Comparison of Propofol ED₅₀ and Insertion Conditions of LMA between Fentanyl and Alfentanil Adjuvant Group

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Background: Recent studies suggest that additional use of alfentanil could provide the best condition for the laryngeal mask airway (LMA) insertion. The aim of this study is to compare the median effective dose (ED₅₀) of propofol for the classic LMA insertion and the insertion condition following between fentanyl and alfentanil adjuvant.

Methods: We enrolled 53 patients scheduled for minor surgery under general anesthesia. Patients were randomly allocated to the fentanyl group (n = 24) and the alfentanil group (n = 29) in double blind manner. For fentanyl group, 1μg/kg of fentanyl was injected intravenously 90 sec before propofol. The alfentanil group received 4μg/kg of alfentanil and propofol coincidentally. The insertion of LMA was attempted 90 sec after propofol administration. In accordance with Dixon's up-and-down method, the dose of propofol for consecutive patients in each group was varied with increments or decrements of 0.5 mg/kg based on the previous insertion results of patients.

Results: In the fentanyl and alfentanil group, the ED₅₀ of propofol for LMA insertion according to Dixon's method was 2.0 ± 0.3 mg/kg and 1.8 ± 0.3 mg/kg, respectively. In addition, the ED₅₀ of propofol of the fentanyl and alfentanil group according to probit regression model, 1.7 mg/kg (95% confidence interval, 1.2-2.2) and 1.7 mg/kg (1.3-2.0) were calculated respectively. There is no significant difference between the two groups.

Conclusions: There was no significant difference in propofol ED₅₀ for insertion of LMA and insertion condition between the alfentanil and the fentanyl group. (Korean J Anesthesiol 2007; 52: S 21~4)

Key Words: alfentanil, ED₅₀, fentanyl, laryngeal mask airway, propofol.

INTRODUCTION

The laryngeal mask airway (LMA) has become increasingly popular for spontaneously breathing patients undergoing minor surgical procedures. The insertion of LMA requires sufficient depth of anesthesia for the relaxed jaw muscles and suppression of upper airway reflexes such as coughing, gagging and laryngospasm.¹⁾ Propofol is considered as the superior intravenous induction agent in achieving the optimum conditions for LMA insertion, compared with thiopentone and other intravenous induction agents.²⁾ Also, among a number of adjuncts to induction agents to further improve LMA insertion condition, the opioid is most commonly used. In general,

fentanyl is more commonly used for LMA insertion than alfentanil. However, there is a study that alfentanil provides better insertion condition than fentanyl.³⁾ Also, owing to its rapid onset and short duration of action, alfentanil is superior to fentanyl as an adjunct agent to LMA insertion in short-duration surgery.

The aim of this study is to compare the median effective dose (ED₅₀) of propofol for classic LMA insertion and the insertion conditions when alfentanil or fentanyl is co-administered in equipotent doses.

MATERIALS AND METHODS

After IRB approval and written informed consent, 53 patients were recruited. The patients were randomly divided into two groups: Group F: patients with fentanyl co-administration, Group A: patients with alfentanil co-administration. Inclusion criteria were: age 18-60, ASA I-II, operation time expected < 2 hr, and free access to both the head and the

Received : October 4, 2006

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device used. Exclusion criteria were: difficult intubation expected (limited airway opening, airway abnormality); history of major neurological, psychiatric, cardiac, pulmonary, renal and hepatic abnormality; aspiration risk (full stomach, obesity); and allergy or hypersensitivity to any of the drugs used.

All patients received diazepam 0.1 mg/kg orally 1 hr before induction of anesthesia and had been fasted for at least 6 hrs and hydrated with Ringer's lactated solution at an appropriate rate determined by body weight and NPO duration. When the patients arrived at operating rooms, electrocardiogram, noninvasive blood pressure in 1 min interval and SpO₂ were monitored. All patients were preoxygenated for 5 min before induction of anesthesia. Fentanyl 1 µg/kg and alfentanil 4 µg/kg were diluted in 10 ml saline. In the fentanyl group, fentanyl 1 µg/kg was administered intravenously. Ninety sec later, saline 10 ml and propofol were administered. In the alfentanil group, saline 10 ml was administered intravenously. Ninety sec later, alfentanil 4 µg/kg and propofol were administered. Ninety sec after propofol injection, the LMA insertion was attempted by a single anesthesiologist, who was blinded to both the dose of propofol and the group (fentanyl vs alfentanil).

The response of the patient to LMA insertion was classified as either 'success' or 'failure'. Success was identified if the jaw was relaxed adequately, and if there were mild or no coughing, gagging, swallowing, laryngospasm, and no or minimal movement such as finger motion within 1 min. Failure was identified if mouth opening was resistant, there was gross swallowing, > 2 coughs or gags, gross head and limb movement within 1 min of LMA insertion, and laryngospasm. All patients were interviewed in the recovery room to assess memory recall. Airway trauma was identified when there was blood stain on the devices after removal of airway devices or when the patients complained about sore throat.

The dose of propofol used for the next patient was predetermined by modification of up-and-down method of Dixon.⁴⁾ If the insertion was a success, the next propofol dose would be decreased by a step of 0.5 mg/kg. If the insertion was a failure, the propofol dose would be increased by a step of 0.5 mg/ml. The process was repeated until the seven cross-over points (success/fail) were obtained.

The Dixon up and down method was used to determine the mean and standard deviation of propofol ED₅₀. This was calculated from the mid points of pairs of the propofol dose in successive patients, in which a failure of insertion was followed by a success. Seven pairs of failure-success are

necessary for each group for the statistical analysis. Data was also analyzed using a probit regression model. The probit regression model is used to estimate the effect of the explanatory variables when the response is a series of binomial results (ex. success or fail). The probit model is defined as $Pr(y = 1|x) = \Phi(xb)$, where Φ is the standard cumulative normal probability distribution and xb is called the probit score or index. Data was plotted and analyzed using Sigma Plot 8.0 and SPSS 11.5 (SPSS Inc., Chigago, IL, USA). Non parametric data was analyzed by using the K² test and parametric data was analyzed using unpaired t-test. Values were expressed as mean $\pm$ SD, mean (95% confidence intervals), or number of patients. A $P < 0.05$ was considered to be statistically significant.

RESULTS

No significant difference in patient characteristics variables was noticed between the two groups (Table 1). No case of airway trauma or recall was observed.

In fentanyl group (Group F), the ED₅₀ of propofol for LMA insertion was 2.0 ± 0.3 mg/kg (Dixon's method) and 1.7 mg/kg (95% confidence interval, 1.2-2.2, probit regression method). In alfentanil group (Group A), the ED₅₀ was 1.8 ± 0.3 mg/kg (Dixon's method) and 1.7 mg/kg (1.3-2.0, probit regression method). The propofol ED₅₀ for insertion classic LMA of group F is not different from that of group A (Fig. 1-3).

Insertion conditions in both groups are shown in Table 2. No significant difference in insertion conditions was noticed

Table 1. Patient Demographics

	Group F (n = 29)	Group A (n = 24)
Age (yr)	39.2 $\pm$ 14.8	34.9 $\pm$ 15.2
Weight (kg)	64.4 $\pm$ 11.8	63.9 $\pm$ 18.8
Height (cm)	166.3 $\pm$ 9.0	168.9 $\pm$ 8.8
Gender (M/F)	16/13	15/9
ASA (I/II)	17/12	15/9
Surgical procedure		
Low abdominal	13	10
Upper/lower extremity	9	11
Genitalia	7	3

Values are mean $\pm$ SD or number of patients. Group F: patients with fentanyl co-administration, Group A: patients with alfentanil co-administration. There are no significant differences between the two groups.

Fig. 1. Consecutive propofol dose in fentanyl group for ED₅₀ determination. The arrow represents the mean propofol dose when crossing from a failure to a success for insertion. The average of these concentrations is ED₅₀.

Fig. 2. Consecutive propofol dose in alfentanil group for ED₅₀ determination. The arrow represents the mean propofol dose when crossing from a failure to a success for insertion. The average of these concentrations is ED₅₀.

between the two groups.

DISCUSSION

Propofol without a muscle relaxant is routinely used as an induction drug for LMA insertion. Different combinations of propofol and adjuncts to induction have been used to facilitate LMA insertion. Among those, the short acting opioids are most commonly used. The major factors that may hinder the insertion are inadequate jaw relaxation and stimulation of airway reflexes by airway devices and cuff inflation. Since opioid

Fig. 3. Dose-response curves for propofol plotted from probit regression analyses of individual dose of propofol (mg/kg) and the respective responses to LMA with fentanyl or alfentanil co-administration.

Table 2. LMA Insertion Conditions following either Alfentanil or Fentanyl Co-administration

	Group F		Group A	
	Success (n = 15)	Failure (n = 14)	Success (n = 13)	Failure (n = 11)
Mouth opening (full/partial/no)	14/1/0	2/9/3	10/3/0	0/7/4
Cough and gag (no/ < 2/ > 2)	14/1/0	0/6/8	13/0/0	0/1/10
Swallowing (no/ < 2/ > 2)	14/1/0	0/6/8	12/1/0	0/3/8
Laryngospasm	0	0	0	0
MAP > 20% increase	0	1	0	0
HR > 20% increase	0	0	0	1

Values are number of patients. Group F: patients with fentanyl co-administration, Group A: patients with alfentanil co-administration. MAP: mean arterial pressure, HR: heart rate. There are no significant differences between the two groups.

suppresses airway reflex and improves jaw relaxation, it is not surprising that opioid improves the condition for LMA insertion with propofol. Tanaka and Nishikawa⁵⁾ reported that fentanyl pretreatment (1 µg/kg) reduced propofol requirement for LMA insertion (3.42 ± 0.26 mg/kg $\rightarrow$ 1.42 ± 0.26 mg/kg). Lee et al⁶⁾ reported that addition of remifentanyl during the propofol induction of anesthesia significantly improved the condition for LMA insertion.

But, there are a few studies comparing among different

opioids for LMA insertion. Hui et al³⁾ reported that co-administration of alfentanil-propofol provided better insertion condition than fentanyl-propofol. Although not direct comparing studies, many studies reported that alfentanil provides the best condition for LMA insertion. Ang et al⁷⁾ reported that pretreatment with alfentanil 5µg/kg resulted in a significantly higher success rate during the first attempt at insertion of the LMA (96%). Sivalingam et al⁸⁾ reported that the addition of alfentanil 5µg/kg to propofol improved insertion condition (excellent condition 88%).

Hui's study indicated that the addition of alfentanil to propofol significantly attenuated the swallowing, gagging, coughing, limb and head movement, and laryngospasm compared to fentanyl.³⁾ But, our study indicates that the addition of alfentanil to propofol did not reduce propofol ED₅₀ for LMA insertion and did not improve insertion conditions compared with the addition of fentanyl in equipotent doses. In Hui's studies, the used doses of fentanyl (1µg/kg) and alfentanil (10µg/kg) are not equipotent.³⁾ Alfentanil was shown to have one-quarter the potency of fentanyl.⁹⁾ Also, LMA insertion was followed 90 sec after drug administration. After bolus injection, the peak effect time of fentanyl is 3.6 min and that of alfentanil is 1.4 min.¹⁰⁾ Thus, in this theory, the peak effect is to be expected at the moment of LMA insertion when comparing to fentanyl, but is not when using fentanyl. Our study used equipotent doses of fentanyl and alfentanil and LMA was inserted 90 sec later in the alfentanil group and 180 sec later in the fentanyl group. Considering potency and peak effect time of drugs, alfentanil is not superior to fentanyl in providing the best condition for the LMA insertion.

We conclude that there are no significant differences in

propofol ED₅₀ for insertion of LMA and insertion conditions between the alfentanil 4µg/kg adjuvant group and the fentanyl 1µg/kg adjuvant group.

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