e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2025; 17(9); 442-447

Original Research Article

A Clinical Comparative Study of Etomidate Versus Propofol Plus Ketamine as an Induction Agent on Quality of Proseal-Laryngeal Mask Airway Insertion and Hemodynamic Stability in Patients Undergoing Laparoscopic Cholecystectomy

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Received: 07-07-2025 / Revised: 06-08-2025 / Accepted: 07-09-2025

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Conflict of interest: Nil

Abstract:

Background: Securing the airway with minimal complications is a primary responsibility of the anesthesiologist. The ProSeal laryngeal mask airway (PLMA), a second-generation supraglottic device, provides effective airway management in elective surgeries. The choice of induction agent influences insertion conditions and haemodynamic responses. Etomidate offers cardiovascular stability but limited muscle relaxation, whereas a propofol–ketamine combination may balance the haemodynamic effects of both drugs while enhancing insertion conditions.

Aim and Objectives: To compare the effectiveness of etomidate and a propofol–ketamine combination as induction agents for PLMA insertion in elective laparoscopic cholecystectomy. The primary objectives were to assess ease and time of insertion, adequacy of relaxation, and the number of attempts. Secondary objectives included evaluation of oropharyngeal leak pressure, haemodynamic stability, and perioperative complications.

Methods: This prospective, randomized, double-blind study enrolled 92 ASA I–II patients aged 18–65 years undergoing elective laparoscopic cholecystectomy. Patients were randomized into two groups: Group A received etomidate (0.3 mg/kg), and Group B received a combination of propofol (1.5 mg/kg) with ketamine (0.5 mg/kg). PLMA insertion time, attempts, ease of insertion, oropharyngeal leak pressure, haemodynamic parameters, and perioperative complications were recorded and analyzed using SPSS version 20.0. A p-value <0.05 was considered statistically significant.

Results: Both groups were comparable in demographic characteristics and baseline vitals (p>0.05). PLMA insertion was significantly faster in Group B (9.15±1.53 sec) compared to Group A (14.09±2.55 sec, p=0.003), and fewer attempts were required (1.11±0.31 vs. 1.33±0.47, p=0.011). Ease of insertion was higher in Group B (80.4% vs. 65.2%), though not statistically significant. Oropharyngeal leak pressures were comparable (p>0.05). Haemodynamic parameters (HR, SBP, DBP, MAP, SpO_2) remained stable in both groups without significant differences. Complications such as sore throat, PONV, and myoclonus were infrequent and not statistically significant.

Conclusion: The combination of propofol and ketamine provided superior conditions for PLMA insertion, with faster placement, fewer attempts, and comparable haemodynamic stability compared to etomidate. It can be considered a more effective induction strategy for airway management in ASA I–II patients undergoing laparoscopic cholecystectomy.

Keywords: ProSeal Laryngeal Mask Airway, Etomidate, Propofol, Ketamine, Induction Agents, Haemodynamic Stability.

Introduction

Airway management is one of the most crucial skills for an anaesthesiologist, as it ensures adequate ventilation, oxygenation, and delivery of anaesthetic gases during general anaesthesia [1]. Securing and

maintaining airway patency with minimal complications is of utmost importance. Although endotracheal intubation is considered the gold standard, it is often associated with undesirable complications such as trauma to the lips, teeth, tongue, epiglottis, larynx, and trachea, haemodynamic instability, and postoperative sore throat, which result from laryngoscopy and manipulation of the vocal cords [2].

To overcome these limitations, supraglottic airway devices (SADs) were introduced in 1983. These devices have been successfully used for resuscitation and in complex airway management as relatively easy tools, and they are increasingly applied in elective general anaesthesia due to their reduced airway complications [3]. Second-generation SADs provide higher oropharyngeal leak pressures, thereby improving airway sealing and offering better separation of respiratory and gastric systems. A higher seal pressure enhances airway protection against contamination or aspiration from the gastric system [4].

The ProSeal laryngeal mask airway (PLMA) is a second-generation SAD featuring a double-lumen, double-cuff design. This structure separates the respiratory and alimentary tracts, providing a dedicated passage for regurgitated fluids [5,6]. The double cuff enhances the seal around the glottis, allowing the administration of intermittent positive pressure ventilation [6]. These features make PLMA especially suitable for patients at risk of aspiration [8,9]. Furthermore, PLMA provides a better seal compared to the classical LMA, increasing its suitability for positive pressure ventilation [5–7].

Choice of induction agent influences both the ease of PLMA insertion and haemodynamic stability. Etomidate, an imidazole derivative, is a commonly used intravenous induction agent. It is valued for its rapid onset, short duration of action, cardiovascular and respiratory stability, and neuroprotective properties [10]. However, etomidate has been shown to cause adrenocortical suppression by inhibiting mitochondrial 11-β hydroxylase, an essential enzyme in adrenal steroid synthesis. This effect may persist for up to 48 hours after a single bolus, with an absent cortisol response to surgical stress during this period [11].

Ketamine, a phencyclidine derivative, is an N-methyl-D-aspartate (NMDA) receptor antagonist that provides reliable anaesthesia, analgesia, and amnesia while maintaining airway reflexes, spontaneous respiration, and muscle tone [12]. Unlike most induction agents, ketamine stimulates the cardiovascular system by releasing catecholamines, leading to increases in heart rate, blood pressure, and cardiac output. Adverse effects include nausea, vomiting, excessive secretions, and emergence phenomena [13].

Propofol is another widely used intravenous anaesthetic that enhances gamma-aminobutyric acid (GABA)-mediated inhibition in the central nervous system [14]. It is characterized by rapid onset and recovery due to its lipophilic nature. Propofol also possesses antiemetic, anticonvulsant, antipruritic, and amnesic properties [14]. However, it can cause dose-dependent hypotension and respiratory depression [15], and challenges remain in achieving optimal dosing for induction [16].

Theoretically, combining drugs with opposing haemodynamic effects can optimize anaesthetic induction by balancing their advantages while minimizing adverse effects. Recent studies have highlighted the benefits of using multiple agents simultaneously for induction rather than monotherapy, demonstrating improved clinical outcomes with fewer side effects [17,18].

With this background, the present study was conducted to compare insertion conditions of PLMA and haemodynamic responses during induction with etomidate versus a propofol–ketamine combination in patients undergoing elective laparoscopic cholecystectomy [8]. The study also aimed to evaluate the adequacy of relaxation, the number of attempts, and the complications associated with both agents.

Materials and Methods

This prospective, randomized, double-blind study was conducted at SVBP Hospital, associated with LLRM Medical College, Meerut, after obtaining approval from the Institutional Ethics Committee (Ref. No. SC1/2024/4482) and registration with the Clinical Trials Registry of India (CTRI/2025/04/084977). Written informed consent was obtained from all participants before enrollment.

A total of 100 patients scheduled for elective laparoscopic cholecystectomy were screened, of which 92 met the eligibility criteria and were randomized for analysis.

Inclusion Criteria: Patients eligible for the study included adults of either sex, aged between 18 and 65 years, belonging to the American Society of Anesthesiologists (ASA) physical status I or II. Only those scheduled to undergo elective laparoscopic cholecystectomy and assessed as Mallampati Grade I or II were considered for inclusion. Additionally, written informed consent was obtained from all participants before enrolment.

Exclusion Criteria: Patients were excluded if they refused to participate or had a history of gastroesophageal reflux disease, significant cardiac illness, pulmonary disorders such as COPD or pneumonia, alcoholism, morbid obesity, or pregnancy. Individuals with abnormalities of the

oral cavity or pharynx, ASA physical status III–V, or those undergoing emergency surgery were also excluded. Additional exclusion factors included uncontrolled hypertension or diabetes, previous stroke, neuropsychiatric disorders requiring medication, cervical spine fracture or instability, obstructive sleep apnea, recent upper respiratory tract infection, and patients assessed as Mallampati Grade III or IV.

Sample Size Estimation: Sample size was calculated using PASS version 23 software. Based on prior studies, a minimum of 92 patients was determined to provide adequate statistical power. The formula considered Zα/2 (1.96 for a 95% confidence interval), Zβ (0.84 for an 80% power), the expected standard deviation, and the minimum clinically significant difference (δ) between groups.

Study Design and Randomization: This was a prospective, randomized, double-blind study. Patients were allocated into two groups using the sealed-envelope technique:

- Group A (Etomidate group): received intravenous etomidate 0.3 mg/kg in slow incremental doses
- Group B (Propofol–Ketamine group): received intravenous propofol 1.5 mg/kg combined with ketamine 0.5 mg/kg

Blinding was ensured as drug syringes were prepared by an independent anaesthesiologist not involved in the study. The investigator performing PLMA insertion was unaware of group allocation. Another independent observer, blinded to group assignment, recorded insertion time, haemodynamic parameters, and complications.

Preoperative Preparation: All patients underwent a detailed pre-anaesthetic check-up (PAC), including systemic evaluation and airway assessment. Routine investigations included complete blood count, coagulation profile, liver and renal function tests, and serum electrolytes. Patients received oral alprazolam 0.25 mg the night before surgery.

Anaesthesia Technique: On arrival in the operating room, standard ASA monitoring (ECG, non-invasive blood pressure, and pulse oximetry) was initiated. Intravenous access (18G/20G) was secured. Premedication included intravenous ondansetron (0.1 mg/kg) and glycopyrrolate (5 µg/kg). All patients were preoxygenated with 100% oxygen for 3 minutes.

Induction was carried out with intravenous fentanyl (2 µg/kg), followed by administration of the allocated study drug as per group. Adequacy of mask ventilation was confirmed by equal bilateral chest rise and air entry.

Once adequate anaesthetic depth was achieved, a ProSeal LMA (PLMA) of appropriate size (based on patient weight) was inserted using a metal introducer in the sniffing position. The device was lubricated with water-based gel and advanced until resistance was felt. The cuff was inflated to 60 cm H_2O, and a Ryle's tube was inserted through the gastric channel. Bilateral chest expansion, equal breath sounds, and square-wave capnography confirmed proper placement.

An attempt was considered successful if PLMA was placed within two attempts with minor maneuvers. More than three unsuccessful attempts were considered failures.

Mechanical ventilation was initiated in volume-controlled mode (6–8 mL/kg tidal volume, 14 breaths/min). Anaesthesia was maintained with isoflurane (0.6–0.8%) in 50% oxygen and 50% nitrous oxide, supplemented with intermittent intravenous vecuronium.

At the end of surgery, isoflurane and nitrous oxide were discontinued. Patients were reversed with neostigmine (50 µg/kg) and glycopyrrolate (10 µg/kg), and the PLMA was removed once patients met standard extubation criteria. Postoperative complications, including sore throat, nausea, vomiting, dysphagia, or mucosal injury, were documented.

Outcome Measures: The primary outcome of the study was the time required for PLMA insertion, measured from the moment the device was picked up until the appearance of a square-wave capnography trace confirmed adequate ventilation. Secondary outcomes included the ease of insertion, assessed on a four-point scale (1 = no resistance, 2 = mild resistance, 3 = moderate resistance, 4 = unable to insert), and the oropharyngeal leak pressure, determined by closing the expiratory valve to 30 cm H_2O at a flow of 4 L/min until an audible or stethoscope-detected leak occurred. Additional secondary parameters were the first-attempt and overall success rate, haemodynamic variables such as systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and heart rate (HR) recorded at baseline, post-induction, and at 1, 5, 10, 15, 20, 25, and 30 minutes following PLMA insertion. Perioperative complications, including sore throat, nausea, vomiting, dysphagia, dysphonia, and myoclonus, were also documented.

Statistical Analysis: Data were analyzed using SPSS version 20.0. Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were presented as numbers and percentages. Comparisons of means between groups were performed using the Student's t-test, and categorical variables were analyzed with the Chi-

square test. A p-value of less than 0.05 was considered statistically significant.

Results

A total of 92 patients were randomized equally into two groups (n=46 each). Both groups were comparable in demographic and baseline clinical characteristics.

Baseline Characteristics: Table 1 summarizes the baseline demographic data. Age, gender distribution, and BMI were similar between groups, with no statistically significant differences (p>0.05).

Table 1: Baseline Characteristics of Study Participants

Variable	Group A (Etomidate) (n=46)	Group B (Propofol+Ketamine) (n=46)	p value
Age (years), mean ± SD	36.4 ± 10.2	34.9 ± 9.6	0.412
Gender (M/F)	10 / 36	11 / 35	0.812
BMI (kg/m²), mean ± SD	21.94 ± 1.39	22.43 ± 1.25	0.078

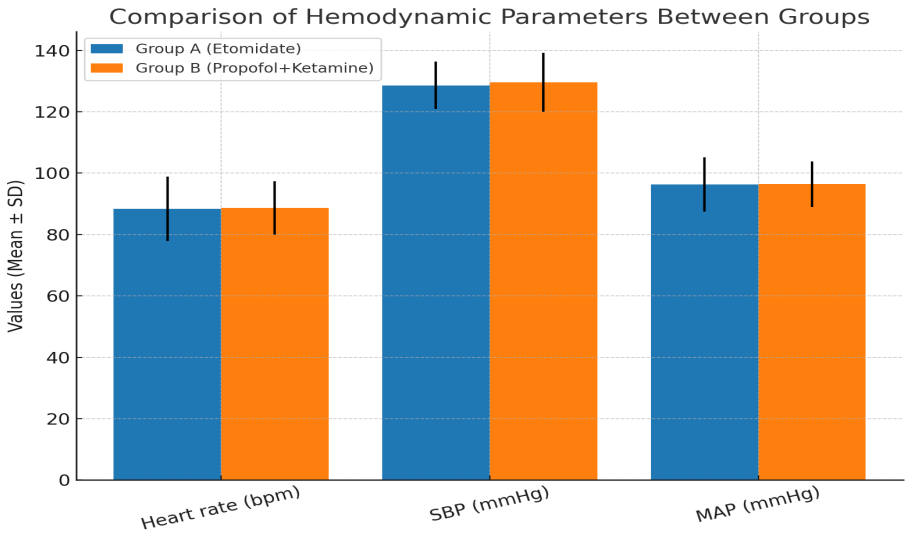
Airway Insertion Outcomes: Group B demonstrated superior performance in airway insertion parameters compared with Group A. Insertion was easier, required fewer attempts, and was significantly faster in the propofol–ketamine group. Airway sealing pressure was higher in Group B, though the difference was not statistically significant (Table 2).

Table 2: Airway Insertion Characteristics

Parameter	Group A (Etomidate)	Group B (Propofol+Ketamine)	p value
Ease of insertion (easy, %)	65.2%	80.4%	0.160
Insertion attempts, mean ± SD	1.33 ± 0.47	1.11 ± 0.31	0.011*
Time of insertion (sec), mean ± SD	14.09 ± 2.55	9.15 ± 1.53	0.003*
Airway sealing pressure (cm H_2O)	22.3 ± 1.98	27.9 ± 1.95	0.056

*Significant at p<0.05

Hemodynamic Parameters: Both groups maintained stable haemodynamics throughout the perioperative period. No significant differences were observed in pulse rate, systolic blood pressure (SBP), or mean arterial pressure (MAP) between groups at any time point (Graph 1).



Graph 1: Comparison of Hemodynamic Parameters Between Groups

Adverse Events: Complications such as myoclonus, postoperative nausea and vomiting (PONV), sore throat, and dysphagia/dysphonia were rare and comparable between groups (p>0.05).

Discussion

This randomized study was conducted to compare the ease and effectiveness of ProSeal laryngeal mask airway (PLMA) insertion under induction with etomidate versus a propofol–ketamine combination. A total of 92 ASA I and II patients aged 18–65 years, scheduled for elective laparoscopic cholecystectomy, were randomized into two groups: Group A (etomidate) and Group B (propofol plus ketamine). After obtaining ethical clearance and informed consent, general anaesthesia was induced,

and insertion time, ease, attempts, haemodynamic stability, and complications were assessed. Statistical analysis was performed using SPSS version 20.0 (IBM, Chicago).

In our study, baseline demographic characteristics such as age, gender distribution, and body mass index were comparable between the two groups ($p>0.05$), ensuring homogeneity. The ease of insertion was higher in Group B, with fewer cases of difficult placement compared to Group A. These findings are consistent with those of Yousef and Elsayed, and Rajmohan and Tumulu Rao, who reported excellent conditions for LMA insertion in the Ketofol group compared with propofol alone, along with faster induction and fewer adverse effects [19,20].

The time of insertion was significantly shorter in Group B than in Group A. Although the number of insertion attempts was higher in Group A, the difference was not statistically significant. This likely reflects better muscle relaxation achieved with propofol compared to etomidate, a finding supported by Yousef and Elsayed, who demonstrated superior jaw relaxation with propofol [19]. Harald et al. also concluded that propofol provided adequate muscle relaxation to allow tracheal intubation without the need for neuromuscular blockers [21].

Regarding haemodynamics, both groups showed reductions in HR, SBP, DBP, MAP, and SpO_2 from baseline to extubation, but no statistically significant intergroup differences were observed. This aligns with the observations of Afsin Gholipour Baradari et al., who noted greater decreases in haemodynamic parameters in the Ketofol group compared with etomidate, though without statistical significance [22]. Similarly, Aggarwal et al. and Baradari et al. reported comparable heart rate and blood pressure values between groups, with non-significant variations in MAP and HR [22,23]. Previous studies by Shivanna et al., Kaushal et al., Kabir et al., and Singhal and Agarwal et al. also concluded that etomidate offers relatively greater haemodynamic stability than propofol. However, the differences were not statistically significant [24,25].

With respect to complications, a higher incidence of sore throat, dysphagia, myoclonus, and postoperative nausea and vomiting (PONV) was observed in the etomidate group compared with the Ketofol group, though these were not statistically significant. Sumer et al. reported similar findings, noting that etomidate is associated with increased PONV compared to propofol, which may be attributed to propofol's sedative effect, weak serotonin antagonism, or modulation of subcortical pathways [24]. Other studies have also highlighted that etomidate, despite its benefits, can suppress adrenocortical steroid synthesis and contribute to higher PONV rates [24,25]. Moreover, Aggarwal et al. and Baradari et al. observed a higher incidence of myoclonic movements with etomidate compared to ketofol, while the incidence of apnoea was similar between groups [22,23].

Taken together, our findings suggest that the propofol–ketamine combination provides better conditions for PLMA insertion, with shorter insertion times, fewer attempts, and comparable haemodynamic stability, along with a lower trend of adverse events compared to etomidate.

Limitations

This study has certain limitations. First, it was conducted at a single tertiary-care center with a relatively small sample size, which may limit the generalizability of findings. Second, only ASA I–II patients undergoing elective laparoscopic cholecystectomy were included; results may differ in higher-risk populations (ASA III–V) or emergency surgeries. Third, endocrine effects of etomidate, particularly adrenocortical suppression, were not assessed, which could have provided additional safety data. Finally, long-term postoperative outcomes were not evaluated, and a larger multicentric trial would be required to validate these results further.

Conclusion

The propofol–ketamine combination demonstrated superior conditions for ProSeal LMA insertion, allowing faster placement with fewer attempts compared to etomidate, while maintaining comparable haemodynamic stability. Although etomidate provided stable cardiovascular parameters, it was associated with slightly longer insertion times and more difficult placement. Both agents showed a low and similar incidence of perioperative complications. Overall, the propofol–ketamine combination may be considered a more effective and reliable induction strategy in ASA I–II patients undergoing laparoscopic cholecystectomy.

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