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The optimal bolus dose of sufentanil for satisfactory laryngeal mask airway (LMA) insertion conditions in chinese pediatric patients

A prospective double-blind randomized controlled trial (CONSORT)

Na Li, MD*, Yong Chen, MM, Bishan Ouyang, MM, Guige Li, BS, Guanwen Lin, MM, Yan Li, MD, Tiejun Li, MM

Abstract

Background: This study aimed to estimate the optimal dose of sufentanil, coadministered with 2.5 mg/kg propofol, for satisfactory laryngeal mask airway (LMA) insertion conditions in Chinese children and to determine the optimal bolus dose.

Methods: Seventy-five Chinese children aged 2 to 6 years with the American Society of Anesthesiologists physical status I or II, undergoing elective minor surgery were recruited. They were randomly divided into 5 different dosage groups (0, 0.05, 0.1, 0.15, 0.2 μg/kg). A predetermined sufentanil diluted with 5 mL saline was injected 30 s, 200 s later, followed by 2.5 mg/kg propofol over 10 s. After that the insertion conditions were assessed, using a 6-category score. The duration of apnea was recorded. A Probit analysis was performed to determine the ED_{50} and ED_{95} with 95% confidence interval for optimal conditions.

Results: There were less hemodynamic changes in all sufentanil groups than propofol-only group, with 0.2 μg/kg patients showing the most stable cardiovascular responses and best insertion conditions. However, the duration of apnea increased with the increasing dosage of sufentanil. From Probit analysis, the ED_{50} and ED_{95} of sufentanil for optimum score were 0.064 μg/kg and 0.177 μg/kg, respectively.

Conclusion: In combination with propofol for anesthesia induction in Chinese children, sufentanil 0.2 μg/kg could prevent patients from dramatic hemodynamic change, providing satisfactory LMA insertion conditions.

Abbreviation: LMA = laryngeal mask airway.

Keywords: laryngeal mask airway, pediatric patients, sufentanil bolus dose

1. Introduction

Laryngeal mask airway (LMA) is an increasingly popular airway device among Chinese pediatric patients, because of its much easier placement, less unwanted effects and lower anesthetic agents needed than a tracheal tube.[1] Successful LMA insertion requires adequate mouth opening and appropriate anesthesia depth to avoid swallowing, gagging, movement, and laryngospasm.[2] There are a number of anesthetics that have been examined, for the purpose of obtaining reliable insertion conditions.[3,4] Propofol is one of the most useful induction drugs for insertion of LMA, with its superior relaxation of the jaw and suppression of airway reflexes.[5] Nevertheless, to use propofol alone can cause injection pain and dramatic hemodynamic changes, especially in unfit and elderly patients.[6]

In China, adding a potent and short-acting opioid is a usual way, and sufentanil is one of the most popular anesthetics with improved blockade of blood pressure.[4,7] Even though there are studies that have focused on investigating its optimal bolus dose or effect-site concentration, during perioperation period in adult patients, as well as its pharmacokinetics during long-term infusion in critically ill pediatric patients,[6,8,9] they were not in Chinese children LMA insertion conditions. The objective of this study was to determine the clinically required bolus dose of sufentanil for providing acceptable LMA insertion conditions in Chinese children, coadministered with 2.5 mg/kg propofol and calculate its ED_{50} and ED_{95}, to provide reliable references for anesthesia induction.

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The study was approved by the institutional ethics Committee at the University of Research Project of Health Planning industry in Hainan and written informed consent was obtained from parents or guardians.

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The authors declare that they have no competing interests.

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Department of Anesthesiology, Hainan General Hospital, Haikou, Hainan Province, China.

** Correspondence: Na Li, Department of Anesthesiology, Hainan General Hospital, Haikou, Hainan Province 570100, China. (e-mail: linasci2016@hotmail.com).*

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2. Materials and methods

2.1. Patients and groups

This study was approved by the institutional ethics Committee at the university of Research project of health planning industry in Hainan and written informed consent was obtained from parents or guardians. Seventy-five children, ASA I or II, aged 2 to 6 years old, undergoing elective minor procedures were included. The exclusion criteria were high risk of aspiration, suspected difficult airway, a history of reactive airway disease and patient refusal.

Patients were randomly assigned to receive 1 of 5 doses sufentanil (0, 0.05, 0.1, 0.15, 0.2 μg/kg), and the study drug was drawn up into a syringe and diluted with normal saline to 5 ml by a second person not involved with assessing LMA insertion. The dosage of the study drug was concealed from the main investigator who assessed the LMA insertion conditions and the physician who inserted the LMA.

2.2. Procedures

No premedication was given. On arrival in the operating room an intravenous access was secured and standard anesthesia monitoring devices were attached, which included noninvasive blood pressure, continuous electrocardiogram and pulse oximeter. Each patient was preoxygenated for 3 minutes. Anesthesia was then induced by first injecting the study drug over 10 seconds, and 200 seconds later, propofol (2.5 mg/kg) was administrated over 10 seconds. After the lungs were ventilated with 100% oxygen, the insertion of the laryngeal mask airway was attempted 5mins after the end of bolus administration of sufentanil. LMA was inserted by an experienced anesthesiologist according to manufacturer's recommendations. A size-2 mask was used for patients with body weight 10 to 20 kg; a size-2.5 for body weight 20 to 30 kg. After insertion, the positioning of the LMA was checked for airway patency by either observing the patient's respiratory movement and the capnogram when breathing spontaneously or, in apneic patients (most cases), observing for chest expansion and the capnogram during manual ventilation. When the LMA was found to be obstructed, due to faulty placement or prolonged laryngospasm, it was removed and another dose of propofol (1 mg/kg) was given, followed by another attempt at LMA insertion made 60 seconds later. After 3 failed attempts at LMA insertion and lung ventilation, the patient's trachea was intubated. After LMA has been successfully inserted, anesthesia was maintained by administrating 4 to 8 mg/kg h propofol continuously and injecting sufentanil when needed.

2.3. Data collection

Patient details, insertion conditions (described below), and duration of apnea (LMA insertion to first spontaneous breath) were recorded on a data collection form. The patient's systolic and mean blood pressure and heart rate were recorded before induction, 1 minute after induction, and 1 minute after LMA insertion. A 3-point, 6-category scale that had been used successfully in other studies was adopted to grade insertion conditions.[2]

A 3-point, 6-category scale (a–f) was used to grade insertion conditions.

a. Resistance to mouth opening grading: no, significant, or undue force required
b. Resistance to insertion grading: no, significant, or undue force required
c. Swallowing grading: nil, slight, or gross
d. Coughing and gagging grading: nil, slight, or gross
e. Head or body movement grading: nil, slight, or gross
f. Laryngospasm grading: nil, partial, or total

Briefly, a total score for insertion conditions were calculated by adding up the swallowing, gagging, movement, and laryngospasm grades (1, 2, or 3). A score of 4 (optimum score) was considered a good condition for LMA insertion. Because mouth opening and resistance to insertion were poor predictors of dose, they were not used for the score calculation.

2.4. Data analysis and statistics

Analysis was performed by SPSS 24 and data were expressed as mean (± SD) or number of patients. Statistical analyses were performed using one-way ANOVA and the Chi-square test. Probit analysis was used to estimate the ED_{50} and ED_{95} (95% confidence intervals) of optimal LMA insertion condition, and dose–response curve was plotted by Prism 7. As the log dose of 0 μg sufentanil was undefined, we substituted 0.0001 μg/kg (one log unit below the lowest nonzero concentration, that is, 0.05 μg/kg) into the data transformation. $P < .05$ was considered significant.

3. Results

3.1. Demographic data

There were 42 male and 33 female patients who were recruited, aged between 2 and 6 years old. The 5 dosage groups were similar with respect to age, sex, American Society of Anesthesiologist physical status, and weight (Table 1).

Table 1

Patient demographic data.

Sufentanil dose, μg/kg	0	0.05	0.1	0.15	0.2
Age, years	3.7 ± 1.2	3.7±1.7	3.9±1.8	3.9±1.6	3.7±1.3
Gender male:female	9:6	11:4	9:6	7:8	6:9
ASA physical status I:II	14:1	14:1	15:0	15:0	14:1
Weight, kg	15.7±3.8	15.5±4.1	16±4	15.5±3.9	14.7±3.2
Unsuccessful first insertion attempt	8	2	1	1	0
Prolonged apnea (> 5 min)	1	1	3	5	7
Optimum score (= 4)	4	5	9	14	15

Mean SD, or incidence, shown for each dose of sufentanil.
ASA = American Society of Anesthesiologists.

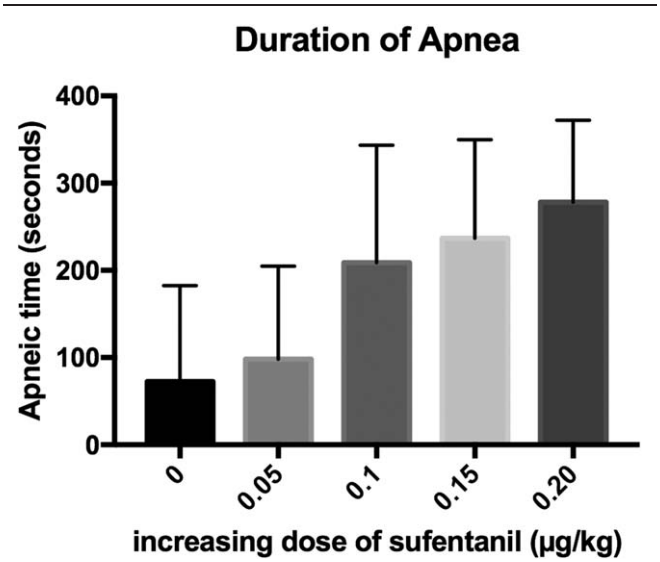

Figure 1. Duration of apnea in 5 different doses of sufentanil groups. The time of apnea prolonged with the increasing dose of sufantanil.

3.2. Successful LMA insertion

In 0 μg/kg group, the number of patients who needed more than one attempt at LMA insertion was much larger than the rest of the groups ($P < .05$, Table 1), with eight children experiencing failure in the first time attempt at LMA insertion. Two patients in the 0.05 μg/kg group and 1 patient in 0.1 or 0.15 μg/kg group received more than one attempt at LMA insertion. Whereas there were no children in 0.2 μg/kg dosage group who had fail insertion at first time.

3.3. Duration of apnea

The duration of apnea became longer (Fig. 1) and the number of patients with prolonged apnea (5 min) increased (Table 1) as the dose of sufentanil grew ($P < .05$).

3.4. Insertion condition

The number of patients (optimum score = 4) rose when the dose of injected sufentanil increased (Table 1). The ED_{50} and ED_{95} of sufentanil were 0.064 μg/kg (95% confidence limits, 0.035-0.088 μg/kg) and 0.177 μg/kg (95% confidence limits, 0.142–0.253 μg/kg), respectively.

3.5. Hemodynamic changes

All 5-group patients had comparable baseline MAP and heart rate in value and the patients in propofol-only group presented even more fluctuation than any sufentanil group (Fig. 2). MAP declined after injection of propofol and the study drug in all the 5 groups ($P < .01$, Fig. 2) by about 15 mm Hg (from a mean of around 107–90 mm Hg). The decrease in MAP ranged from 8% to 14%. After the insertion of the LMA, MAP in 0.2 μg/kg group keep stable, while the number of the other 4 groups increased ($P < .01$).

Similarly, the data of heart rate dropped slightly after induction, but this decrease did not differ among groups ($P > .05$, Fig. 2). After LMA insertion, the change among groups was noticeably different. The number of heart rate in 0.2 μg/kg group showed slight decrease, compared with the patients in the rest 4 groups whose rose ($P < .01$). By contrast, the figure for 0 μg/kg patients grew significantly, whereas the heart rates showed relatively stable in sufentanil groups ($P < .01$).

3.6. Dose response

The dose-response for sufentanil co-administration with propofol on LMA insertion conditions was estimated, using an overall optimal conditions score based on the last 4 categories of a 6-category of outcome (Fig. 3).

4. Discussion

In this study, the ED_{50} and ED_{95} of sufentanil, providing optimal LMA insertion condition for Chinese pediatric patients, were determined. Also, an optimal sufentanil dose for this condition was recommended according to the hemodynamic changes, apnea duration, and optimum scores. We adopted the 3-point, 6-category scale method to grade insertion conditions, which had worked in other study.[2]

Sufentanil as a potent opioid analgesia has been frequently used in clinical anesthesia in the world for years and it is also a usual preference in China. Even though its blood concentration is at low level, it can still exert its pharmacological effect.[10,11] Sufentanil prevents major changes in blood pressure, heart rate, ejection times and ejection fractions during induction phase of anesthesia.[12–14] In addition, pretreatment of sufentanil reduces propofol induced pain.[15] Therefore, it has become an increasingly popular agent not only for pediatric patients who undergo operation, but also for those suffering from severe diseases in intensive care unit.[9,12,16]

In this study, the bolus administration of sufentanil showed dose-related attenuation of laryngeal mask airway insertion responses: after induction, MAP experienced a slight decrease, and then recovered at the level of baseline in all sufentanil dose groups, expect 0.2 μg/kg group, which had even lower blood pressure than baseline (Fig. 2). Similarly, sufentanil injection kept heart rates stable among all sufentanil groups, compared with propofol-only group. This finding confirms the study of Al-Metwalli[6] and Xue et al,[17] who demonstrated that sufentanil co-administered with propofol could blunt cardiovascular responses to laryngoscopy and intubation in children. On the other hand, the duration of apnea prolonged when the concentration of sufentanil rose. It can be seen from Fig. 2 and Table 1 that 0.2 μg/kg sufentanil could completely abolish the cardiovascular insertion responses and produce satisfactory conditions (optimal score) for LMA insertion in all 15 children (Table 1). Also, it approximated to the ED_{95} for the optimal score.

There are a number of researchers who focus on determining optimal dose of sufentanil for anesthesia induction these days. Some of them based on adult patients' LMA insertion, and the others showed interests in trachea intubation. However, none of them has dealt with sufentanil combined with propofol for LMA insertion in children. A study found the effective site-concentration of sufentanil for successful LMA insertion in 50% patients (EC_{50}) during induction with target-controlled propofol is 0.16 ng/mL in adult patients, and Xu et al[17] showed that 0.3 μg/kg could abolish cardiovascular responses to laryngoscopy and intubation in children. Previous studies had proved that sufentanil has age-related differences in pharmadynamics[18] and that the stimulus of trachea cannula is much stronger than

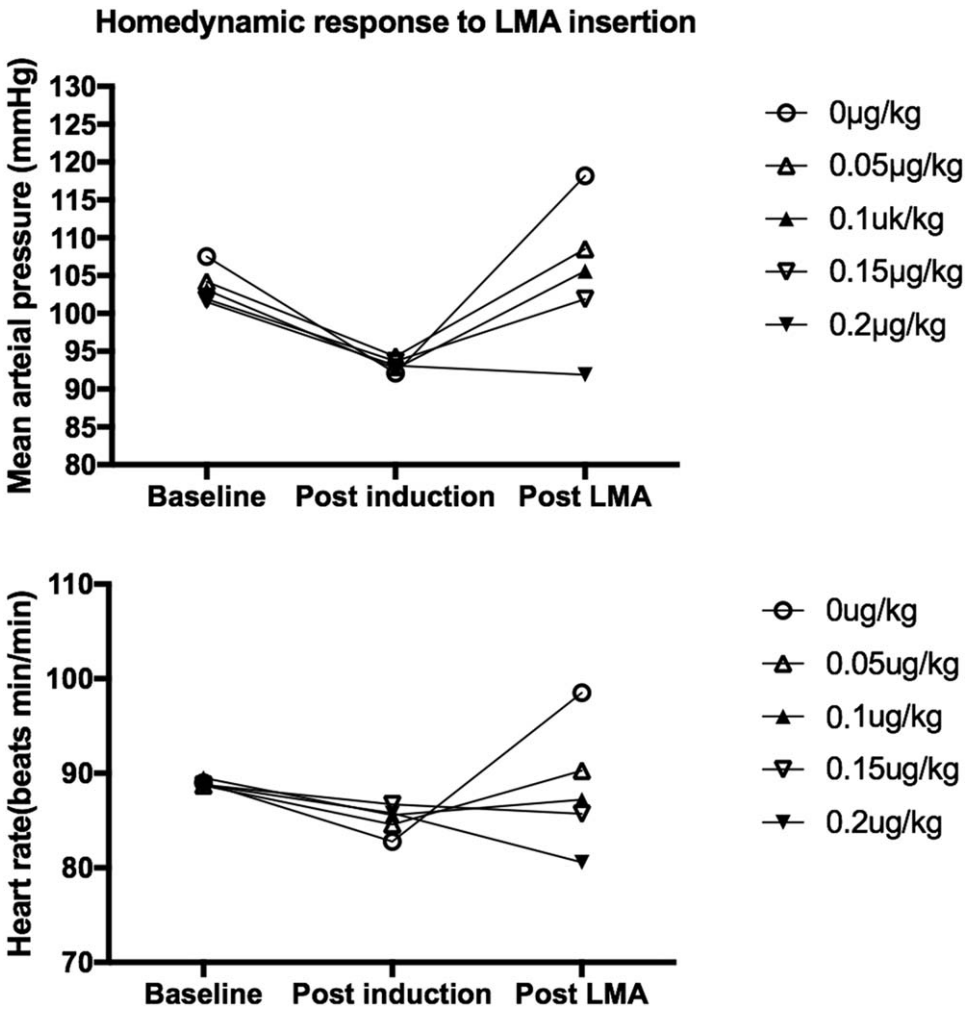

Figure 2. Mean arterial pressure and heart rate during laryngeal mask airway (LMA) insertion at baseline, after induction and LMA insertion as the dose of sufentanil was increased. LMA = laryngeal mask airway.

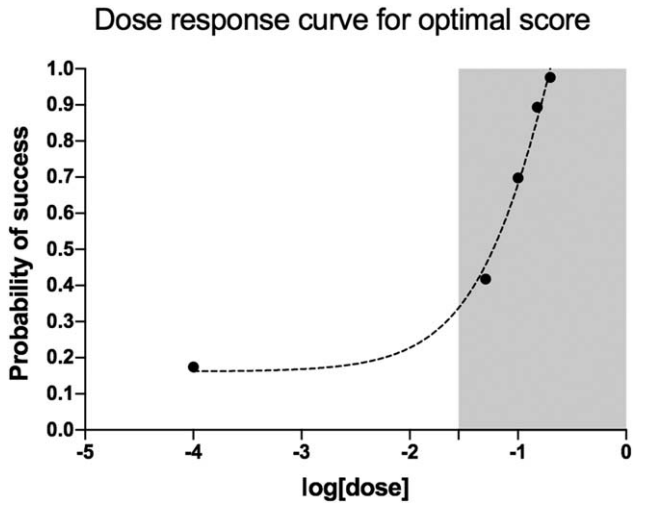

Figure 3. Dose-response curves for optimum score. The 5 sufentanil doses are plotted (points). Log scale used for *X*-axis. The shadow area shows the 95% confidence interval of $\log ED_{50}$.

the LMA insertion.[1] Therefore, the data of our study, which concluded the optimal bolus dose, were reliable and practicable.

Our study was based on Chinese children, aged 3 to 6 years old. Since age-related differences in pharmacodynamics has proved before, the result cannot be extrapolated to other age groups.[18] Nevertheless, we are not aware of any ethnic differences between children, so we would recommend the same dosage for other ethnic groups in the world.

The present study had a few limitations, in this study the serum level of the study drug was not measured. In addition, we did not calculate dose-response in those who did not have an optimum score or received more propofol than others, so further dose finding studies with more study groups recruited may provide more comprehensive data for sufentanil dosage during LMA insertion in children. Moreover, we did not evaluate the sedation level after propofol injection, which might affect the assessment of insertion condition, because there are individual differences in the effect of propofol.[19]

5. Conclusion

In combination with 2.5 mg/kg propofol, the ideal bolus dose of sufentanil for laryngeal mask insertion was 0.2 μg/kg in Chinese

pediatric patients, which could produce optimal insertion conditions and hemodynamic stability.

Author contributions

Conceptualization: Na Li, Yong Chen.
Data curation: Tiejun Li.
Formal analysis: Tiejun Li.
Investigation: Guige Li, Guanwen Lin.
Methodology: Yan Li.
Project administration: Na Li.
Resources: Yong Chen, Bishan Ouyang.
Software: Yong Chen, Bishan Ouyang.
Supervision: Guanwen Lin.
Validation: Guige Li.
Visualization: Yan Li.
Writing – original draft: Na Li.
Writing – review & editing: Na Li.
Na Li orcid: 0000-0003-2567-3351.

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