
19. Marsh B, White M, Morton N, Kenny GN. Pharmacokinetic model driven infusion of propofol in children. Br J Anaesth. 1991; 67: 41-8.
20. Higuchi H, Adachi Y, Arimura S, Nitahara K, Satoh T. Oral clonidine premedication reduces the EC50 of propofol concentration for laryngeal mask airway insertion in male patients. Acta Anaesthesiol Scand. 2002; 46: 372-7.
21. Casati A, Fanelli G, Casaletti E, Cedrati V, Veglia F, Torri G. The target plasma concentration of propofol required to place laryngeal mask versus cuffed oropharyngeal airway. Anesth Analg. 1999; 88: 917-20.
22. Kodaka M, Handa F, Kawasaki J, Miyao H. Cp50 of propofol for laryngeal mask airway insertion using predicted concentrations with and without nitrous oxide. Anaesthesia. 2002; 57:956-9.
23. Brimacombe J. Laryngeal Mask Anesthesia: Principles and Practice, 2nd edition. New York:Saunders, 2005.
24. Ludbrook GL, Upton RN. A physiological model of induction of anaesthesia with propofol in sheep. 2. Model analysis and implications for dose requirements. Br J Anaesth. 1997; 79: 505-13.