ORIGINAL ARTICLE

EFFICIENCY OF PROPOFOL CO-ADMINISTERED WITH REMIFENTANIL AND FENTANYL OVER LARYNGEAL MASK AIRWAY INSERTION

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Abstract

In this study we assessed and compared the conditions during insertion of the Laryngeal Mask Airway (LMA) to patients undergoing minor surgery, who received either remifentanil, fentanyl, or normal saline co-administered with propofol. Ninety patients with American Society of Anesthesiology (ASA) class-I/II aged from 18 to 60 years undergoing minor surgery were included in this prospective study. Patients were randomly allocated to receive either normal saline (Group I), fentanyl 1μg/kg (Group II), or remifentanil 1 μg/kg (Group III) over 30 s following induction of anaesthesia with propofol 2.5 μg/kg + lidocaine 1 μg/kg. LMA insertion conditions including mouth opening, ease of placement, coughing, swallowing, laryngospasm, airway obstruction and patients' movement were assessed. Time to eyelash reflex loss, time to successfully place LMA, number of attempts and haemodynamic variables were also recorded. Demographic data were all similar between the groups. Heart rate and blood pressure values were lower in remifentanil and fentanyl groups in comparison with the saline group. Induction rates were found to be the highest in the remifentanil group, followed by fentanyl and saline groups. Both remifentanil and fentanyl increased the LMA insertion tolerance when co-administered with propofol, with remifentanil producing slightly better conditions.

Rezumat

În acest studiu au fost evaluate şi comparate condiţiile din timpul procedurii de introducere a măştii de ventilaţie laringeală (*Laryngeal Mask Airway*, LMA) la pacienţii supuşi unor intervenţii chirurgicale minore, care au primit remifentanil, fentanil sau ser fiziologic concomitent cu administrarea de propofol. In acest studiu prospectiv au fost incluşi nouăzeci de pacienţi cu vârsta cuprinsă între 18 şi 60 de ani, supuşi unor intervenţii chirurgicale minore. Pacienţii au fost repartizaţi aleatoriu pentru a primi fie ser fiziologic (grupul I), fentanil 1 μg / kg (grupul II) sau remifentanil 1 μg / kg (grupul III) pentru 30 de secunde, consecutiv inducerii anesteziei cu propofol 2,5 μg / kg + lidocaină 1 μg. Au fost evaluate evenimentele consecutive folosirii LMA: deschiderea gurii, tusea, înghiţirea, laringospasmul, obstrucţia căilor respiratorii şi mişcările pacienţilor. A fost înregistrat timpul scurs până la pierderea reflexelor palpebrale, uşurinţa şi timpul folosit pentru aplicarea măştii şi variabilele hemodinamice. Datele demografice au fost toate similare între grupuri. Ritmul cardiac şi tensiunea arterială au fost mai scăzute în grupurile de remifentanil şi fentanil în comparaţie cu grupul I. Ratele de inducere a anesteziei au fost crescute în cazul grupului de remifentanil, urmat de fentanil şi de grupul cu ser fiziologic. Atât remifentanilul, cât şi fentanilul au crescut toleranţa la inserţia LMA atunci când aceste substanţe au fost administrate concomitent cu propofolul.

Keywords: propofol, remifentanil, fentanyl, laryngeal mask insertion

Introduction

Useful airway device in many applications, the Laryngeal mask airway (LMA), is used in the emergency department, surgery room and out of hospital, because it is comfortable to use and easy to place, even for the inexperienced care provider [1, 7, 21]. Its use determines less gastric distention than with bag-valve-mask ventilation, reducing but not eliminating the threat of aspiration. This can be specifically important for patients who have not fasted before being ventilated [2, 3, 8, 10].

Even though LMA is a very popular airway device in the practice of anaesthesia, its installation is not always easy [4, 22]. This will need some degree of skills and suppression of upper airway reflex. When placed with propofol alone, this anaesthetic dosage required for setting up of LMA was reported to vary between 2 - 2.5 μg/kg [5]. Higher doses of propofol may result in several haemodynamic changes. In spite of this, propofol is not able to manage alone airway responses and may not prevent gagging, breath holding, breathing, and patients' movement [6]. Amounts of adjuncts including low dose opioids or muscle-relaxants were used to facilitate LMA set. Of those, opioid drugs are the most chosen options [1, 3, 9, 11].

In recent studies, various doses of fentanyl and remifentanil have been reported to improve the

achievement of insertion-rate for the present LMA applications [2, 7, 8]. In this prospective and placebo-control study, we evaluated the conditions for insertion of the LMA and haemodynamics with propofol, fentanyl and remifentanil, and propofol alone administered on anaesthesia induction.

Materials and Methods

Clinical design

This study was performed in the Medical Faculty of Mustafa Kemal University, Turkey. Ninety adult patients, which were ASA (American Society of Anesthesiology) class I/II aged from 18 to 60 years, were included in this prospective study. Written consent was obtained from all patients, after obtaining approval from the Local Ethics Committee. All patients were scheduled for minor surgery in which an LMA and spontaneously breathing anaesthetic technique was planned. Participants with potential of difficult intubation (Mallampati score III - IV, thyro-mental distance ≤ 60 mm, mouth opening ≤ 35 mm), pulmonary aspiration risk, gastrointestinal reflux history, continuous sedatives or anti-epileptic drugs use, ischemic and/or valvular heart disease, renal disease, pregnancy or any known anaesthetic drug allergy were excluded.

Blood pressure, peripheral-oxygen-saturation (SpO_2), heart rate (HR) and electro cardiogram (ECG) were all monitored for patients who were taken into the surgery chamber, after recording the demographic characteristics (age, weight, ASA). All were fasted for over six hours without premedication. Using sealed envelope technique, patients were randomly allocated into one of the three groups: Group I (saline group) received 5 mL saline, Group II (fentanyl group) received fentanyl 1 μg/kg (made up to 5 mL with normal saline), and Group III (remifentanil group) received remifentanil 1 μg/kg (made up to 5 mL with normal saline) over 30 s following induction of anaesthesia with propofol 2.5 μg/kg + lidocaine 1 μg/kg.

Subsequently, anaesthesia was maintained by the inhalation of 6 L/min to ensure fresh gas flow and sevoflurane 2% for 90 seconds with mixture of N_2O 50% and O_2 50%. Attempt to place the LMA was performed afterwards. Tidal volume was organized to be 8 - 10 mL/kg. No-3 LMA was used for patients under 65 kg weight, while No-4 LMA was used for patients over 65 kg. LMA was placed after application of a water-soluble lubricating gel and manual ventilation was performed. When the device has been effectively set up, the patient was periodically ventilated *via* the LMA to maintain saturation and the end-tidal carbon dioxide concentration from 35 to 45 mmHg until resumption of spontaneous respiration. No muscle relaxant agents were used in this study. In case of inability to provide adequate induction or any movement monitored before or after LMA insertion, additional 0.5 μg/kg dose propofol was administered and we waited 30 seconds for the next attempts [9]. Peak heart pulse under 50 pulse/min was evaluated to be bradycardia and i.v. atropine 0.01 μg/kg was administered. Systolic blood pressure lower than 90 mmHg was defined as hypotension and i.v. ephedrine 10 μg was administered. All additional propofol, atropine and ephedrine drugs administered were recorded.

The patients tolerance to LMA insertion was evaluated using an improved scoring system of Muzi *et al.*, based on criteria including mouth opening during LMA insertion, ease of placement, coughing, swallowing, laryngospasm, airway obstruction and patients movement [10]. In all cases, time to eyelash reflex loss, time to successfully place LMA and number of successful attempts in order to place LMA were noted. A total of 7 time periods including anaesthesia onset, after eyelash reflex loss, during LMA placing, after LMA placing, 2^{nd}, 5^{th} and 10^{th} minute after administration of induction agent were all recorded for the heart rate, SpO_2, systolic blood pressure and diastolic blood pressure of the patients. Sevoflurane was finished and 100% oxygen started to be prepared 5 minutes before surgery end. The durations of anaesthesia, surgery and patient recovery (eye opening, extubating, name telling, and capability to count backward from number 10) were also recorded.

Statistics

Statistical analysis was performed using SPSS 13 for Windows (Statistical Package for Social Sciences). All data were analysed by descriptive statistical methods (mean, standard deviation). For quantitative data, One-way ANOVA test was used for comparison between groups of parameters with normal distribution. Analysis of variance was used for comparison of qualitative data and Chi-square test was used for repeated measurements. The results were evaluated in the range of 95% confidence and at $p < 0.05$ significance level.

Results and Discussion

Data were collected from the patients admitted to department of anaesthesiology and reanimation, Mustafa Kemal University, Faculty of Medicine. Age, weight, loss of eyelash reflex time and number of attempts were statistically similar among the groups, as given in Table I.

Table I

Demographic features of the groups

Parameters	Group I	Group II	Group III
Age (year)	41.6 ± 14.8	38.1 ± 10.9	41 ± 10.9
Weight (kg)	69.8 ± 10.4	69.4 ± 11.1	72.0 ± 10.1
Loss of Eyelash Reflex Time	48 ± 24.4	50.2 ± 17	42.6 ± 18.4
Number of Attempts	1.3 ± 0.6	1.2 ± 0.5	1.1 ± 0.3

Comparing the groups in terms of time spent for the successful LMA placement, anaesthesia time and surgery time, the shortest durations were remarked for Group I while the longest durations were remarked for Group II. Group II and Group I were different in terms of time for successful LMA placement, anaesthesia time, surgery time, eye opening time, extubating time, name telling time and time for ability to count backward from 10. Concerning the recovery parameters like eye-opening time, name telling time and time for ability to count backward from 10, the shortest durations were obtained for Group III while the longest durations were obtained for Group I. A significant difference was found between Group II reported to Group I and between Group I reported to Group III. Extubating time was observed as the shortest for Group II, and the longest for Group I. In this case a significant difference was remarked between Group II and Group I (Table II).

Table II

Time results of LMA placement, anaesthesia, surgery and resting periods and statistical analyses

Parameters	Group I	Group II	Group III	Statistical analyses		
				Group I *vs.* Group II	Group I *vs.* Group III	Group II *vs.* Group III
Time for successful LMA placement	88 ± 62	128 ± 42	102 ± 42	$p < 0.05$	NS	NS
Anaesthesia time	972 ± 518	1510 ± 850	1342 ± 792	$p < 0.05$	NS	NS
Operation time	967 ± 490	1485 ± 879	1200 ± 775	$p < 0.05$	NS	NS
Eye-opening time	238 ± 142	133 ± 72	129 ± 130	$p < 0.05$	$p < 0.05$	NS
Extubation time	110 ± 86	52,7 ± 46	69 ± 109	$p < 0.05$	NS	NS
Name telling time	289 ± 164	178 ± 120	180 ± 140	$p < 0.05$	$p < 0.05$	NS
Time for ability to count backward from 10	344 ± 167	220 ± 148	204 ± 148	$p < 0.05$	$p < 0.05$	NS

* **NS** means there is no significance for comparison.

According to the scale used to assess LMA tolerance, the highest and the lowest scores were 18 and 15 points respectively. The total score was excellent for 66.7% of patients as 20% was evaluated as enough. Total score was below 16 for 7 patients belonging to Group I, 3 patients belonging to Group II and 2 patients belonging to Group III this result being evaluated as a poor response for these patients. An excellent LMA induction of 73.3% was recorded for Group III patients (the highest rate). Despite these different rates, there was no significance in terms of the response classified as excellent, enough or bad response. 77.8% of patients had complete loss of motion. This ratio was 70% in Group I as the lowest and 90% in Group III as the highest. Because excessive mobility was observed in 3 patients of Group I (10%) and 1 patient of Group II (3.3%), additional propofol 0.5 μg/kg i.v. was administered to these patients. No patient in Group III needed additional propofol. There was no statistically significant difference between groups in terms of jaw opening, convenience of LMA placement and patient mobility.

One patient in Group I (3.3%) and two (6.7%) in Group III had coughing symptoms and one patient in Group III (3.3%) had hiccups. In the study, laryngospasm was not observed for any of the patients. There was no significant difference between these three groups in terms of cough, hiccup or incidence of laryngospasm, which are side effects of induction agents.

Rigidity was not observed for any patient of this study among complications defined due to induction agent. Found for a total of seven patients (7.8%) including two in Group II and five in Group III, hypotension was the most common complication due to induction agent. Blood pressure reached normal limits without having to apply any intervention for 4 patients. 10 μg of i.v. ephedrine was administered to one patient in Group II and two patients in Group III, whose systolic blood pressure was recorded lower than 90 mmHg. In our study, bradycardia and hypertension were observed for two patients. Of the patients with hypertension, one was from Group I, and other from Group II; two of the patients with bradycardia were from Group III.

Heart rates of the patients did not significantly differ between the groups after anaesthesia onset and loss of eyelash reflex (Table III). Heart rates were significantly lower in Group II and Group III in comparison with Group I during LMA placement, after LMA placement and 5th and 10th minute after the administration of the induction agents ($p < 0.05$). Heart rate was the lowest in Group III by the 2nd

minute after administration of induction agent ($p < 0.001$).

Table III

Comparison of heart rate at different times and statistical analyses

Time Period	Group I	Group II	Group III	Statistical analyses		
				Group I *vs.* Group II	Group I *vs.* Group III	Group II *vs.* Group III
Anaesthesia Onset	90 ± 19	86 ± 15	84 ± 13	NS	NS	NS
After Loss of Eyelash Reflex	90 ± 15	85 ± 12	85 ± 13	NS	NS	NS
During LMA Placing	89 ± 14	78 ± 10	80 ± 15	$p < 0.05$	$p < 0.05$	NS
After LMA Placed	85 ± 13	77 ± 10	72 ± 11	$p < 0.05$	$p < 0.05$	NS
2th Minute (AIF)	86 ± 13	79 ± 12	72 ± 12	NS	$p < 0.05$	$p < 0.05$
5th Minute (AIF)	83 ± 11	74 ± 10	69 ± 10	$p < 0.05$	$p < 0.05$	NS
10th Minute (AIF)	78 ± 11	69 ± 9	70 ± 10	$p < 0.05$	$p < 0.05$	NS

* **NS** means there is no significance for comparison. **AIF** – After induction agent; **LMA** – Laryngeal mask airway

Systolic blood pressure (SBP) did not differ between groups at 5th and 10th minute after induction. Comparison of the observed changes over time and differences between groups in SBP values are presented in Table IV. After loss of eyelash reflex, SBP was significantly lower in both Group II and Group III than in Group I ($p < 0.05$). During LMA placement and after the LMA placement, SBP values were significantly lower in Group III than in Group I ($p < 0.05$). SBP value was the lowest for Group III during 2nd minute after the induction ($p < 0.05$).

Table IV

Comparison of systolic blood pressure at different times and statistical analyses

Time Period	Group I	Group II	Group III	Statistical analyses		
				Group I *vs.* Group II	Group I *vs.* Group III	Group II *vs.* Group III
Anaesthesia Onset	136 ± 17	129 ± 13	128 ± 9	NS	NS	NS
After Loss of Eyelash Reflex	125 ± 15	115 ± 15	116 ± 14	$p < 0.05$	$p < 0.05$	NS
During LMA Placing	120 ± 15	112 ± 18	109 ± 16	NS	$p < 0.05$	NS
After LMA Placed	115 ± 13	110 ± 16	106 ± 15	NS	$p < 0.05$	NS
2th Minute (AIF)	115 ± 14	112 ± 14	103 ± 12	NS	$p < 0.05$	$p < 0.05$
5th Minute (AIF)	112 ± 14	106 ± 15	105 ± 12	NS	NS	NS
10th Minute (AIF)	113 ± 15	106 ± 12	106 ± 11	NS	NS	NS

* **NS** means there is no significance for comparison. **AIF** – After induction agent; **LMA** – Laryngeal mask airway

Diastolic blood pressure (DBP) did not differ between groups in terms of initial induction, 5th and 10th minute after induction agent administration. Comparison of the observed changes over time and differences between groups in DBP values are presented in Table V. After loss of eyelash reflex, DBP was significantly lower in Group II than in Group I ($p < 0.05$). 2nd minute after induction agent administration, the lowest DBP was noted for Group III ($p < 0.05$).

Table V

Comparison of diastolic blood pressure at different times and statistical analyses

Time Period	Group I	Group II	Group III	Statistical analyses		
				Group I *vs.* Group II	Group I *vs.* Group III	Group II *vs.* Group III
Anaesthesia Onset	84 ± 10	80 ± 8,7	83 ± 7,8	NS	NS	NS
After Loss of Eyelash Reflex	79 ± 11	71 ± 10	74 ± 13	$p < 0.05$	NS	NS
During LMA Placing	77 ± 12	72 ± 13	70 ± 13	NS	NS	NS
After LMA Placed	71 ± 11	70 ± 13	67 ± 13	NS	NS	NS
2th Minute (AIF)	73 ± 12	70 ± 10	64 ± 10	NS	$p < 0.05$	$p < 0.05$
5th Minute (AIF)	70 ± 11	65 ± 12	65 ± 11	NS	NS	NS
10th Minute (AIF)	70 ± 12	66 ± 11	66 ± 10	NS	NS	NS

* **NS** means there is no significance for comparison. **AIF** – After induction agent; **LMA** – Laryngeal mask airway

Initial SpO_2 did not differ between groups. There was a significant difference for SpO_2 during 5th and 10th minute after induction agent administration, when Group I and II were compared ($p < 0.05$). However, this difference was not statistically significant for the clinical evaluation. There was no statistical difference between other times.

Insertion of LMA needs sufficient depth of anaesthesia to suppress the airway reflexes and relax the jaw muscles [11]. Recent studies have found that

propofol is the first choice as induction agent for insertion of LMA [12, 13]. However, especially alone, propofol provides less satisfactory conditions for LMA insertion and results in cardio-respiratory depression [14]. In order to decrease such side events of propofol, we need to administer opioids or muscle relaxants. We compared the group of propofol (2.5 μg/kg) co-administered with fentanyl (1μg/kg) and remifentanil (0.5 μg/kg) with the group of propofol alone (2.5 μg/kg), and highlighted their efficiency to LMA insertion comfort.

The studies to promote LMA insertion with opioid combined with propofol were performed in two main parts. These studies compared various doses of comparable opioids co-administered with propofol to reduce the propofol dose for LMA application [2, 5]. A study of Kodaka indicated amounts of 0.5, 1, and 2 μg/kg fentanyl to be co-administered with propofol as being efficient for 50% of the attempts to attain the LMA insertion and demonstrated that 0.5 μg/kg fentanyl was the most suitable to obtain minimal respiratory depression [15]. In our design, 1 μg/kg fentanyl used in combination with 2 μg/kg propofol dose was sufficient for the majority of patients. 2.5 μg/kg propofol with 1 μg/kg lidocaine was administered for 10 seconds in induction of anaesthesia. In our fentanyl group, anaesthesia was induced by administration of 2.5 μg/kg propofol with 1 μg/kg lidocaine for 10 seconds and additionally to 30 seconds by administration of 1 μg/kg of fentanyl. In the remifentanil group, anaesthesia was induced by administration of 2.5 μg/kg propofol with 1 μg/kg lidocaine for 10 seconds and additionally to 30 seconds by administration of 1 μg/kg of remi-fentanil.

The highest and the lowest scores were 18 and 15 points respectively, according to the scale used to assess LME tolerance. Total score was excellent for 66.7% of patients, while 20% was evaluated as enough, similarly to the results reported in the study of Kodaka [14]. An excellent LMA induction of 73.3% was recorded for remifentanil (the highest rate). Because excessive mobility was observed for 3 patients treated with propofol alone and fentanyl, additional 0.5 μg/kg propofol i.v. was administered to these patients. There was no statistically significant difference between groups in terms of jaw opening, convenience of LME placement and patient mobility.

Among the recent studies, Qattan *et al.* evaluated the LMA installation situations after using 0.5 μg/kg remifentanil and 5 μg/kg alfentanil adscititious to a combination of 0.5 μg/kg propofol and set conditions for remifentanil group and alfentanil group compared to the baseline group - propofol only [16]. Mean force per unit area significantly reduced in the groups, and thus pulse was lower inside groups of remifentanil and alfentanil. The study of Hui reported LMA installation conditions after using 10 μg/kg alfentanil plus 1 μg/kg fentanyl adscititious to a combination of 5 μg/kg propofol, the results indicating that alfentanil propofol administration resulted in better insertion conditions compared to fentanyl propofol, even though apnoea symptom was longer [17]. Mouth opening and insertion easiness were not increased by alfentanil. Alfentanil and propofol combination reduced occlusion, gagging, swallowing and movement, in comparison with fentanyl and propofol combination. In our study, when comparing the times for the successful LMA placement, anaesthesia and surgery, we determined that the longest period was recorded for the fentanyl group while the shortest period was recorded for the lidocaine group.

The recovery, eye opening, counting backwards from 10 and saying the name times were the shortest for remifentanil group and the longest for lidocaine group. The shortest time to extubating was recorded for the fentanyl group. We found no statistically significant difference between the groups in terms of assessment of LMA insertion tolerance including opening up of patients, installation of LME, patient mobility, coughing, hiccup and laryngospasm.

In the study of Lee [18], different doses of remi-fentanil (as 0.25 μg/kg - 0.5 μg/kg) and 2.5 μg/kg propofol or 2.5 μg/kg propofol only were compared, and found that 0.25 μg/kg remifentanil supported the condition for LMA installation with the lowest hemodynamic [18]. Another study done by Grewal reported that 0.3 μg/kg remifentanil with propofol provides, in comparison to propofol only, installation opportunity with nominal hemodynamics [19]. The achievement rate throughout the primary try was satisfactory within doses of 5 and 10 μg/kg alfentanil. However, 10 μg/kg alfentanil with propofol resulted in a major decrease within both blood pressure and heart rate. In another study, Yazicioglu reported that each remifentanil dose with propofol offered good conditions for LMA with low clinical disturbances [20]. Propofol alone is not a suitable drug for the LMA conditions.

Conclusions

In our study, we have shown that propofol with both fentanyl and remifentanil increased the LMA insertion tolerance, despite the reduction of the hemodynamic parameters in comparison with the initial value.

Heart rates were significantly lower in both remifentanil (1 μg/kg) and fentanyl (1 μg/kg) group than propofol only during LMA placement, after LMA placement and fifth and tenth minute after the administration of the induction agents.

The lowest heart rate was recorded for remifentanil (1 μg/kg) group by the second minute after administration of induction agent.

In our study, additionally, 5th and 10th minutes measured SBP and DBP values did not differ between groups after induction agent administration. After loss of eyelash reflex, we found a significant decrease in SBP and DBP in both fentanyl and remifentanil group. Significantly lower SBP values were found in the remifentanil group during and after LME placement.

After induction agent administration, the 2nd minute SBP and DBP recorded were the lowest for remifentanil group. The results of our study demonstrated similar hemodynamic for propofol administered with fentanyl and remifentanil.

However, for blood pressure decreases in the remifentanil amount can be dangerous for older and sicker patients, although this is tolerated by younger patients. Although both drugs reduced SBP, this reduction was not at all clinically expressed.

In conclusion, the addition of either remifentanil or fentanyl developed better conditions for LMA insertion when compared to propofol only, whereas remifentanil slightly improved the conditions, despite its haemodynamic effects.

Conflict of interest

All authors declare that there is no conflict of interests.

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