Sevoflurane–fentanyl versus propofol–fentanyl for tracheal intubation without neuromuscular blocking agents in elective surgery: A randomized controlled trial.

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Abstract

Background

Objectives: To compare sevoflurane–fentanyl versus propofol–fentanyl for tracheal intubation without a muscle relaxant and to assess intubating conditions, laryngoscopic view, apnea, and hemodynamic responses.

Methods

This prospective comparative observational study enrolled 80 ASA I–II adults over 18 months. After fentanyl 2 ug/kg, Group P received propofol 3 mg/kg IV with intubation at 90 seconds, while Group S underwent incremental sevoflurane induction up to 8% with intubation at 5 minutes. Intubating conditions were graded as optimal/good/poor/inadequate, Cormack–Lehane grade was recorded, and apnea was documented. Heart rate and blood pressure were recorded at baseline, after induction, after intubation, and at 1 and 5 minutes. Group comparisons used the t-test and chi-square.

Results

Results: Baseline characteristics were comparable between the two groups. Optimal intubating conditions were achieved more frequently with sevoflurane (92.5%) than with propofol (52.5%), while acceptable conditions were observed in 100% and 82.5% of patients, respectively. Apnea occurred in 12.5% of patients in the sevoflurane group compared with 100% in the propofol group. Laryngoscopic view was comparable between the groups. Heart rate and systolic blood pressure remained similar throughout the observation period. However, diastolic blood pressure and mean arterial pressure were significantly higher in the sevoflurane group at 1 and 5 minutes after intubation compared with the propofol group (p < 0.05), although the values remained within clinically acceptable limits in both groups.

Conclusion

Sevoflurane–fentanyl provided superior intubating conditions with markedly lower apnea incidence and acceptable hemodynamic stability compared with propofol–fentanyl for tracheal intubation without neuromuscular blockade.

Recommendations

In ASA I–II elective cases where a muscle relaxant-free approach is planned, sevoflurane–fentanyl can be considered to optimize intubating conditions and reduce apnea, with continuous monitoring and readiness for rescue neuromuscular blockade.

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Introduction

Tracheal intubation is conventionally facilitated by neuromuscular blocking agents (NMBAs), which improve laryngoscopic conditions and suppress airway reflexes. Nevertheless, avoidance of NMBAs remains relevant in carefully selected elective patients, including short procedures and situations where clinicians aim to reduce exposure to paralytic drugs or avoid residual neuromuscular blockade [1,2]. When paralysis is not used,

the induction regimen must provide adequate jaw relaxation and suppression of laryngeal reflexes without compromising ventilation and hemodynamic stability.

Muscle relaxant-free intubation can be associated with coughing, movement, or laryngospasm when anesthetic depth is insufficient, and repeated attempts can increase airway trauma. Postoperative upper airway discomfort and laryngeal symptoms have been reported more frequently when intubation conditions are suboptimal, emphasizing the need for consistent and well-defined endpoints when studying NMBA-free techniques [3,4]. Accordingly, comparative studies that quantify intubation conditions and peri-intubation physiology can guide practical protocol selection.

Intravenous induction with propofol combined with opioids is widely practiced because of the rapid onset and ease of use. Propofol depresses airway reflexes and provides favorable jaw relaxation, while opioids attenuate sympathetic responses and suppress cough. However, trials using propofol with fentanyl or alfentanil have shown variable rates of excellent-to-acceptable conditions, influenced by opioid choice, dosing, timing, and adjuncts such as lidocaine or benzodiazepines [5-7]. A key operational concern is respiratory depression, which can present as apnea and necessitate assisted ventilation or rescue neuromuscular blockade.

Fentanyl is a commonly selected opioid for this purpose because it reduces the sympathetic response to laryngoscopy and decreases the dose requirement of hypnotic agents. The balance is narrow: deeper hypnosis and higher opioid effect can improve intubating conditions, but also increase the risk of apnea and the need for assisted ventilation. Therefore, comparing commonly used, clinically feasible regimens helps clinicians select an approach that optimizes airway conditions while maintaining stable physiology.

Sevoflurane inhalational induction provides an alternative strategy. Sevoflurane has low blood–gas solubility, supporting rapid increases in alveolar concentration and smooth induction. Opioids reduce sevoflurane requirements for intubation and improve the probability of acceptable intubating conditions [5]. Clinical trials using sevoflurane-based approaches, including timing guidance, have demonstrated that intubation without NMBAs is feasible with stable hemodynamics and preserved ventilation in many patients [6,7].

Against this background, this study compared propofol–fentanyl with sevoflurane–fentanyl for tracheal intubation without muscle relaxant in elective surgeries. Objectives of the study were (1) to compare intubating conditions, (2) to compare laryngoscopic view using the Cormack–Lehane grading [13], (3) to determine the incidence of apnea after induction, and (4) to evaluate peri-intubation hemodynamic responses.

Methodology

Study design and setting

This study was designed as a prospective, parallel-group, randomized controlled trial with a 1:1 allocation ratio. It was conducted in the Department of Anaesthesiology and Critical Care, Gandhi Medical College, Secunderabad, Telangana, India, over an 18-month recruitment period from January 2023 to June 2024. Participant recruitment, intervention, outcome assessment, and in-hospital follow-up were completed during the same perioperative admission.

Participants

Eighty adult patients of either sex, aged above 18 years, belonging to American Society of Anesthesiologists (ASA) physical status I or II, and scheduled for elective surgery under general anesthesia requiring endotracheal intubation were enrolled. All participants underwent preanesthetic evaluation, including medical history, clinical examination, airway assessment, and routine preoperative investigations. Patients with an anticipated difficult airway, increased risk of aspiration, significant cardiovascular or respiratory instability, pregnancy, obesity with anticipated ventilation difficulty, known allergy or contraindication to propofol, sevoflurane, fentanyl, or succinylcholine, and those refusing consent were excluded.

Sample size justification

The sample size was set at 80 patients, with 40 patients in each group. The calculation was based on the primary outcome of intubating conditions, assuming a clinically meaningful difference between the two groups in the proportion of patients achieving acceptable intubating conditions. Considering an alpha error of 0.05, power of 80%, and feasibility within the study period, a minimum of 40 participants per group was considered adequate to detect a significant between-group difference. The final sample size also accounted for possible minor attrition, although all randomized participants completed the study and were included in the final analysis.

Randomization, allocation concealment, and implementation

Eligible participants were randomly allocated into two groups: Group P (propofol–fentanyl) and Group S (sevoflurane–fentanyl), using simple randomization in a 1:1 ratio. The random allocation sequence was generated before the start of the trial using a lottery-based method in

which 80 identical opaque slips were prepared by a faculty member not involved in patient recruitment, anesthesia administration, or outcome assessment. Forty slips were marked for Group P and forty for Group S, and all slips were folded identically and mixed thoroughly in a sealed container. For each enrolled participant, one slip was drawn immediately before induction to determine group assignment.

Allocation concealment was maintained by keeping the slips enclosed and inaccessible until the point of assignment. The random sequence was prepared by an independent faculty member, participants were enrolled by the principal investigator, and group assignment was implemented by the attending anesthesiologist immediately before induction of anesthesia.

Blinding

Blinding was not feasible in this study because the two induction techniques differed in route and conduct of administration, making masking of the anesthesiologist impractical. Participants were under anesthesia during airway instrumentation and were therefore not aware of the allocated induction regimen at the time of outcome assessment. However, the intubating anesthesiologist and the observer recording peri-intubation parameters were not blinded. This should be considered while interpreting the findings.

Conduct of anesthesia and intubation

All patients were kept fasting as per standard preoperative guidelines. In the operating room, standard monitoring was instituted, including electrocardiography, non-invasive blood pressure, and pulse oximetry. An 18-gauge intravenous cannula was secured, and intravenous normal saline 10 mL/kg was administered before induction. All patients received intravenous ondansetron 4 mg and glycopyrrolate 0.2 mg as premedication. Patients were placed in the supine position with the head in Magill's position and were preoxygenated with 100% oxygen for 5 minutes. Fentanyl 2 µg/kg intravenously was administered 3 minutes before induction in both groups.

In Group P, induction was performed with intravenous propofol 3 mg/kg administered over 10 seconds, and laryngoscopy with tracheal intubation was attempted 90 seconds later.

In Group S, the breathing circuit was primed, and inhalational induction was carried out using oxygen and nitrous oxide in a 40:60 ratio with a fresh gas flow of 6 L/min. Sevoflurane was started at 1% and increased by 1% every 2 to 3 breaths up to a maximum concentration of 8%. Assisted ventilation was provided when necessary to maintain end-tidal carbon dioxide between 25 and 35 mmHg. Laryngoscopy and tracheal intubation were attempted at 5 minutes after starting sevoflurane induction.

Following successful intubation, the tracheal tube cuff was inflated gently. Maintenance anesthesia was continued with propofol infusion at 4 mg/kg/hour in Group P and sevoflurane 2% in Group S, according to the allocated regimen.

Rescue neuromuscular blockade

If tracheal intubation could not be achieved because of inadequate intubating conditions, severe coughing, or airway obstruction, rescue neuromuscular blockade was provided with succinylcholine 1 mg/kg intravenously, and intubation was then completed. This rescue strategy was predefined in the protocol to ensure patient safety.

Outcome measures

The primary outcome measure was the quality of intubating conditions. Intubating conditions were assessed within 1 minute of intubation attempt using jaw relaxation, vocal cord position, and patient response to intubation, and were categorized as optimal, good, poor, or inadequate according to established structured criteria [14].

Secondary outcome measures included laryngoscopic view, incidence of apnea after induction, and peri-intubation hemodynamic responses. Laryngoscopic view was graded according to the Cormack–Lehane classification [13]. Apnea was defined clinically as the absence of spontaneous respiration after induction requiring assisted ventilation. Hemodynamic parameters, including heart rate, systolic blood pressure, diastolic blood pressure, and mean arterial pressure, were recorded at baseline, after induction, immediately after intubation, and at 1 minute and 5 minutes after intubation.

Statistical analysis

Data were entered and analyzed using SPSS for Windows version 15.0. Continuous variables were expressed as mean ± standard deviation and compared between groups using Student's unpaired t-test. Categorical variables were expressed as frequency and percentage and were compared using the chi-square test. A two-sided p-value of less than 0.05 was considered statistically significant.

Ethical considerations

Ethical approval was obtained from the Institutional Ethics Committee of Gandhi Medical College, Secunderabad, Telangana, India, before commencement

of the study, and written informed consent was obtained from all participants before enrollment.

Results

Participant flow

A total of 92 patients scheduled for elective surgery were assessed for eligibility during the study period. Twelve patients were excluded before randomization because they did not meet the inclusion criteria (n = 8) or declined to participate (n = 4). The remaining 80 eligible patients were randomized in a 1:1 ratio into two groups. Forty patients were allocated to the propofol–fentanyl group (Group P) and forty patients were allocated to the sevoflurane–fentanyl group (Group S). All randomized patients received the allocated intervention and completed the study protocol. No participants were lost to follow-up

or excluded after randomization. Therefore, all 80 patients were included in the final statistical analysis.

Confidence intervals for key outcomes

Optimal intubating conditions were achieved in 21 of 40 patients (52.5%) in the propofol group and in 37 of 40 patients (92.5%) in the sevoflurane group. The absolute difference between groups was 40.0% (95% CI: 23.4%–56.6%; p = 0.0001). Acceptable intubating conditions (optimal + good) were observed in 82.5% of patients in the propofol group and in 100% of patients in the sevoflurane group, corresponding to an absolute difference of 17.5% (95% CI: 5.7%–29.3%; p = 0.011). Apnea after induction occurred in 40 patients (100%) in the propofol group and in 5 patients (12.5%) in the sevoflurane group. The absolute difference between groups was 87.5% (95% CI: 76.1%–98.9%; p < 0.0001).
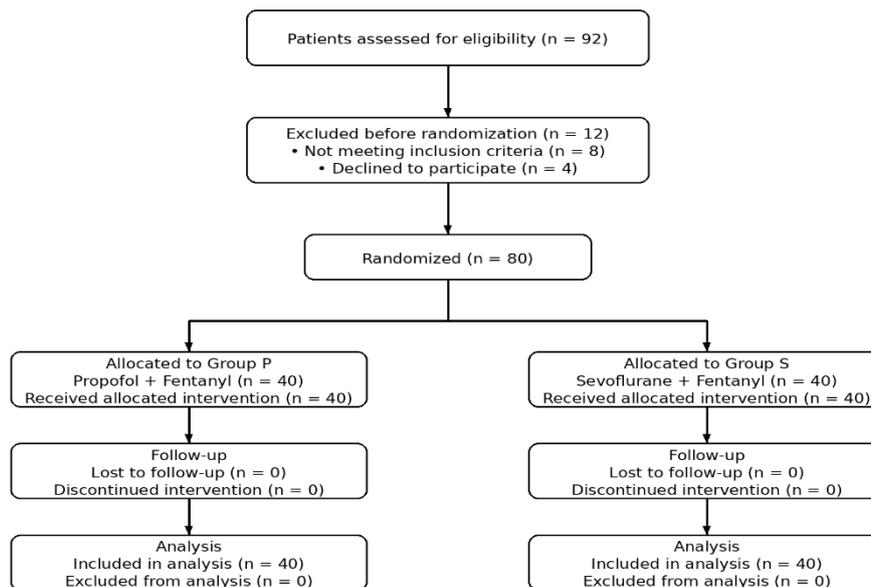

Figure 1: Participant flow diagram

A total of 80 patients were included and analyzed, with 40 patients in each group. All enrolled patients completed the study protocol without protocol violations. Baseline

demographic characteristics were comparable between groups (Table 1).

Table 1. Baseline demographic characteristics

Variable	Propofol (Group P) (n=40)	Sevoflurane (Group S) (n=40)	p value
Age (years), mean ± SD	32.0 ± 12.43	33.4 ± 11.48	0.602
Weight (kg), mean ± SD	57.0 ± 9.63	58.1 ± 8.96	0.590
Height (cm), mean ± SD	157.5 ± 6.08	158.8 ± 5.99	0.376
Sex (M/F)	18 / 22	16 / 24	>0.05

Intubating conditions differed significantly between groups. Optimal conditions were achieved in 37/40 (92.5%) of patients in the sevoflurane group compared with 21/40 (52.5%) in the propofol group. Acceptable intubating conditions (optimal+good) were achieved in 100% with sevoflurane versus 82.5% with propofol. Apnea was observed in all propofol patients and in 12.5% of sevoflurane patients (Table 2).

Table 2. Intubating conditions and apnea

Parameter	Propofol (Group P) (n=40)	Sevoflurane (Group S) (n=40)	p value
Intubating conditions – Optimal	21 (52.5%)	37 (92.5%)	0.0001
Intubating conditions – Good	12 (30.0%)	3 (7.5%)	—
Intubating conditions – Poor	6 (15.0%)	0	—
Intubating conditions – Inadequate	1 (2.5%)	0	—
Acceptable (Optimal + Good)	33 (82.5%)	40 (100%)	0.011
Apnea after induction – Yes	40 (100%)	5 (12.5%)	<0.0001
Apnea after induction – No	0	35 (87.5%)	—

Laryngoscopic view assessed by Cormack–Lehane grading was similar between groups, with Grade 1 views predominating (Table 3).

Table 3. Cormack–Lehane laryngoscopic grading

Cormack–Lehane grade	Propofol (Group P)	Sevoflurane (Group S)	p value
Grade 1	27	30	0.458
Grade 2	11	10	—
Grade 3	2	0	—
Grade 4	0	0	—

Hemodynamic parameters are summarized in Table 4. Heart rate and systolic blood pressure were comparable at all time points. Between-group differences were noted for diastolic blood pressure and mean arterial pressure at 1 and 5 minutes after intubation ($p < 0.05$), with values remaining clinically acceptable in both groups. No patient required vasoactive medication or atropine.

Table 4. Hemodynamic parameters (mean ± SD)

Time point	Heart rate (beats/min)	Systolic BP (mmHg)	Diastolic BP (mmHg)	Mean arterial pressure (mmHg)
Baseline	P: 90.42 ± 18.44 S: 91.42 ± 13.21	P: 119.35 ± 13.94 S: 122.78 ± 15.37	P: 78.92 ± 9.05 S: 81.42 ± 8.57	P: 92.10 ± 9.85 S: 95.12 ± 10.40
After induction	P: 87.75 ± 16.20 S: 87.40 ± 16.35	P: 98.50 ± 11.48 S: 98.20 ± 13.10	P: 67.28 ± 9.66 S: 67.18 ± 10.44	P: 77.55 ± 9.54 S: 77.55 ± 10.75
Immediately after intubation	P: 92.28 ± 17.61 S: 91.45 ± 17.59	P: 105.58 ± 17.60 S: 103.85 ± 17.09	P: 70.75 ± 11.19 S: 71.75 ± 13.90	P: 82.28 ± 12.28 S: 82.02 ± 14.15
1 min after intubation	P: 89.95 ± 14.66 S: 88.15 ± 15.03	P: 101.28 ± 12.88 S: 103.65 ± 14.20	P: 66.90 ± 9.71 S: 73.00 ± 9.08*	P: 78.08 ± 10.03 S: 82.82 ± 10.05*
5 min after intubation	P: 87.78 ± 12.32 S: 84.70 ± 14.48	P: 101.12 ± 13.77 S: 106.32 ± 12.11	P: 69.18 ± 10.67 S: 74.75 ± 9.36*	P: 79.95 ± 11.08 S: 84.42 ± 9.61*

Between-group p < 0.05 at the indicated time points.

Discussion

This study compared sevoflurane–fentanyl with propofol–fentanyl for muscle relaxant-free tracheal intubation in ASA I–II adults. Sevoflurane induction produced superior intubating conditions, with a higher proportion of optimal scores and universal acceptability. These findings are consistent with earlier work showing that opioids lower sevoflurane requirements and improve the likelihood of acceptable conditions for intubation without NMBAs [5]. The clinical relevance of better intubating conditions extends beyond immediate success. Poorer conditions can increase airway stimulation and trauma, and previous randomized trials have reported greater postoperative upper airway discomfort when intubation is performed without muscle relaxants under less favorable conditions [3,12]. Although postoperative airway symptoms were not recorded in the present study, the dominance of optimal conditions in the sevoflurane group suggests a potentially smoother airway course in the immediate peri-intubation period.

Propofol–opioid techniques remain attractive for their rapid onset and ease of implementation. However, prior studies demonstrate variability in intubation quality without NMBAs, influenced by opioid selection, timing, and use of adjuncts such as lidocaine or benzodiazepines [8-11]. In the current cohort, acceptable conditions were achieved in 82.5% with propofol, and one patient had inadequate conditions requiring succinylcholine, emphasizing that IV-only approaches can yield inconsistent suppression of airway reflexes in some individuals.

Apnea was the most prominent between-group difference and has important operational implications. Universal apnea after propofol–fentanyl is consistent with dose-dependent respiratory depression from propofol, accentuated by opioids, and has been described in similar sequences [8,9]. In contrast, incremental sevoflurane induction preserved spontaneous ventilation in most patients, resulting in a low apnea incidence. This profile is advantageous when maintenance of ventilation is prioritized during induction and airway instrumentation.

Hemodynamic responses remained clinically acceptable in both groups. Heart rate and systolic blood pressure were similar, while diastolic pressure and mean arterial pressure were higher in the sevoflurane group at 1 and 5 minutes post-intubation. Prior studies of sevoflurane-based induction and timing-guided intubation have also reported stable hemodynamics when ventilation is assisted to maintain appropriate carbon dioxide levels [6,7]. Laryngoscopic view did not differ between groups, indicating that differences in intubating conditions were predominantly related to anesthetic depth and reflex suppression rather than anatomical exposure [13,14].

Generalizability: These findings are most relevant to ASA I–II adults undergoing elective surgery with experienced airway operators, standard monitoring, and immediate access to rescue neuromuscular blockade. The results reflect the specific protocol used (incremental sevoflurane up to 8% with nitrous oxide and fentanyl 2 ug/kg, or propofol 3 mg/kg with fentanyl). Application to obese patients, severe reflux, difficult airways, emergencies, or low-resource settings requires caution. Findings are best applied where ventilation can be promptly supported.

Conclusion

In ASA physical status I–II adults undergoing elective surgery, sevoflurane induction with fentanyl provided superior conditions for tracheal intubation without a muscle relaxant compared with propofol induction with fentanyl. The sevoflurane regimen achieved a higher proportion of optimal conditions and ensured universal acceptability, while substantially reducing apnea and the need for assisted ventilation. Laryngoscopic view was comparable between groups, and peri-intubation hemodynamics remained clinically stable without requiring pharmacological intervention. When neuromuscular blockade is intentionally avoided, a sevoflurane–fentanyl strategy offers a practical airway-friendly option. Protocolized monitoring, readiness for bag-mask ventilation, and availability of rescue paralysis remain essential to maintain safety and consistency. Overall, sevoflurane appears preferable for NMBA-free elective intubation here.

Limitations

This single-centre study included only ASA I–II elective patients and used non-blinded assessment, introducing observer bias. Intubation timing differed between groups by protocol, confounding attribution of effects to the induction drugs alone. Postoperative airway outcomes (sore throat, hoarseness, laryngeal injury) were not assessed. Objective depth-of-anesthesia indices and end-tidal sevoflurane concentrations were not recorded, and inter-operator variability was not evaluated in detail.

Recommendations

For elective ASA I–II cases where neuromuscular blockade is intentionally avoided, incremental sevoflurane induction with fentanyl can be used to improve intubating conditions and reduce apnea. Standardized scoring of intubation conditions should be adopted to strengthen audit and research quality. Assisted ventilation to maintain appropriate EtCO2 and strict adherence to protocolized timing of laryngoscopy are

recommended. A predefined rescue plan with immediate availability of a short-acting muscle relaxant is essential, along with clear criteria for abandoning attempts. Training in inhalational induction and airway rescue should be ensured in all operating lists. Future studies should incorporate blinded assessment, end-tidal agent measurement, and postoperative airway symptom tracking.

Acknowledgement

Abbreviations

ASA – American Society of Anesthesiologists;
BP – blood pressure;
DBP – diastolic blood pressure;
ECG – electrocardiogram;
EtCO2 – end-tidal carbon dioxide;
FGF – fresh gas flow;
HR – heart rate;
MAP – mean arterial pressure;
NMBA – neuromuscular blocking agent;
N2O – nitrous oxide;
O2 – oxygen;
SD – standard deviation;
SPSS – Statistical Package for the Social Sciences.

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Conflict of interest

The authors declare no conflict of interest.

Author contributions

KR-Concept and design of the study, results interpretation, review of literature, and preparing the first draft of the manuscript. Statistical analysis and interpretation, revision of manuscript. DR- Design of the study, results interpretation, review of literature, preparing the first draft of the manuscript, and revision of the manuscript. KR-Review of literature and preparing the first draft of the manuscript. Statistical analysis and interpretation.

Data availability

Data available on request

Author biography

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