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EFFICACY OF FENTANYL VERSUS NALBUPHINE AS ADJUVANT AGENTS IN THE INDUCTION PHASE OF GENERAL ANESTHESIA: A COMPARATIVE STUDY

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Abstract

Background: Propofol is the most commonly preferred intravenous induction agent but may cause dose-dependent cardiovascular depression. Opioid premedication reduces propofol requirements during induction. This study compared the propofol-sparing efficacy of fentanyl and nalbuphine during induction of general anaesthesia.

Methods: In this prospective comparative study, 100 ASA physical status I–II adults undergoing elective surgery under general anaesthesia were randomized into two groups (n=50 each). Group F received intravenous fentanyl 3 µg/kg and Group N received intravenous nalbuphine 0.3 mg/kg six minutes before induction. Using propofol titrated to loss of the eyelash reflex. Primary outcomes were before propofol dose, Ramsay Sedation Scale score, and induction time. Secondary outcomes included haemodynamic changes and opioid-related adverse effects.

Results: Fentanyl significantly reduced the propofol dose required for induction compared with nalbuphine 80.78 ± 14.30 mg vs 95.44 ± 15.69 mg ($p < 0.001$). Ramsay Sedation Scale scores were higher with nalbuphine 2.34 ± 0.35 vs 2.87 ± 0.56 ($p < 0.001$). Induction time was significantly shorter in the fentanyl group 43.52 ± 8.53 s vs 48.76 ± 10.24 s ($p = 0.007$). The incidences of hypotension, bradycardia, respiratory depression, postoperative nausea and vomiting, and pruritus were low and comparable between groups.

Conclusion: Fentanyl demonstrated superior propofol-sparing efficacy compared with nalbuphine while maintaining comparable haemodynamic stability and safety. Nalbuphine produced greater pre-induction sedation and represents a suitable alternative opioid adjunct.

Keywords: Propofol; Fentanyl; Nalbuphine; General anaesthesia; Induction; Haemodynamic stability

Introduction

Propofol is currently the most widely used intravenous induction agent for general anaesthesia because of its rapid onset of action, smooth induction, short duration of effect, and rapid recovery profile.1 Compared with earlier induction agents, propofol provides excellent conditions for airway instrumentation, suppresses airway reflexes, possesses antiemetic properties, and facilitates early postoperative recovery, making it the induction agent of choice for a broad range of surgical procedures.1

Despite these advantages, propofol produces dose-dependent cardiovascular depression that frequently manifests as hypotension during induction of anaesthesia.2 The reduction in arterial blood pressure results primarily from systemic vasodilation, diminished sympathetic activity, and mild myocardial depression.2 These haemodynamic effects are particularly pronounced in elderly, hypovolaemic, or cardiovascularly compromised patients and may lead to inadequate organ perfusion if not anticipated and managed appropriately.2 Consequently, several pharmacological strategies have been investigated to minimise the induction dose of propofol while maintaining satisfactory depth of anaesthesia and haemodynamic stability.2

Balanced anaesthesia, first described by Lundy in 1926, remains one of the foundational principles of modern anaesthetic practice, wherein different classes of drugs are combined to achieve hypnosis, analgesia, amnesia, and muscle relaxation while reducing the dose-dependent adverse effects of individual agents.3 Opioids constitute an integral component of balanced anaesthesia because they provide profound analgesia, blunt sympathetic responses to laryngoscopy and tracheal intubation, and reduce the hypnotic requirement of intravenous induction agents.3 Administration of an opioid before induction has therefore become a common strategy to decrease propofol requirements and improve cardiovascular stability during induction of general anaesthesia.3

Fentanyl, a synthetic phenylpiperidine opioid and highly selective μ-opioid receptor agonist, has long been considered the standard opioid adjunct during induction of general anaesthesia. Owing to its rapid onset, potent analgesic action, and ability to attenuate the haemodynamic response to airway manipulation, fentanyl is routinely administered before propofol induction.4 Experimental and clinical studies have demonstrated an additive interaction between fentanyl and propofol, resulting in a reduction in the dose of propofol required to achieve loss of consciousness while improving intubating conditions.4

Nalbuphine is a semisynthetic opioid with a unique agonist–antagonist pharmacological profile, acting predominantly as a κ-opioid receptor agonist and a μ-opioid receptor antagonist.5 This receptor activity provides effective analgesia while producing a ceiling effect on respiratory depression and reducing the incidence of several μ-receptor-mediated adverse effects, including pruritus, nausea, vomiting, and opioid dependence.5 Because of these characteristics, nalbuphine has gained increasing interest as an alternative perioperative opioid, particularly in patients in whom minimising opioid-related complications is desirable.5

Duda et al. have examined nalbuphine as an adjunct in anaesthesia, showing that it can provide effective analgesia and acceptable haemodynamic stability.6 However, direct evidence for its propofol-sparing effect during induction remains limited, and comparative data between nalbuphine and fentanyl in this specific setting are scarce. This makes it worthwhile to evaluate whether nalbuphine can offer induction conditions comparable to fentanyl while maintaining a favourable adverse-effect profile.6

Therefore, the present prospective comparative study was undertaken to evaluate the propofol-sparing efficacy of intravenous nalbuphine (0.3 mg/kg) and intravenous fentanyl (3 μg/kg) administered before induction of general anaesthesia.

METHODS

Study Design and Ethical Approval

This prospective, randomized, comparative study was conducted in the Department of Anaesthesiology, Narayana Medical College and Hospital, Nellore, Andhra Pradesh, India, over a period of six months (June 2025 to December 2025), after obtaining approval from the Institutional Ethics Committee. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki. Written informed consent was obtained from all participants before enrolment.

Study Population

A total of 100 adult patients scheduled for elective surgery under general anaesthesia with endotracheal intubation were enrolled. Patients aged 18–65 years with American Society of Anesthesiologists (ASA) physical status I or II were included. The inclusion criteria were: age 18–65 years, ASA physical status I or II, elective surgery requiring general anaesthesia with endotracheal intubation, and provision of written informed consent. The exclusion criteria were refusal to participate, known allergy or hypersensitivity to opioids, contraindications to opioid administration (including severe obesity or chronic obstructive pulmonary disease), anticipated difficult airway, ASA physical status III or higher, and planned rapid sequence induction and intubation.

Sample Size

As there were limited published data directly comparing the propofol-sparing efficacy of fentanyl and nalbuphine during induction of general anaesthesia, this study was designed as a pilot comparative study. A total of 100 patients were recruited and equally allocated into two groups, with 50 patients in each group.

Randomization and Blinding

Patients were randomized into two equal groups using a computer-generated random number table, with allocation concealment maintained throughout the study. Group A received intravenous fentanyl 3 μg/kg, and Group B received intravenous nalbuphine 0.3 mg/kg. The study drug was prepared by an anaesthesia resident who was not involved in patient management or data collection. Both study drugs were diluted with normal saline to a total volume of 5 mL and administered in identical unlabelled syringes. The attending anaesthesiologist and the observer responsible for data collection were blinded to group allocation.

Anaesthetic Technique

Following application of standard ASA monitors, baseline heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, and peripheral oxygen saturation were recorded. Patients were preoxygenated with 100% oxygen for 3 minutes before administration of the allocated study drug. Six minutes after administration of fentanyl or nalbuphine, sedation was assessed using the Ramsay Sedation Scale which is a clinical scoring system used to assess the depth of sedation, ranging from 1 (anxious/agitated) to 6 (no response to stimuli), with higher scores indicating deeper sedation. Propofol was then administered intravenously in incremental doses of 30 mg every 10 seconds until loss of the eyelash reflex. The total dose of propofol required and the time to induction were recorded. Neuromuscular blockade was achieved using atracurium (0.5 mg/kg)/ cisatracurium (0.2 mg/kg), or vecuronium (0.1 mg/kg), followed by endotracheal intubation three minutes later. Heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, and peripheral oxygen saturation were recorded at baseline, immediately before propofol administration, immediately after induction, immediately after intubation, and at 5, 10, 15, and 20 minutes following intubation. The occurrence of hypotension, bradycardia, respiratory desaturation, postoperative nausea and vomiting, pruritus, pain during propofol injection, number of intubation attempts, and airway adjuncts used were also documented throughout the intraoperative period.

Outcome Measures

The primary outcomes were the cumulative propofol dose required to achieve loss of the eyelash reflex, Ramsay Sedation Score before induction, and time required for induction following propofol administration. The secondary outcomes included the incidence of hypotension and bradycardia, haemodynamic response to laryngoscopy and endotracheal intubation, and opioid-related adverse effects including respiratory depression, postoperative nausea and vomiting, and pruritus. Hypotension and bradycardia were managed according to standard institutional protocols, and all adverse events were documented.

STATISTICAL ANALYSIS

Data were analysed using SPSS version 22.0 (IBM Corp., Armonk, NY, USA). Continuous data were presented as mean ± standard deviation, while categorical data were summarised as frequencies and percentages. The independent-samples t-test was used for comparison of continuous variables, and the Chi-square test or Fisher's exact test was applied for categorical variables as appropriate. A two-tailed p value of less than 0.05 was considered statistically significant.

RESULTS

A total of 100 patients were enrolled in this prospective comparative study and randomized equally into the fentanyl group (n = 50) and the nalbuphine group (n = 50). All randomized patients completed the study protocol and were included in the final statistical analysis. No patient was excluded after randomization as depicted in figure 1.

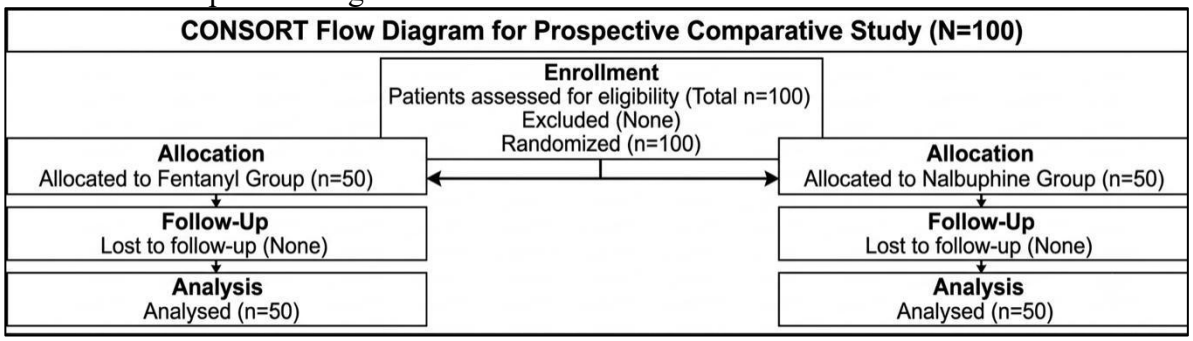

Figure 1 : Patient CONSORT diagram of the study.

The baseline demographic and clinical characteristics of the study population are summarized in Table 1. The two groups were comparable with respect to age, sex distribution, body weight, and ASA physical status, with no statistically significant differences observed between the groups (all $p > 0.05$), indicating adequate baseline homogeneity.

The primary outcome measures are presented in Table 2. Patients receiving intravenous fentanyl required a significantly lower dose of propofol to achieve loss of eyelash reflex compared with those receiving intravenous nalbuphine (80.78 ± 14.30 mg vs. 95.44 ± 15.69 mg; mean difference −14.66 mg, 95% CI −20.60 to −8.72; $p < 0.001$). Pre-induction sedation, assessed using the Ramsay Sedation Score, was significantly greater in the nalbuphine group than in the fentanyl group (2.87 ± 0.56 vs. 2.34 ± 0.35; mean difference −0.53, 95% CI −0.71 to −0.35; $p < 0.001$). Furthermore, induction of anaesthesia was achieved significantly earlier in patients receiving fentanyl than in those receiving nalbuphine (43.52 ± 8.53 s vs. 48.76 ± 10.24 s; mean difference −5.24 s, 95% CI −9.01 to −1.47; $p = 0.007$).

Peri-induction adverse events are summarized in Table 3. Hypotension was defined as a decrease in systolic blood pressure (SBP) of >20% from baseline or an SBP <90 mmHg. Bradycardia was defined as a heart rate <50 beats/min. Hypotension was observed in both study groups with an identical incidence (10.0% vs. 10.0%; odds ratio [OR] 1.00, 95% CI 0.27–3.69; p = 1.000). Bradycardia occurred in three patients (6.0%) in the fentanyl group and two patients (4.0%) in the nalbuphine group, with no statistically significant difference (OR 1.53, 95% CI 0.25–9.34; p = 1.000). Hypotensive episodes were managed with intravenous fluid boluses and incremental doses of vasopressors (phenylephrine/ephedrine) as required, while bradycardia was treated with intravenous atropine when clinically indicated. No patient in either group experienced respiratory depression during the study period.

Postoperative nausea and vomiting (PONV) was defined as the occurrence of nausea, vomiting, or retching during the postoperative observation period. The severity of PONV was assessed based on clinical symptoms and requirement for rescue antiemetic therapy. PONV occurred exclusively in the nalbuphine group (4 patients, 8.0%), whereas no cases were observed in the fentanyl group; however, the difference was not statistically significant (Fisher's exact test, p = 0.117). Episodes of PONV were managed with rescue antiemetic medication as per institutional protocol. Pruritus was defined as the subjective sensation of itching reported by the patient during the postoperative period and was graded based on clinical severity. One patient (2.0%) in the fentanyl group experienced pruritus, while no cases were observed in the nalbuphine group (p = 1.000). Mild cases were managed conservatively, while antihistamines were considered for clinically significant symptoms. Overall, both study drugs demonstrated a favourable safety profile, with a low incidence of opioid-related adverse effects.

Serial peri-induction hemodynamic parameters are summarized in Table 4. Baseline heart rate, systolic blood pressure, diastolic blood pressure (measured by non-invasive blood pressure monitoring), and peripheral oxygen saturation were comparable between the fentanyl and nalbuphine groups. Following administration of propofol, both groups demonstrated the expected reduction in heart rate and blood pressure, reflecting the known cardiovascular effects of induction. A transient increase in heart rate and blood pressure was observed immediately after endotracheal intubation in both groups, following which the hemodynamic variables gradually returned toward baseline values during the observation period. Peripheral oxygen saturation remained well maintained throughout the peri-induction period in both groups without clinically significant desaturation. Overall, both fentanyl and nalbuphine provided comparable peri-induction haemodynamic stability, with no statistically significant differences observed in serial haemodynamic parameters between the study groups.

Overall, intravenous fentanyl demonstrated a statistically significant propofol-sparing effect compared with nalbuphine and resulted in a shorter induction time, whereas nalbuphine produced higher pre-induction sedation scores. Both opioids exhibited comparable peri-induction hemodynamic stability and a similarly low incidence of adverse events.

Table 1. Baseline demographic and clinical characteristics of the study population

Variable	Group A (n = 50)	Group B (n = 50)	p value
Age (years)	40.41 ± 11.62	40.67 ± 11.78	0.914
Body weight (kg)	64.74 ± 9.31	65.92 ± 11.83	0.581
Male sex, n (%)	28 (56.0)	27 (54.0)	0.842
Female sex, n (%)	22 (44.0)	23 (46.0)	
ASA Physical Status I, n (%)	30 (60.0)	28 (56.0)	0.685
ASA Physical Status II, n (%)	20 (40.0)	22 (44.0)	

Values are presented as mean ± standard deviation or number (%). Continuous variables were compared using the independent-samples t-test. Categorical variables were compared using the Chi-square test.

Table 2. Primary outcome measures

Outcome	Group A (n = 50)	Group B (n = 50)	p value
Propofol required for induction (mg)	80.78 ± 14.30	95.44 ± 15.69	<0.001
Ramsay Sedation Score	2.34 ± 0.35	2.87 ± 0.56	<0.001
Time to induction (s)	43.52 ± 8.53	48.76 ± 10.24	0.007

Values are expressed as mean ± standard deviation. Mean differences are presented with 95% confidence intervals. Statistical comparisons were performed using the independent-samples t-test.

Table 3. Peri-induction adverse events

Variable	Group A (n = 50)	Group B (n = 50)	p value
Hypotension	5 (10.0)	5 (10.0)	1.000
Bradycardia	3 (6.0)	2 (4.0)	1.000
Respiratory depression	0	0	—
Postoperative nausea and vomiting	0	4 (8.0)	0.117
Pruritus	1 (2.0)	0	1.000

Values are expressed as number (%). Fisher's exact test was used where expected cell frequencies were less than five.

*Odds ratio could not be reliably estimated because one treatment group contained zero events.

Table 4. Serial hemodynamic parameters during induction and endotracheal intubation

Time point	Heart Rate (beats/min)		SBP (mmHg)		DBP (mmHg)		SpO_2 (%)	
	Group A (n=50)	Group B (n=50)	Group A (n=50)	Group B (n=50)	Group A (n=50)	Group B (n=50)	Group A (n=50)	Group B (n=50)
Baseline	80.88 ± 5.58	79.24 ± 5.59	125.56 ± 4.14	124.80 ± 3.99	77.72 ± 3.37	77.98 ± 4.21	99.00 ± 0.00	99.00 ± 0.00
5 min after premedication	78.88 ± 5.58	76.24 ± 5.59	122.56 ± 4.14	119.80 ± 3.99	75.72 ± 3.37	75.98 ± 4.21	99.00 ± 0.00	99.00 ± 0.00
After propofol	75.88 ± 5.58	71.24 ± 5.59	115.56 ± 4.14	109.80 ± 3.99	72.72 ± 3.37	72.98 ± 4.21	99.00 ± 0.00	99.00 ± 0.00
Immediately after intubation	88.88 ± 5.58	93.24 ± 5.59	133.56 ± 4.14	138.80 ± 3.99	82.72 ± 3.37	82.98 ± 4.21	98.00 ± 0.00	98.00 ± 0.00
5 min after intubation	84.88 ± 5.58	87.24 ± 5.59	129.56 ± 4.14	132.80 ± 3.99	80.72 ± 3.37	80.98 ± 4.21	99.00 ± 0.00	99.00 ± 0.00
10 min after intubation	82.88 ± 5.58	84.24 ± 5.59	127.56 ± 4.14	128.80 ± 3.99	79.72 ± 3.37	79.98 ± 4.21	99.00 ± 0.00	99.00 ± 0.00
15 min after intubation	80.88 ± 5.58	81.24 ± 5.59	125.56 ± 4.14	126.80 ± 3.99	77.72 ± 3.37	77.98 ± 4.21	99.00 ± 0.00	99.00 ± 0.00
20 min after intubation	80.88 ± 5.58	79.24 ± 5.59	125.56 ± 4.14	124.80 ± 3.99	77.72 ± 3.37	77.98 ± 4.21	99.00 ± 0.00	99.00 ± 0.00

Values are expressed as mean ± standard deviation. HR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; SpO_2, peripheral oxygen saturation.

DISCUSSION

The present prospective comparative study evaluated the propofol-sparing efficacy of fentanyl (3 μg/kg) and nalbuphine (0.3 mg/kg) administered before induction of general anaesthesia in adult patients undergoing elective surgical procedures. The study demonstrated that fentanyl required a significantly lower cumulative propofol induction dose to achieve loss of eyelash reflex compared with nalbuphine (80.78 ± 14.30 mg vs. 95.44 ± 15.69 mg; $p < 0.001$). Conversely, nalbuphine produced significantly higher pre-induction Ramsay Sedation Scores compared with fentanyl (2.87 ± 0.56 vs. 2.34 ± 0.35; $p < 0.001$). The time required for induction was also shorter with fentanyl compared with nalbuphine (43.52 ± 8.53 s vs. 48.76 ± 10.24 s; $p = 0.007$). Despite these differences, the peri-induction haemodynamic profile, and incidence of adverse events, including hypotension (10.0% vs. 10.0%; $p = 1.000$), bradycardia (6.0% vs. 4.0%; $p = 1.000$), postoperative nausea and vomiting (0% vs. 8.0%; $p = 0.117$), and pruritus (2.0% vs. 0%; $p = 1.000$), were comparable between the two groups. These findings suggest that while fentanyl provides superior dose-sparing of propofol, nalbuphine offers comparable peri-induction safety and haemodynamic stability during induction of general anaesthesia.

Propofol remains the most commonly used intravenous induction agent because of its rapid onset, favourable recovery profile, and predictable pharmacokinetics.7 However, its dose-dependent cardiovascular depression, particularly hypotension resulting from systemic vasodilation and myocardial depression, continues to be a major concern during induction.7 The use of opioid adjuncts before induction has therefore become an integral component of balanced anaesthesia to reduce propofol requirements while maintaining adequate hypnosis and haemodynamic stability.7

The principal finding of the present study was the significantly lower induction dose of propofol observed in the fentanyl group. This finding is consistent with the established pharmacological interaction between fentanyl and propofol.9 Fentanyl, a potent μ-opioid receptor agonist, exhibits synergistic effects with propofol by reducing afferent nociceptive input and enhancing hypnotic efficacy, thereby lowering the amount of propofol required to achieve unconsciousness.9 Darlong et al. demonstrated that administration of fentanyl before induction significantly reduced the induction dose of propofol, with maximal dose reduction observed when an adequate interval was allowed between fentanyl administration and propofol injection.8 Similarly, previous studies have shown that opioid premedication can reduce propofol requirement during induction while providing favourable induction conditions and haemodynamic stability.9 The findings of the present study therefore reinforce the role of fentanyl as an effective propofol-sparing opioid during induction.

Although nalbuphine required a comparatively greater dose of propofol, patients receiving nalbuphine demonstrated significantly higher Ramsay sedation scores before induction. Nalbuphine possesses a unique agonist-antagonist pharmacological profile, acting predominantly as a κ-opioid receptor agonist with μ-receptor antagonistic activity.5 Activation of κ receptors contributes to sedation and analgesia while limiting several classical μ-opioid-mediated adverse effects.5 Consequently, greater pre-induction sedation with nalbuphine is pharmacologically expected and has been consistently reported in previous clinical studies.5 However, the present findings indicate that greater subjective sedation does not necessarily translate into a greater reduction in hypnotic drug requirement. This distinction highlights that opioid-induced sedation and propofol-induced hypnosis represent different pharmacodynamic endpoints.

The significantly shorter induction time observed in the fentanyl group reflects its greater synergistic interaction with propofol during induction of general anaesthesia. Patients receiving fentanyl achieved loss of the eyelash reflex more rapidly than those receiving nalbuphine, despite both drugs being administered using a standardized induction protocol. This finding is consistent with the superior propofol-sparing effect of fentanyl observed in the present study and suggests that enhanced μ-opioid receptor-mediated potentiation of propofol facilitates faster onset of hypnosis. Similar observations have been reported by Darlong et al. and Kaur et al., who demonstrated that fentanyl administered before induction reduced propofol requirements and facilitated efficient induction of anaesthesia without compromising haemodynamic stability.8,9 Therefore, the shorter induction time observed with fentanyl further supports its role as the preferred opioid adjunct when rapid and efficient induction of general anaesthesia is desired.

Maintenance of cardiovascular stability during induction and tracheal intubation remains an important objective of balanced anaesthesia. In the present study, both groups exhibited the expected reduction in heart rate and arterial blood pressure following propofol administration, followed by transient increases immediately after laryngoscopy and tracheal intubation. These haemodynamic changes remained within clinically acceptable limits throughout the observation period, and no clinically meaningful differences were observed between fentanyl and nalbuphine. Likewise, the incidence of hypotension and bradycardia was low bradycardia (6.0% vs. 4.0%) and comparable between groups. These findings suggest that both opioids provide adequate attenuation of peri-induction cardiovascular responses when combined with titrated propofol administration.10

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Earlier studies comparing fentanyl and nalbuphine have demonstrated similar observations. Khan et al. compared both opioids during total intravenous anaesthesia and reported comparable intraoperative haemodynamic stability, although fentanyl produced slightly greater suppression of sympathetic responses during laryngoscopy owing to its potent μ-opioid agonist activity.11 Duda et al. also observed that fentanyl attenuated haemodynamic responses to endotracheal intubation more effectively than nalbuphine, although both agents maintained acceptable cardiovascular stability throughout anaesthesia.6 The absence of clinically significant differences in the present study may be attributed to gradual propofol titration, standardized anaesthetic management, and adequate timing

between opioid administration and induction.Opioid-related adverse effects remain an important determinant when selecting an induction adjunct. Respiratory depression, postoperative nausea and vomiting, pruritus, and excessive sedation are among the most frequently encountered complications associated with perioperative opioid administration. In the present study, respiratory depression was not observed in either group, while the incidences of hypotension, bradycardia

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consumption, recovery characteristics, and patient satisfaction were not evaluated. Future multicentre randomized controlled trials with larger sample sizes, incorporation of depth-of-anaesthesia monitoring, and assessment of postoperative recovery outcomes would further clarify the optimal role of nalbuphine as an alternative induction adjunct to fentanyl.

CONCLUSION

Fentanyl demonstrated significantly greater propofol-sparing efficacy than nalbuphine during induction of general anaesthesia, requiring a lower propofol dose to achieve loss of eyelash reflex. Nalbuphine, however, produced significantly higher pre-induction sedation while maintaining haemodynamic stability, and peri-induction safety comparable to fentanyl. The incidences of hypotension, bradycardia, respiratory depression, postoperative nausea and vomiting, and pruritus were low and similar between the two groups. These findings suggest that fentanyl remains the preferred opioid adjunct when minimizing propofol requirement is the primary objective, whereas nalbuphine may represent a safe and effective alternative when greater pre-induction sedation and the pharmacological advantages of a κ-agonist/μ-antagonist opioid are desired. Further multicentre randomized studies with larger sample sizes are warranted to validate these findings and determine the optimal role of nalbuphine in balanced anaesthesia.

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ABBREVIATIONS

Abbreviation	Full Form
ASA	American Society of Anesthesiologists
ASA PS	American Society of Anesthesiologists Physical Status
BMI	Body Mass Index
BP	Blood Pressure
DBP	Diastolic Blood Pressure
GA	General Anaesthesia
HR	Heart Rate
IV	Intravenous
MAP	Mean Arterial Pressure
PONV	Postoperative Nausea and Vomiting

Abbreviation	Full Form
RSS	Ramsay Sedation Scale
SBP	Systolic Blood Pressure
SD	Standard Deviation
SpO_2	Peripheral Oxygen Saturation
µg	Microgram
mg	Milligram

References

1. Langley MS, Heel RC. Propofol. A review of its pharmacodynamic and pharmacokinetic properties and use as an intravenous anaesthetic. Drugs 1988;35:334-72.
2. Goodchild CS. Propofol-induced cardiovascular depression: science and art. Br J Anaesth 2015;115:641-2.
3. Lundy JS. Balanced anesthesia. Minn Med 1926;9:399-404.
4. Ben-Shlomo I, Finger J, Bar-Av E, et al. Propofol and fentanyl act additively for induction of anaesthesia. Anaesthesia 1993;48:111-3.
5. Errick JK, Heel RC. Nalbuphine. A preliminary review of its pharmacological properties and therapeutic efficacy. Drugs 1983;26:191-211.
6. Duda D, Müller H, Brandt L. Comparative clinical study of nalbuphine and fentanyl. Effects and side effects with special reference to the induction phase. Anaesthesist 1987;36:407-11.
7. Marik PE. Propofol: therapeutic indications and side-effects. Curr Pharm Des 2004;10:3639-49.
8. Darlong V, Som A, Baidya DK, et al. Effect of varying time intervals between fentanyl and propofol administration on propofol requirement for induction of anaesthesia: a randomised controlled trial. Indian J Anaesth 2019;63:826-33.
9. Kaur J, Srilata M, Padmaja D, et al. Dose sparing of induction dose of propofol by fentanyl and butorphanol: a comparison based on entropy analysis. J Anaesthesiol Clin Pharmacol 2013;29:128-33.
10. Stoelting RK, Hillier SC. Pharmacology and Physiology in Anesthetic Practice. 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2015.
11. Khan FA. Comparison of fentanyl and nalbuphine in total intravenous anaesthesia (TIVA). Journal of Pakistan Medical Association. 2002;52(10):459
12. Yaksh TL, Wallace MS. Opioids, analgesia and pain management. In: Brunton LL, Hilal-Dandan R, Knollmann BC, eds. Goodman & Gilman's The Pharmacological Basis of Therapeutics. 13th ed. New York: McGraw-Hill; 2018.