

Role of opioids as coinduction agent with propofol and their effect on apnea time, recovery time, and sedation score

Manisha Bhatt Dwivedi, Anisha Puri, Sankalp Dwivedi¹, Harinder Deol

ABSTRACT

Background: Laryngeal mask airway (LMA) is a supraglottic device which requires lesser depth of anaesthesia, evokes lesser hemodynamic response and causes lesser stimulation of airway as compared to traditional definitive airway device endotracheal tube. Its placement is possible without muscle relaxants thereby allowing maintenance of anaesthesia on spontaneous respiration thus preventing apnoea or minimizing apnoea time. Propofol, the commonly used induction agent, causes cardiorespiratory depression at higher induction doses. To attenuate this, co-induction agents combined with propofol has been a regular I/V anaesthetic technique these days.

Aim: Comparing apnoea time, recovery time and sedation scores using propofol-fentanyl and propofol-butorphanol combination.

Methodology: Hundred patients scheduled for various elective surgical procedures were randomly selected and divided into two groups of 50 each. As coinduction drug Group F received fentanyl and Group B received butorphanol. In both the groups induction was achieved with I/V propofol and LMA was placed. Apnoea time was noted after induction. Recovery time and sedation scores were recorded after anaesthetic agents were turned off.

Results: As compared to group F apnoea time was significantly less and recovery time was significantly more in group B ($P < 0.05$). Statistically postoperative sedation was significantly higher in group B than in group F at 1/2 hr but clinically, majority were responding to verbal commands. At 1 hour no significant difference in sedation was noted between the groups.

Conclusion: Considering respiratory and recovery profile propofol -butorphanol combination is a safer alternative to propofol-fentanyl combination for LMA insertion.

Key Words: Apnea time, butorphanol, fentanyl, laryngeal mask airway, propofol, recovery

INTRODUCTION

Airway management is an indispensable and integral element of general anesthesia. Any ineptitude in establishing airway can cause catastrophic results.^[1] Conventionally, face mask and endotracheal tube (ETT) are the two methods for securing airway. Apart from these two traditional concepts, another invention called laryngeal mask airway (LMA) which is a supraglottic device has led to drastic reforms in the fundamental aspects of general anesthesia. Although not a definitive airway device, LMA has established its role in routine anesthesia care and management of difficult airway^[2] as it does not

demand jaw thrust for airway patency and maintains hemodynamic stability.^[3] Of the various induction agents that have been used to achieve optimization prior to LMA insertion, propofol provides rapid induction of anesthesia

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

Cite this article as: Dwivedi MB, Puri A, Dwivedi S, Deol H. Role of opioids as coinduction agent with propofol and their effect on apnea time, recovery time, and sedation score. *Int J Crit Illn Inj Sci* 2018;8:4-8.

Access this article online

Website: www.ijciis.org

DOI: 10.4103/IJCIIS.IJCIIS_4_17

Quick Response Code:



Department of Anaesthesiology and
¹General Surgery, MMIMSR, Ambala,
Haryana, India

Address for correspondence:

Dr. Manisha Bhatt Dwivedi,
Department of Anaesthesiology, dmims
MMIMSR, Mullana, Ambala, Haryana,
India.
E-mail: manishabhattedwivedi@gmail.
com

and easy insertion of LMA by depressing airway reflexes.^[4] When used alone, Propofol dosing often exceeds 2.5 mg/kg which can lead to cardiorespiratory depression, prolonged apnea, longer duration of sedation, and hypotension.^[5] Other problems associated with propofol are excessive patient movement, pain at injection site, no analgesic properties,^[6] and laryngospasm.

Hence, propofol as a sole anesthetic agent is unsatisfactory, and therefore, drugs such as opioids,^[7] midazolam, ketamine, inhalational anesthetics, or muscle relaxants are used with propofol to decrease its dose and minimize undesirable effects. In addition, the use of muscle relaxants mandates that the patient be placed on mechanical ventilatory support, creating further stress on the pulmonary system.

In a spontaneously breathing patient respiratory muscle activity is preserved, diaphragm is being stimulated continuously, and tidal volume and duration of the breaths are continuously changed. All these factors considered together reduce the degree of atelectasis during spontaneous breathing as compared to positive pressure ventilation. Spontaneous ventilation also prevents the development of distention. Light anesthesia and titration of analgesia according to the respiratory rate of the patients are possible with spontaneous breathing. This reduces overall drug dosage and decreases the pulmonary and cardiovascular side effects.

In this study, we compared the combination of propofol and butorphanol with propofol and fentanyl during LMA insertion without using muscle relaxant and allowing the patient to resume spontaneous ventilation. Apnea time, recovery time, and sedation scores were noted and analyzed statistically.

MATERIALS AND METHODS

The present study was conducted after the approval from our local Ethics Committee. One hundred patients classified as American Society of Anesthesiologists (ASA) I and ASA II, ages 18-60 years, Mallampati-I and II who were scheduled for various elective surgical procedures were randomly selected and divided into two groups of fifty each, i.e., Group F (propofol and fentanyl) and Group B (propofol and butorphanol). Written informed consent for the present study, surgery, and anesthesia procedure was obtained from all the patients.

The detailed clinical examination was performed, and vital parameters were recorded for all patients included in the present study. All patients were kept nil by mouth (NPO) overnight before surgery. Detailed education and instructions were provided to each patient regarding the surgery, anesthesia procedure, and the present study.

After the establishment of the standard monitoring, the patients were preoxygenated with 100% O₂ for 3 min and 18G or 20G intravenous (IV) cannula was secured. The baseline measurements were recorded on arrival for all study patients. In Group B, patients were given IV butorphanol (30 µg/kg), and in Group F, patients were given IV fentanyl (1.5 µg/kg) as coinduction agents.

One minute after coinduction, induction was achieved with IV propofol 2.5 mg/kg over 60 s, the depth of anesthesia was assessed using the loss of eyelash reflex and jaw relaxation, and LMA was inserted.

Classic LMA no. 3 or 4 was inserted with standard technique according to the weight of the patients (30–50 kg or 50–70 kg, respectively). After LMA placement, the cuff was inflated with 20 ml of air in case of LMA no. 3 and 30 ml of air in LMA no. 4 over 3–5 s. The LMA was then connected to Bains circuit.

Anesthesia was maintained with oxygen and nitrous oxide (50:50) and isoflurane 0.5%–1%. Apnea time was noted, and gentle intermittent positive pressure ventilation (IPPV) was given until patients regained spontaneous ventilation. Monitoring of pulse rate, systolic and diastolic blood pressure, oxygen saturation (SPO₂), and end-tidal CO₂ was performed. Any incidence of hypotension, hypertension, dysrhythmia, coughing/gagging, head and limb movements, and laryngospasm were noted and treated accordingly.

Toward the end of the surgical procedure, isoflurane and N₂O were turned off, and LMA was removed. After the surgery was concluded, the recovery time was noted, defined as time from discontinuation of nitrous oxide and isoflurane to spontaneous eye opening in all patients.

All results were compared and compiled, and statistical analysis was carried out to reach the conclusion. Student's *t*-test for age, weight, apnea time, and recovery time and Mann-Whitney U-test for ordinal data for postoperative sedation score were applied. *P* < 0.05 was considered statistically significant. Observation tables were made, and conclusions were drawn.

RESULTS

Demographic characteristics of study patients, including age, weight, and sex were comparable between the two groups [Table 1].

Apnea time (57.74 ± 13.08 s) was significantly less (*Z* = 8.78; *P* = 0.000) in Group B. Recovery time (6.52 ± 0.90 min) was significantly more (*Z* = 14.97; *P* = 0.000) in Group B as compared to Group F [Table 2].

Table 1: Distribution of patients according to demographic characteristics

Variables	Group (n = 50)	Group B (n = 50)	Z	P
Age (years)	33.48 ± 11.15	31.84 ± 11.49	0.72	0.42 (NS), >0.05
Weight (kg)	47.66 ± 7.51	50.42 ± 7.65	1.81	0.07 (NS), >0.05
Gender (male/female)	6/44	12/38	$\chi^2 = 2.43$	0.11 (NS), >0.05

NS: Not significant

Table 2: Comparative evaluation of apnea time and recovery

Variables	Time taken in both the groups		Z	P
	Group F	Group B		
Apnea time (sec)	78.12 ± 9.91	57.74 ± 13.08	8.78	0.000 (S), <0.05
Recovery time (min)	3.74 ± 0.95	6.52 ± 0.90	14.97	0.000 (S), <0.05

S: Significant

Table 3: Postoperative sedation score data

Time (h)	Grade	Group F	Group B	χ^2	P
½	1	1	0	88.73	<0.0001 (S)
	2	46	0		
	3	3	46		
	4	0	4		
	5	0	0		
1	1	1	0	5.09	0.16 (NS), >0.05
	2	49	46		
	3	0	3		
	4	0	1		
	5	0	0		
2	1	0	0	1.01	0.31 (NS), >0.05
	2	50	49		
	3	0	1		
	4	0	0		
	5	0	0		

NS: Not significant, S: Significant

Table 4: Changes in SPO₂ during procedure

Variables	Group F	Group B	Z	P
Before premedication	99.06 ± 0.89	98.76 ± 0.71	1.85	0.066 (NS), >0.05
After premedication	99.04 ± 1.00	98.94 ± 0.71	0.57	0.56 (NS), >0.05
1 min after insertion	99.26 ± 0.87	98.98 ± 0.68	1.78	0.07 (NS), >0.05
After 3 min of insertion	99.40 ± 0.69	99.14 ± 0.78	1.75	0.080 (NS), >0.05
After 5 min of insertion	99.46 ± 0.57	97.54 ± 12.64	1.07	0.286 (NS), >0.05
After extubation	99.46 ± 0.50	99.26 ± 0.82	1.45	0.148 (NS), >0.05

The SPO₂ was maintained >97 in all the patients throughout the procedure and both groups were comparable. NS: Not significant

In our study, postoperative sedation as measured by Ramsay Sedation Score was significantly higher in Group B than in Group F at ½ h ($\chi^2 = 88.73$; $P = 0.0001$). At ½ h, in Group F, majority (46) of patients had a sedation score of Grade 2 implying tranquil and oriented patient whereas in Group B, majority (46) had Grade 3 sedation which implies that patient is responding to verbal commands.

At 1 h, in Group B, some cases showed persistent level of sedation, but no significant difference was noted ($\chi^2 = 5.09$; $P = 0.16$) between the groups. None of the patients were deeply sedated (score 5) at 2 h in either group [Table 3]. Furthermore, no statistically significant difference was observed between the groups when comparing SPO₂ measurements [Table 4].

DISCUSSION

Securing definitive airway by laryngoscopy and ETT placement requires clinical expertise^[8] and can elicit undesirable sympathoadrenal stress responses^[9] such as hypertension and tachycardia which are of a great concern if patients have coexisting cardiovascular or neurological disease.^[10] To alleviate this stress response, various supraglottic airways are gaining popularity. LMA is a supraglottic device which does not require muscle relaxants, requires lesser depth of anesthesia, evokes less hemodynamic response, and causes less stimulation of airway. All these factors when considered together affect apnea time, recovery time, and sedation score.

In our study, apnea time (57.74 ± 13.08 s) was significantly less in Group B; recovery time (6.52 ± 0.90 min) was significantly more in Group B as compared to Group F [Table 2]. Postoperative sedation was significantly higher in Group B than in Group F at ½ h, and at 1 h, in Group B, no significant difference was noted ($\chi^2 = 5.09$; $P = 0.16$) between the groups.

The LMA allows both spontaneous as well as positive pressure ventilation with an airway pressure <15 cm H₂O. One of the advantages of spontaneous ventilation is that it obviates the need of muscle relaxants. The cases we chose for our study does not mandate absolute indication for muscle relaxant on either anesthetic grounds or considering the nature of surgical procedure. Hence, we opted not to use muscle relaxant and maintain patient on spontaneous ventilation. Spontaneous ventilation improves dead space and shunts, thus improving gas exchange, preserving natural link between heart rate and respiration, preserving ventilation and blood flow distribution, reducing IPPV-induced lung damage, achieving better lung function test postoperatively, and avoiding any chances of inadequate reversal. All these factors collectively pave the way to good recovery.

Another advantage of maintaining spontaneous ventilation is minimizing apnea time. Apnea time, if extends for >1 min, can precipitate critical hypoxia^[11] in an adult breathing air with normal functional residual capacity and normal oxygen consumption. Critical hypoxia and ventilatory failure can lead to death^[12] or neurological insufficiency if airway is not secured timely.

During apnea, 250 ml/min of O₂ is transferred from alveolar space to capillaries, but CO₂ moved to alveolar space is just 20 ml. This reduces the lung volume, decreases the intrathoracic pressure if airway is obstructed, decreases partial pressure of oxygen in the lungs, and precipitates critical hypoxia if apnea time is prolonged.^[13]

The apnea time in our study was (57.74 ± 13.08 s) in Group B and (78.12 ± 9.91 s) in Group F. This was significantly less with butorphanol as $Z = 8.78$ and $P = 0.000$. In both the groups, in our study, at no point in time, patients encountered hypoxia; SpO₂ was never <97% [Table 4]. This was because we opted a two-way approach to increase FAO₂, i.e., preoxygenated the patient with 100% oxygen and tried to minimize apnea time with a reasonable dose of opioids in combination with propofol without muscle relaxant.

Results of the present study correlate with the study conducted by Chari and Ghai. As in our study, they found significantly less apnea time with butorphanol-thiopentone combination as compared to fentanyl-thiopentone combination ($P = 0.002$).^[4]

Gupta *et al.*^[14] compared ketamine-propofol, fentanyl-propofol, and butorphanol-propofol for LMA insertion. They found that the mean duration of apnea was 61.67 ± 13.28 s in Group PF, was 33.75 ± 1.58 s in Group PK, and was 41.22 ± 3.99 s in Group PB. Apnea time was prolonged with fentanyl as in our study.

The prolonged apnea time with fentanyl as observed in Group F of the present study was also found by Goh *et al.*^[15] They found that the incidence of prolonged apnea (>120 s) was higher in the fentanyl group (23.1%) than in either the ketofol group (6.3%) or the normal saline group (3.3%).

Dryden *et al.* on the basis of a double-blind study concluded that butorphanol is safer in terms of respiratory profile and adverse effects as compared to fentanyl.^[16]

Tanaka and Nishikawa^[17] found higher degree of respiratory depression reflected as prolonged apnea time of 179 (74) s when propofol was used alone as compared to apnea time of 152 (45) s when fentanyl pretreatment was given. Pretreatment with fentanyl 1 mcg/kg significantly reduced the propofol requirement from >3 mg/kg to 1.42 mg/kg.

It is evident from the above explanation that escalated dose of propofol prolongs the apnea time whereas pretreatment decreases apnea time. This formed the basis for our selection of opioid pretreatment. Dose selection for butorphanol 30 mcg/kg and fentanyl 1.5 mcg/kg were chosen because butorphanol 20–40 mcg/kg IV is comparable to fentanyl 1–2 mcg/kg IV.^[18,19]

In the present study, recovery time (6.52 ± 0.9 min) was significantly more ($Z = 14.97$; $P = 0.000$) in Group B as compared to Group F (3.74 ± 0.9 min), but all patients were awake and following commands at ½ h postoperatively. This correlates with the study conducted by Harish and Gautam. Subrahmanyam, who found that the recovery time in Group B was 5.86 ± 1.3 min and in Group F was 3.33 ± 0.8 min, which was statistically highly significant ($P < 0.0001$).^[20]

In our study, although sedation scores were higher in butorphanol group as compared to fentanyl group, the majority of the patients of butorphanol group were responding to verbal commands at ½ h postoperatively. Rao *et al.* also found prolonged sedation with butorphanol, but as evident from the graphical representation, 15 out of 25 patients (60%) of butorphanol group had a Michigan sedation score of 2 at the end of 30 min. This implies that even with butorphanol, 60% patients were awake and responding to verbal commands at 30 min postoperatively which is clinically acceptable.^[21]

CONCLUSION

Butorphanol, when used as a coinduction agent with propofol, causes less apnea time, prolonged recovery time, and prolonged sedation as compared to fentanyl-propofol combination. Prolonged recovery time and higher sedation scores as seen with butorphanol clinically fall within the acceptable limit.

Butorphanol is a preferred coinduction agent due to its safer respiratory profile as evident from less apnea time and easy availability as compared to fentanyl.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Sood J. Laryngeal mask airway and its variants. *Indian J Anaesth* 2005;49:275-80.
2. Doshi C, Phadtare S, Ahluwalia G, Swami S, Vyas V, Patil S, *et al.* Fentanyl and butorphanol as co-induction agents for LMA insertion: A comparative study. *J Evid Based Med Healthc* 2015;2:5640-53.
3. Parasa M. Ideal induction agent for LMA insertion: A comparative study between thiopental sodium and propofol. *Int J Sci Res* 2014;3:7-8.
4. Chari P, Ghai B. Comparison of butorphanol and thiopentone vs. fentanyl and thiopentone for laryngeal mask airway insertion. *J Clin Anesth* 2006;18:8-11.
5. Ghafoor H, Afshan G, Kamal R. General anesthesia with Laryngeal Mask Airway: Etomidate vs. propofol for hemodynamic stability. *Open J Anesthesiol* 2012;2:161-5.
6. Yousef GT, Elsayed KM. A clinical comparison of ketofol (ketamine and

- propofol admixture) versus propofol as an induction agent on quality of laryngeal mask airway insertion and hemodynamic stability in children. *Anesth Essays Res* 2013;7:194-9.
7. Ramaswamy AH, Shaikh SI. Comparison of dexmedetomidine-propofol versus fentanyl-propofol for insertion of laryngeal mask airway. *J Anaesthesiol Clin Pharmacol* 2015;31:217-20.
 8. Pournajafian A, Alimian M, Rokhtabnak F, Ghodraty M, Mojri M. Success rate of airway devices insertion: Laryngeal mask airway versus supraglottic gel device. *Anesth Pain Med* 2015;5:e22068.
 9. Henderson J. Airway management in adult. In: Miller RD, editor. *Miller Textbook of Anesthesia*. 6th ed. Philadelphia: Elsevier; 2009. p. 1573-603.
 10. Khan FA, Ullah H. Pharmacological agents for preventing morbidity associated with the haemodynamic response to tracheal intubation. *Cochrane Database of Systematic Reviews* 2013:CD004087. Doi: 10.1002/14651858.CD004087.pub2.
 11. Sirian R, Wills J. Physiology of apnea and the benefits of preoxygenation. *Contin Educ Anaesth Crit Care Pain* 2009;9:105-8.
 12. Ziyaeifard M, Azarfarin R, Ferasatkish R, Dashti M. Management of difficult airway with laryngeal mask in a child with mucopolysaccharidosis and mitral regurgitation: A case report. *Res Cardiovasc Med* 2014;3:e17456.
 13. Whitten C. Preoxygenation can more than double the time to hypoxia during apnea. *Anyone Can Intubate*. 5th ed. Mooncat Publications: 2013.
 14. Gupta A, Kaur S, Attri JP, Saini N. Comparative evaluation of ketamine – Propofol, fentanyl – Propofol and butorphanol-propofol on haemodynamics and laryngeal mask airway insertion conditions. *J Anaesthesiol Clin Pharmacol* 2011;27:74-8.
 15. Goh PK, Chiu CL, Wang CY, Chan YK, Loo PL. Randomized double-blind comparison of ketamine-propofol, fentanyl-propofol and propofol-saline on haemodynamics and laryngeal mask airway insertion conditions. *Anaesth Intensive Care* 2005;33:223-8.
 16. Dryden GE. Voluntary respiratory effects of butorphanol and fentanyl following barbiturate induction: A double-blind study. *J Clin Pharmacol* 1986;26:203-7.
 17. Tanaka M, Nishikawa T. Propofol requirement for insertion of cuffed oropharyngeal airway versus laryngeal mask airway with and without fentanyl: A dose-finding study. *Br J Anaesth* 2003;90:14-20.
 18. Day OL 2nd, Nespeca JA, Ringgold C, Behr DA, Evens RP. Outpatient sedation for oral surgery: A comparison of butorphanol and fentanyl. *Acute Care* 1988;12 Suppl 1:63-9.
 19. Philip BK, Scott DA, Freiburger D, Gibbs RR, Hunt C, Murray E, *et al.* Butorphanol compared with fentanyl in general anesthesia for ambulatory laparoscopy. *Can J Anaesth* 1991;38:183-6.
 20. Gautam PH, Subrahmanyam BS. Randomised comparative study of fentanyl versus butorphanol on recovery characteristics and analgesic efficacy under total intravenous anesthesia for laparoscopic cholecystectomy. *Indian J Appl Res* 2015;5:542-4.
 21. Rao MH, Satyanarayana V, Srinivas B, Muralidhar A, Samantaray A, Reddy AS, *et al.* Comparison of butorphanol and fentanyl for balanced anesthesia in patients undergoing laparoscopic surgeries under general anesthesia: A prospective, randomized, double-blind study. *J Clin Sci Res* 2013;2:8-15.