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Comparative Study of Butorphanol, Fentanyl, and Nalbuphine for Total Intravenous Anesthesia in Laparoscopic Cholecystectomy

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Abstract

Background: Total intravenous anaesthesia (TIVA) with propofol and opioids is widely used in laparoscopic surgeries, but the choice of opioid significantly impacts analgesia, sedation, and recovery. Agonist-antagonist opioids like butorphanol and nalbuphine may offer safer alternatives to traditional agonists like fentanyl.

Aim: To compare the efficacy, safety, and recovery profiles of butorphanol, fentanyl, and nalbuphine as adjuvants to propofol-based TIVA in patients undergoing laparoscopic cholecystectomy.

Material and Methods: A prospective randomized study was conducted in 120 patients. Patients were allocated into three groups: Group I (butorphanol), Group II (fentanyl), and Group III

(nalbuphine). Demographic data, duration of anaesthesia, analgesia, sedation, emergence and recovery times were recorded. Statistical analysis was performed using ANOVA and chi-square tests.

Results: All groups were demographically comparable. Nalbuphine provided the longest analgesia and sedation, but with slightly longer emergence and recovery times. Fentanyl showed the fastest emergence and recovery but the shortest analgesic duration. Statistically significant differences were observed in analgesia, sedation, emergence, and recovery times ($p < 0.05$).

Conclusion: Both butorphanol and nalbuphine are effective and safe alternatives to fentanyl in TIVA, offering longer analgesia and sedation with acceptable recovery profiles. Their use may help reduce adverse effects and opioid misuse potential in surgical settings.

Keywords: Butorphanol, fentanyl, nalbuphine, TIVA, laparoscopic cholecystectomy, analgesia, recovery

Introduction

Laparoscopic cholecystectomy has become the gold standard for the treatment of gallbladder diseases, offering faster recovery, minimal pain, and shorter hospital stays compared to open surgery [1]. Total intravenous anaesthesia (TIVA), which uses hypnotic agents and opioids without inhalational agents, has gained popularity in laparoscopic procedures due to its advantages of smoother induction, stable hemodynamics, reduced postoperative nausea and vomiting (PONV), and faster emergence from anaesthesia [2].

Opioids are the mainstay of analgesia in TIVA, with fentanyl being one of the most widely used due to its potent analgesic and rapid onset of action [3]. However, fentanyl and other pure agonist opioids have notable limitations, including dose-dependent respiratory depression, bradycardia, chest

wall rigidity, and high misuse potential, making them scheduled medications with restricted availability in many centers [4].

Butorphanol and nalbuphine are mixed agonist-antagonist opioids that offer analgesic and sedative properties with a lower risk of respiratory depression and fewer adverse effects [5]. Butorphanol, a κ-receptor agonist and μ-receptor partial agonist, has been shown to provide excellent analgesia, sedation, and cardiovascular stability during surgical procedures [6]. Nalbuphine, another κ-agonist and μ-antagonist, similarly provides analgesia with a ceiling effect on respiratory depression, making it an attractive alternative to pure μ-agonist opioids [7].

Recent studies have highlighted the potential of these agents as opioid alternatives or adjuvants to propofol-based TIVA, especially in laparoscopic surgeries where stable hemodynamics and rapid recovery are critical [8]. Compared to fentanyl, butorphanol and nalbuphine have demonstrated comparable or superior analgesic efficacy, with lower incidence of PONV, pruritus, and respiratory complications [9]. Moreover, their reduced abuse liability makes them particularly valuable in settings with restricted opioid regulations or concerns about opioid diversion [10].

Despite these promising findings, there is limited comparative research evaluating the role of butorphanol and nalbuphine against standard opioids like fentanyl in the Indian context, especially in laparoscopic cholecystectomy under TIVA. This study aims to assess the efficacy, safety, and clinical profile of butorphanol, fentanyl, and nalbuphine as adjuvants to propofol-based TIVA, providing evidence that could help optimize opioid selection and improve perioperative care in resource-limited settings.

Material and Methods

This was a prospective, randomized, double-blind comparative study conducted in the Department of Anaesthesiology at a tertiary care hospital in India.

A total of 120 adult patients, aged 18–60 years, of ASA physical status I and II, undergoing elective laparoscopic cholecystectomy under total intravenous anaesthesia (TIVA) were enrolled in the study.

Inclusion Criteria:

- Patients aged 18–60 years.
- ASA grade I or II.
- Scheduled for elective laparoscopic cholecystectomy under TIVA.
- Provided written informed consent.

Exclusion Criteria:

- Known allergy to study drugs.
- History of opioid abuse or chronic analgesic use.
- Severe hepatic, renal, or cardiopulmonary disease.
- Pregnancy or lactation.

Patients were randomly divided into three groups (n=40 each) using a computer-generated randomization table:

- Group I (Butorphanol group): Received butorphanol 1 mg IV as an adjuvant to propofol-based TIVA.
- Group II (Fentanyl group): Received fentanyl 2 μg/kg IV as an adjuvant to propofol-based TIVA.
- Group III (Nalbuphine group): Received nalbuphine 0.2 mg/kg IV as an adjuvant to propofol-based TIVA.

Anaesthetic Protocol:

- All patients were premedicated with midazolam 0.02 mg/kg IV and glycopyrrolate 0.004 mg/kg IV.
- After preoxygenation, induction was done with propofol 2–2.5 mg/kg IV and the assigned study drug.
- Muscle relaxation was achieved using vecuronium 0.1 mg/kg IV, and maintenance was done with propofol

infusion (100–150 µg/kg/min) along with oxygen and air.

- Hemodynamic parameters (heart rate, blood pressure), depth of anaesthesia (BIS monitoring if available), and adverse events (hypotension, bradycardia, respiratory depression, nausea, vomiting) were recorded.

Outcome Measures:

- Primary outcome: Efficacy of analgesia and hemodynamic stability.
- Secondary outcomes: Sedation scores, intraoperative opioid requirement, postoperative pain scores (VAS), time to recovery, incidence of adverse events.

Statistical Analysis

Data were analyzed using SPSS software. Continuous variables were expressed as mean ± SD and compared using ANOVA or Student's t-test. Categorical variables were compared using chi-square or Fisher's exact test. A p-value <0.05 was considered statistically significant.

the Institutional Ethics Committee approved the study protocol. Written informed consent was obtained from all participants prior to enrollment.

Results

Table 1 shows the demographic characteristics of patients across the three groups. The mean ages and weights were comparable among groups, with no significant differences. Gender distribution was balanced, maintaining homogeneity between the study arms.

Table 2 summarizes the duration of anaesthesia, analgesia, and sedation. While the duration of anaesthesia was comparable across groups ($p = 0.07$), significant differences were seen in analgesia and sedation duration. Group III (nalbuphine) showed the longest duration of analgesia (156.2 min), followed by Group I (butorphanol, 122.5 min), and Group II

(fentanyl, 72.4 min), with a p-value of 0.002. Sedation was absent in Group II (fentanyl) but was significantly longer in Group III compared to Group I (p = 0.001).

Table 3 presents recovery characteristics. Emergence time was shortest in Group II (3.7 min) and longest in Group III (5.1 min), while recovery time was fastest in Group II (1.2 min), followed by Group III (1.5 min) and Group I (1.8 min). Both variables showed statistically significant differences across groups (p = 0.001).

Table 1: Demographic Parameters

Variable	Group I (Mean ± SD)	Group II (Mean ± SD)	Group III (Mean ± SD)	p value
Age (years)	38.6 ± 10.1	37.4 ± 10.5	39.9 ± 9.5	0.11
Weight (kg)	59.2 ± 8.1	58.9 ± 8.0	62.3 ± 6.2	0.50
Gender (M:F)	40:40	38:42	37:43	0.18

Table 2: Duration of Anaesthesia, Analgesia, and Sedation

Variable	Group I (Mean ± SD)	Group II (Mean ± SD)	Group III (Mean ± SD)	p value
Duration of anaesthesia (min)	62.1 ± 10.5	65.2 ± 13.1	66.4 ± 9.4	0.07
Duration of analgesia (min)	122.5 ± 8.3	72.4 ± 7.0	156.2 ± 18.6	0.002*
Duration of sedation (min)	6.0 ± 1.1	0	12.9 ± 5.1	0.001*

Table 3: Recovery Characteristics: Emergence Time and Recovery Time

Variable	Group I (Mean ± SD)	Group II (Mean ± SD)	Group III (Mean ± SD)	p value
Emergence time (min)	4.6 ± 0.3	3.7 ± 0.9	5.1 ± 1.1	0.001*
Recovery time (min)	1.8 ± 0.5	1.2 ± 0.5	1.5 ± 0.6	0.001*

Discussion

This study aimed to compare the efficacy, safety, and recovery profiles of butorphanol, fentanyl, and nalbuphine as adjuvants to propofol-based total intravenous anaesthesia (TIVA) in patients undergoing laparoscopic cholecystectomy. The findings provide valuable insights into the role of agonist-antagonist opioids as alternatives to traditional μ-agonist opioids, particularly in the Indian tertiary care setting.

The demographic characteristics, including age, weight, and gender distribution, were comparable across all three groups, ensuring that the groups were homogenous and that outcome differences were attributable to the choice of opioid rather than baseline characteristics. This consistency aligns with prior randomized trials where demographic homogeneity was essential for valid comparisons [11].

The duration of analgesia was significantly longer in the nalbuphine group (Group III), followed by the butorphanol group (Group I), and shortest in the fentanyl group (Group II), with a p-value of 0.002. This supports recent evidence that nalbuphine, a κ-agonist and μ-

antagonist, offers prolonged analgesia with minimal respiratory depression compared to fentanyl [12]. Butorphanol's intermediate analgesic duration may reflect its partial μ-agonist action, providing balanced sedation and pain relief [13].

Regarding sedation, nalbuphine again showed the longest effect, while fentanyl provided no measurable sedation in this study. This is consistent with prior reports indicating that nalbuphine and butorphanol offer moderate sedation, which can be advantageous in intraoperative settings where patient immobility is essential [14].

Importantly, recovery characteristics demonstrated significantly shorter emergence and recovery times in the fentanyl group compared to butorphanol and nalbuphine. While fentanyl's rapid offset is well-known, this finding raises practical considerations: although fentanyl offers faster emergence, its shorter analgesic duration may necessitate additional postoperative pain management [15]. Conversely, nalbuphine's slower recovery may be balanced by its prolonged analgesic benefits and lower risk of opioid-induced respiratory depression.

One key advantage of butorphanol and nalbuphine over fentanyl is their lower potential for misuse and more favorable regulatory status, making them especially appealing in resource-limited settings with restricted opioid availability. This is particularly relevant in India, where strict opioid regulations can limit fentanyl use in non-cancer pain settings [12].

Overall, this study supports the view that both butorphanol and nalbuphine are effective alternatives to fentanyl in propofol-based TIVA, offering longer analgesia and acceptable sedation without significantly compromising recovery times. Further large-scale trials are warranted to confirm these results and optimize dosing strategies.

Conclusion

In conclusion, nalbuphine provided the longest duration of analgesia and sedation, followed by butorphanol, while fentanyl offered the fastest emergence and recovery. Both butorphanol and nalbuphine demonstrated efficacy as alternatives to fentanyl in propofol-based TIVA, with the added advantage of a lower adverse effect profile and reduced misuse potential. Incorporating agonist-antagonist opioids into TIVA protocols may improve patient outcomes and increase access to safe anaesthetic practices, particularly in regions with opioid restrictions.

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