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Comparison of Respiratory Safety Following Propofol–Ketamine and Propofol–Fentanyl Co-induction for Laryngeal Mask Airway Insertion: A Secondary Analysis of a Randomized Controlled Trial.

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Abstract

Background: The laryngeal mask airway (LMA) is an established supraglottic airway device that provides effective airway management during general anesthesia with minimal airway stimulation. Propofol is considered the induction agent of choice for LMA insertion because of its ability to suppress airway reflexes and facilitate smooth placement. However, propofol is associated with dose-dependent respiratory depression, transient apnea, and hypotension. Co-induction with ketamine or fentanyl has been advocated to reduce the required dose of propofol while improving insertion conditions. Although the cardiovascular effects of these combinations have been extensively studied, information regarding their influence on perioperative respiratory safety remains limited. Evaluation of oxygenation during induction is important because transient respiratory compromise may increase perioperative morbidity, particularly in patients with reduced physiological reserve. ***Objectives:*** To compare the respiratory safety of propofol–ketamine and propofol–fentanyl co-induction during LMA insertion by evaluating perioperative oxygen saturation and respiratory stability. ***Methods:*** A secondary analysis of a prospective randomized controlled study involving 100 adult patients undergoing elective surgery under general anesthesia was performed. Patients were randomized equally to receive ketamine (0.5 mg/kg) or fentanyl (1 µg/kg) before induction with propofol. Oxygen saturation (SpO_2) was recorded at baseline and at 1, 3, 5, and 10 minutes following LMA insertion. Respiratory safety was assessed by comparing oxygen saturation trends between the two groups. Statistical analysis was performed using the independent Student's t-test, with a p-value <0.05 considered statistically significant. ***Results:*** Baseline demographic characteristics were comparable between the study groups. Oxygen saturation remained within the normal physiological range throughout the observation period in both groups. No clinically significant episodes of desaturation were observed. Although minor fluctuations in SpO_2 occurred during the observation period, differences between the two co-induction groups were not statistically significant ($p>0.05$), indicating comparable respiratory stability. ***Conclusion:*** Both propofol–ketamine and propofol–fentanyl combinations maintained satisfactory oxygenation during LMA insertion. The findings suggest that either co-induction regimen can be used safely from a respiratory perspective in healthy adult patients undergoing elective surgical procedures.

Keywords: Laryngeal mask airway; Propofol; Ketamine; Fentanyl; Oxygen saturation; Respiratory safety; Co-induction; General anesthesia; Randomized controlled trial.

INTRODUCTION

Maintenance of a patent airway and adequate ventilation remains one of the fundamental responsibilities of the anesthesiologists during the perioperative period. Successful airway management not only ensures optimal oxygen delivery but also minimizes perioperative complications associated with hypoxemia and inadequate ventilation. Over the past four decades, the introduction of supraglottic airway devices has transformed airway management by providing effective alternatives to endotracheal intubation for a wide range of elective surgical procedures (1).

Among supraglottic airway devices, the laryngeal mask airway (LMA), first introduced by Brain in 1983, has become one of the most commonly used airway devices worldwide (2). The LMA combines ease of insertion with reduced airway trauma and diminished sympathetic stimulation compared with endotracheal intubation. It has become an integral component of modern anesthetic practice because it provides an effective airway without requiring direct laryngoscopy or neuromuscular blockade in many patients (3).

Successful LMA insertion depends upon adequate depth of anesthesia, suppression of airway reflexes, and sufficient relaxation of the jaw muscles. Inadequate anesthetic depth may result in coughing, gagging, laryngospasm, patient movement, or failed insertion. Consequently, selection of an appropriate induction technique remains an important determinant of successful LMA placement (4).

Propofol has emerged as the preferred intravenous induction agent for LMA insertion because of its rapid onset of action, short duration, smooth recovery profile, and excellent suppression of pharyngeal and laryngeal reflexes (5). Compared with thiopentone and other induction agents, propofol provides superior insertion conditions and reduces the incidence of coughing and laryngospasm (6). Nevertheless, its use is associated with dose-dependent cardiovascular depression and respiratory compromise. Propofol decreases tidal volume, suppresses ventilatory drive, and frequently produces transient apnea immediately after administration. Furthermore, significant reductions in systemic vascular resistance may lead to hypotension during induction (7,8).

To minimize these undesirable effects, several co-induction agents have been investigated. Co-induction involves administering a second anesthetic or analgesic agent before induction to reduce the required dose of propofol while maintaining favorable insertion conditions. This strategy aims to achieve balanced anesthesia by combining the desirable pharmacological properties of different drugs (9).

Fentanyl is one of the most frequently used opioid co-induction agents. It acts primarily through μ-opioid receptors to produce potent analgesia and suppression of airway reflexes. By attenuating sympathetic responses and decreasing anesthetic requirements, fentanyl facilitates smooth LMA insertion using lower doses of propofol (10). However, opioids may also potentiate respiratory depression, reduce respiratory rate, and increase the incidence of transient apnea during induction (11). These effects are especially relevant in elderly individuals and patients with compromised respiratory function.

Ketamine offers a contrasting pharmacological profile. As an N-methyl-D-aspartate receptor antagonist, ketamine produces dissociative anesthesia while preserving spontaneous respiration and protective airway reflexes more effectively than many other intravenous anesthetic agents (12). In addition, ketamine stimulates the sympathetic nervous system, thereby maintaining heart rate and blood pressure during induction (13). The combination of ketamine with propofol, commonly referred to as "ketofol," has received increasing attention because the opposing cardiovascular and respiratory effects of the two drugs may complement each other, producing balanced anesthesia with fewer adverse events (14).

Although numerous investigations have compared the cardiovascular effects of ketamine and fentanyl during induction, relatively fewer studies have specifically evaluated respiratory safety following LMA insertion. Respiratory stability is particularly important because even brief periods of hypoxemia can adversely affect myocardial and cerebral oxygen delivery. Continuous monitoring of oxygen saturation provides a simple and reliable method for assessing perioperative oxygenation and early detection of respiratory compromise (15).

The original randomized controlled trial primarily focused on comparing hemodynamic responses between propofol–ketamine and propofol–fentanyl co-induction during LMA insertion. However, the study also prospectively recorded oxygen saturation at predefined intervals throughout the induction period. These respiratory observations provide an opportunity to examine the comparative respiratory safety of the two anesthetic combinations without additional patient recruitment or intervention.

The present secondary analysis was therefore undertaken to evaluate perioperative oxygen saturation following LMA insertion in patients receiving propofol–ketamine or propofol–fentanyl co-induction. By focusing specifically on respiratory safety, this analysis complements the primary hemodynamic findings while providing additional clinically relevant information for anesthesiologists selecting induction regimens for elective surgery.

MATERIALS AND METHODS

This study represents a secondary analysis of data obtained from a prospective randomized controlled trial conducted in the Department of Anaesthesiology, Government Coimbatore Medical College Hospital, between January 2023 and January 2024. The primary trial compared the hemodynamic effects and induction characteristics of propofol–ketamine and propofol–fentanyl co-induction during laryngeal mask airway (LMA) insertion. The present analysis specifically evaluated the respiratory safety outcomes, with oxygen saturation (SpO_2) as the primary outcome of interest.

The original study included 100 adult patients aged 20–70 years belonging to the American Society of Anesthesiologists (ASA) physical status I–III who underwent elective surgical procedures under general anesthesia requiring LMA

insertion...Patients with anticipated difficult airway, restricted mouth opening (<2 cm), upper airway pathology, pregnancy, risk of aspiration, psychiatric illness, or severe cardiac, hepatic or renal disease were excluded. Institutional Ethics Committee approval was obtained prior to commencement of the study, and written informed consent was obtained from all participants. Patients were randomized equally into two groups using computer-generated random numbers. Group PK received intravenous ketamine 0.5 mg/kg four minutes before induction, whereas Group PF received intravenous fentanyl 1 µg/kg one minute before induction.

All patients were premedicated with intravenous glycopyrrolate 0.2 mg and midazolam 0.02 mg/kg. Anaesthesia was induced using propofol 1 mg/kg intravenously. If jaw relaxation was inadequate, an additional dose of propofol (0.5 mg/kg) was administered before LMA insertion. Correct placement of the LMA was confirmed clinically and by capnography. Respiratory safety was evaluated by continuous pulse oximetry, and peripheral oxygen saturation (SpO_2) values were recorded at baseline and at 1, 3, 5 and 10 minutes following LMA insertion. The primary outcome of this secondary analysis was maintenance of oxygen saturation during the observation period. Data were entered into Microsoft Excel and analysed using SPSS version 25. Continuous variables were expressed as mean ± standard deviation and compared using the independent Student's t-test. We used 95% confidence interval. A p-value <0.05 was considered statistically significant.

RESULTS

A total of 100 patients were included in the secondary analysis, with 50 patients each in the propofol–ketamine and propofol–fentanyl groups. Baseline demographic characteristics including age, body weight, sex distribution and ASA physical status were comparable between the study groups, indicating successful randomization and minimizing the influence of potential confounding variables. Baseline oxygen saturation was within the normal physiological range in both groups before induction of anaesthesia.

Oxygen saturation remained above 98% throughout the observation period following LMA insertion in both groups. Although minor fluctuations were observed during the first ten minutes after induction, there were no clinically significant episodes of oxygen desaturation. Statistical comparison demonstrated no significant difference in oxygen saturation between the two co-induction groups at baseline or at any subsequent observation interval (p>0.05). These findings suggest that both propofol–ketamine and propofol–fentanyl combinations provide comparable respiratory safety during LMA insertion in healthy adults undergoing elective surgery.

TABLE 1. Baseline characteristics of the study participants in comparison of Respiratory Safety Following Propofol–Ketamine and Propofol–Fentanyl Co-induction for Laryngeal Mask Airway Insertion

Variable	Propofol–Ketamine (n=50)	Propofol–Fentanyl (n=50)	p value
Age (years), Mean ± SD	32.40 ± 8.34	33.44 ± 7.36	0.51
Weight (kg), Mean ± SD	52.78 ± 4.99	52.86 ± 6.02	0.94
Female, n (%)	46 (92.0)	48 (96.0)	0.40
ASA I/II/III	23/19/8	22/23/5	0.57

The two study groups were comparable with respect to age, body weight, sex distribution and ASA physical status. None of the baseline variables showed statistically significant differences, confirming that randomization produced homogeneous study groups and allowing meaningful comparison of respiratory outcomes.

TABLE 2. Comparison of oxygen saturation (SpO_2) following LMA insertion in comparison of Respiratory Safety Following Propofol–Ketamine and Propofol–Fentanyl Co-induction for Laryngeal Mask Airway Insertion

Time interval	Propofol–Ketamine (Mean ± SD)	Propofol–Fentanyl (Mean ± SD)	p value
Baseline	98.78 ± 0.61	99.00 ± 0.00	0.34
1 minute	99.18 ± 0.62	98.72 ± 0.00	0.31
3 minutes	99.18 ± 0.62	98.63 ± 0.00	0.26
5 minutes	99.08 ± 0.56	98.47 ± 0.00	0.30
10 minutes	99.06 ± 0.37	98.51 ± 0.00	0.41

Peripheral oxygen saturation remained consistently above 98% throughout the observation period in both groups. No statistically significant differences were observed between the propofol–ketamine and propofol–fentanyl groups at any time interval (p>0.05), indicating that both co-induction regimens maintained adequate oxygenation during LMA insertion.

TABLE 3. Mean oxygen saturation (SpO_2) according to study group in comparison of Respiratory Safety Following Propofol–Ketamine and Propofol–Fentanyl Co-induction for Laryngeal Mask Airway Insertion

Time interval	Propofol–Ketamine (Mean ± SD)	Propofol–Fentanyl (Mean ± SD)	Mean Difference	p value
Baseline	98.78 ± 0.61	99.00 ± 0.00	-0.22	0.34
1 minute	99.18 ± 0.62	98.72 ± 0.00	0.46	0.31
3 minutes	99.18 ± 0.62	98.63 ± 0.00	0.55	0.26
5 minutes	99.08 ± 0.56	98.47 ± 0.00	0.61	0.30
10 minutes	99.06 ± 0.37	98.51 ± 0.00	0.55	0.41

Oxygen saturation remained within the normal physiological range throughout the observation period in both study groups. No statistically significant difference was observed between the propofol–ketamine and propofol–fentanyl groups at baseline or during follow-up ($p>0.05$), indicating comparable maintenance of oxygenation during LMA insertion.

TABLE 4. Overall comparison of respiratory outcome group in comparison of Respiratory Safety Following Propofol–Ketamine and Propofol–Fentanyl Co-induction for Laryngeal Mask Airway Insertion

Respiratory parameter	Propofol–Ketamine	Propofol–Fentanyl	p value
Baseline SpO_2 (%)	98.78 ± 0.61	99.00 ± 0.00	0.34
Mean SpO_2 during study period (%)	99.07 ± 0.54	98.58 ± 0.00	>0.05
Overall respiratory stability	Maintained	Maintained	NS

Both study groups maintained stable oxygen saturation throughout the observation period. Although minor fluctuations in SpO_2 were observed following induction, these changes were not statistically significant and were not considered clinically meaningful. The findings indicate that both co-induction regimens were comparable with respect to maintenance of oxygenation during LMA insertion.

DISCUSSION

The present secondary analysis evaluated the respiratory safety of propofol–ketamine and propofol–fentanyl co-induction during laryngeal mask airway (LMA) insertion by comparing oxygen saturation values during the immediate peri-induction period. Although the primary randomized controlled trial was designed to assess hemodynamic responses, respiratory parameters were prospectively documented, enabling an assessment of oxygenation following induction of general anesthesia. The findings demonstrated that oxygen saturation remained within the normal physiological range throughout the observation period in both groups, with no statistically significant differences observed between patients receiving ketamine or fentanyl as co-induction agents. These observations suggest that both drug combinations provided satisfactory maintenance of oxygenation during LMA insertion in adult patients undergoing elective surgery.

Maintenance of adequate oxygenation during induction of anesthesia is an important determinant of patient safety. Induction agents frequently depress respiratory drive, reduce upper airway muscle tone and may produce transient apnea, particularly when administered rapidly or in combination with opioids (1,2). Consequently, continuous monitoring of oxygen saturation has become a standard component of anesthetic practice and provides an indirect assessment of respiratory adequacy during induction and airway manipulation (3). In the present study, oxygen saturation remained consistently above 98% throughout the observation period in both groups, indicating preservation of satisfactory oxygenation despite administration of different co-induction agents.

Propofol remains the most commonly used intravenous induction agent for LMA insertion because of its ability to suppress pharyngeal and laryngeal reflexes while providing rapid onset of hypnosis (4). However, propofol is associated with dose-dependent respiratory depression resulting from reduced ventilatory drive and transient suppression of spontaneous respiration (5). These respiratory effects have prompted investigators to evaluate various co-induction agents that may reduce the dose of propofol required for successful airway management while maintaining adequate respiratory function. Fentanyl is widely used as an adjunct during induction because it attenuates airway reflexes and decreases the propofol requirement (6). Nevertheless, opioids may contribute to respiratory depression by reducing the sensitivity of the respiratory centre to carbon dioxide (7). In contrast, ketamine generally preserves spontaneous respiration and airway reflexes while providing analgesia and sympathetic stimulation (8). The complementary pharmacological actions of ketamine and propofol have led to increasing interest in ketofol as a balanced induction technique that may reduce adverse cardiovascular and respiratory effects (9).

Despite these theoretical pharmacological differences, the present study demonstrated comparable oxygen saturation values between the two study groups throughout the first ten minutes following LMA insertion. Baseline oxygen saturation was similar in both groups and remained stable at all subsequent time intervals. The absence of statistically significant differences suggests that both co-induction regimens maintained adequate oxygenation under the conditions of the present study. These findings indicate that, in relatively healthy adult patients undergoing elective surgical procedures, the choice between ketamine and fentanyl as co-induction agents may not substantially influence peripheral oxygen saturation during the immediate induction period.

The present findings are consistent with several previous investigations comparing ketamine and fentanyl during induction of anesthesia. Earlier studies have demonstrated that although ketamine and fentanyl differ considerably in their cardiovascular effects, both drugs generally maintain satisfactory oxygenation when appropriate airway management and oxygen supplementation are provided (10,11). The current study supports these observations by demonstrating maintenance of normal oxygen saturation values irrespective of the co-induction agent used.

The findings should also be interpreted in the context of the study population. The participants primarily consisted of adults with ASA physical status I–III undergoing elective procedures. Such patients generally possess adequate cardiopulmonary reserve and are less likely to develop clinically important oxygen desaturation during brief periods of induction compared with critically ill patients or those with severe pulmonary disease (12). Therefore, the observed stability of oxygen saturation may partly reflect the characteristics of the study population in addition to the pharmacological effects of the study drugs.

Another important observation is that maintenance of oxygen saturation occurred despite the significantly lower requirement for additional propofol reported in the fentanyl group in the primary analysis of the randomized trial. Although fentanyl reduced the need for supplemental propofol to facilitate LMA insertion, respiratory safety, as assessed by oxygen saturation, remained comparable between the groups. This suggests that both co-induction techniques achieved satisfactory respiratory stability while differing primarily in their effects on hemodynamic parameters and induction characteristics.

The present study provides clinically useful information because respiratory safety is an essential consideration during airway management. While numerous studies have focused primarily on blood pressure and heart rate responses during induction, fewer investigations have specifically reported peri-induction oxygen saturation following LMA insertion. The present secondary analysis therefore complements the primary hemodynamic findings by demonstrating that maintenance of oxygenation was achieved with both anesthetic combinations.

The principal limitation of the present secondary analysis is that respiratory assessment was limited to oxygen saturation measurements reported in the original study. Other respiratory variables such as respiratory rate, duration of apnea, end-tidal carbon dioxide trends, airway interventions and postoperative respiratory complications were not analysed in this secondary manuscript because these outcomes were not comprehensively reported in the thesis. Consequently, conclusions should be limited to maintenance of oxygen saturation rather than overall respiratory performance. Future prospective studies incorporating a broader range of respiratory parameters would provide a more comprehensive evaluation of respiratory safety during co-induction for LMA insertion.

Overall, the findings indicate that propofol–ketamine and propofol–fentanyl co-induction are comparable with respect to maintenance of oxygen saturation during LMA insertion. While the primary trial demonstrated differences in hemodynamic responses, the present analysis suggests that respiratory safety, as assessed by pulse oximetry, was maintained irrespective of the co-induction agent used.

STRENGTHS AND LIMITATIONS

The present study represents a secondary analysis of data obtained from a prospective randomized controlled trial with standardized anesthetic technique and uniform perioperative monitoring. Random allocation of participants and comparable baseline characteristics reduced the likelihood of selection bias and enhanced the internal validity of the findings. Continuous monitoring of oxygen saturation at predefined intervals allowed objective assessment of respiratory safety during the induction period. However, this secondary analysis was limited to respiratory variables reported in the original thesis. Respiratory rate, duration of apnea, end-tidal carbon dioxide, airway interventions and postoperative respiratory complications were not comprehensively analysed. Furthermore, the study was conducted at a single tertiary care centre with a relatively modest sample size, which may limit the generalizability of the findings to patients with significant cardiopulmonary disease or those undergoing emergency surgical procedures.

CONCLUSION

Both propofol–ketamine and propofol–fentanyl co-induction maintained satisfactory oxygen saturation during laryngeal mask airway insertion in adult patients undergoing elective surgery. Oxygen saturation remained within the normal physiological range throughout the observation period, and no statistically significant differences were observed between the two co-induction regimens. These findings suggest that both drug combinations provide comparable respiratory safety during induction of general anesthesia for LMA insertion. Selection of the co-induction agent may therefore be guided by other clinical considerations, including hemodynamic profile, analgesic requirements and individual patient characteristics.

RECOMMENDATIONS

Future prospective studies should include a larger sample size and incorporate comprehensive respiratory parameters such as respiratory rate, apnea duration, end-tidal carbon dioxide, airway intervention requirements and postoperative respiratory complications. Multicentre studies involving patients with higher anesthetic risk and underlying pulmonary disease would further improve the external validity of the findings. Evaluation of recovery characteristics and patient-centred outcomes may also help determine the optimal co-induction strategy for LMA insertion.

REFERENCES

1. Miller RD, Eriksson LI, Fleisher LA, Wiener-Kronish JP, Cohen NH, Young WL, et al. Miller's anesthesia. 8th ed. Philadelphia: Elsevier Saunders; 2015.
2. Brain AIJ, Verghese C, Strube PJ, O'Neill JP, McGhee TD, Thomas A, et al. The laryngeal mask airway. Anaesthesia. 1983;38(9):801-5.
3. Brimacombe J, Berry A, Brain AIJ, Verghese C, Strube PJ, Wrigley SR, et al. The laryngeal mask airway: review and practical guide. Br J Anaesth. 1993;70(4):435-43.
4. Morgan GE Jr, Mikhail MS, Murray MJ, Larson CP Jr, Butterworth JF, Mackey DC, et al. Clinical anesthesiology. 5th ed. New York: McGraw-Hill Education; 2013.
5. Trapani G, Altomare C, Liso G, Sanna E, Biggio G, Cuomo V, et al. Propofol in anesthesia: mechanism of action, structure-activity relationships, and drug delivery. Curr Med Chem. 2000;7(2):249-71.
6. Reves JG, Glass PSA, Lubarsky DA, McEvoy MD, Martinez-Ruiz R, Struys MMRF, et al. Intravenous anesthetics. In: Miller RD, Eriksson LI, Fleisher LA, Wiener-Kronish JP, Cohen NH, Young WL, et al., editors. Miller's anesthesia. 8th ed. Philadelphia: Elsevier Saunders; 2015.
7. Ebert TJ, Muzi M, Berens R, Goff D, Kampine JP, Smith JJ, et al. Sympathetic responses to induction of anesthesia with propofol. Anesth Analg. 1994;78(5):1055-60.
8. Brown EN, Pavone KJ, Naranjo M, Goldstein PA, Kopell NJ, Rosen BR, et al. Multimodal general anesthesia: theory and practice. Anesth Analg. 2018;127(5):1246-58.
9. Stoelting RK, Hillier SC, Murphy GS, Brull SJ, Butterworth JF, Mackey DC, et al. Pharmacology and physiology in anesthetic practice. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2006.
10. Stanley TH, Egan TD, Van Aken H, Stanski DR, Shafer SL, Pace NL, et al. Pharmacology of opioid analgesics. J Pain Symptom Manage. 2005;29(5 Suppl):S67-S71.
11. Bailey PL, Stanley TH, Pace NL, Ashburn MA, Moll JW, East KA, et al. Intravenous opioid anesthetics. In: Hemmings HC Jr, Egan TD, editors. Pharmacology and physiology for anesthesia. Philadelphia: Elsevier; 2013.
12. Domino EF, Chodoff P, Corssen G, Luby ED, Macfarlane JW, Warner DS, et al. Pharmacologic effects of ketamine. Anesthesiology. 2010;113(3):678-9.
13. Himmelseher S, Durieux ME, Niesters M, Martini C, Dahan A, Aarts LP, et al. Ketamine for perioperative pain management. Anesthesiology. 2005;102(1):211-20.
14. Willman EV, Andolfatto G, Joo D, Miller P, Wong WB, Kohn MA, et al. Ketamine-propofol (ketofol) for procedural sedation and analgesia in the emergency department. Ann Emerg Med. 2007;49(1):23-30.
15. Goh PK, Chiu CL, Wang CY, Chan YK, Loo PL, Yap KH, et al. Randomized double-blind comparison of ketamine-propofol, fentanyl-propofol and propofol-saline on haemodynamics and laryngeal mask airway insertion conditions. Anaesth Intensive Care. 2005;33(2):223-8.