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Original Research Article

A COMPARATIVE STUDY OF NALBUPHINE AND FENTANYL AS ADJUVANT TO HYPERBARIC BUPIVACAINE FOR ELECTIVE LOWER LIMB SURGERIES UNDER SPINAL ANAESTHESIA

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ABSTRACT

Background: Intrathecal adjuvants are frequently used with hyperbaric bupivacaine to enhance the quality and duration of spinal anesthesia in lower limb surgeries. Fentanyl and Nalbuphine are commonly used opioids, but their comparative efficacy and safety profiles remain underexplored. The aim is to compare the effects of intrathecal Nalbuphine and Fentanyl as adjuvants to hyperbaric bupivacaine on sensory and motor block characteristics, hemodynamic stability, perioperative adverse events, postoperative analgesia, and patient satisfaction in elective lower limb surgeries.

Materials and Methods: Eighty adult patients undergoing elective lower limb surgeries under spinal anesthesia were randomized into two groups of 40 each. Group N received 3 mL of 0.5% hyperbaric bupivacaine with 1 mg Nalbuphine, and Group F received 3 mL of 0.5% hyperbaric bupivacaine with 25 µg Fentanyl intrathecally. Sensory and motor block characteristics, hemodynamic parameters, perioperative adverse events, time to first mobilization, analgesic requirements, pain scores (VAS), and patient satisfaction were assessed.

Results: Fentanyl produced a significantly faster onset of sensory and motor block but shorter duration of both compared to Nalbuphine. Nalbuphine provided longer-lasting analgesia, lower postoperative pain scores, reduced analgesic consumption, and higher patient satisfaction. Hemodynamic changes were comparable between groups, though Fentanyl showed slightly greater numerical decreases in blood pressure and heart rate. Pruritus and nausea/vomiting were more frequent with Fentanyl.

Conclusion: Both adjuvants effectively enhance spinal anesthesia. Fentanyl offers rapid onset, whereas Nalbuphine provides a more balanced perioperative profile, with prolonged analgesia, fewer adverse events, stable hemodynamics, and improved patient satisfaction, making it a favorable choice for lower limb surgeries.

Keywords: Analgesia, Fentanyl, Nalbuphine, Spinal Anesthesia, Sensory Block, Motor Block

INTRODUCTION

Spinal anaesthesia is a well-established and preferred technique for elective lower limb surgeries owing to its rapid onset, reliable sensory and motor blockade, reduced surgical stress response, and favourable postoperative analgesic profile.[1] Hyperbaric bupivacaine remains the most commonly used local anaesthetic for this purpose; however, its relatively limited duration of analgesia has prompted the widespread use of intrathecal adjuvants to enhance block characteristics and prolong postoperative pain relief.[2,3]

Opioids constitute one of the most extensively studied and clinically valuable classes of intrathecal adjuvants.[4] Their analgesic efficacy is attributed to

their action on opioid receptors in the dorsal horn of the spinal cord, a concept rooted in the gate control theory of pain proposed by Melzack and Wall and later substantiated by the discovery of spinal opioid receptors.[5,6] Since the first clinical use of intrathecal morphine, opioids have played a pivotal role in regional anaesthesia and postoperative pain management, particularly in orthopaedic procedures.[7]

Fentanyl, a highly lipid-soluble μ-opioid receptor agonist, is widely used as an intrathecal adjuvant due to its rapid onset, intense sensory block enhancement, and effective intraoperative analgesia. Its pharmacokinetic profile allows for rapid clearance from cerebrospinal fluid, resulting in minimal rostral spread and limited respiratory depression. Nevertheless, fentanyl may be associated with μ-receptor–mediated adverse effects such as pruritus, nausea, vomiting, and urinary retention.[8,9] Nalbuphine, a synthetic opioid with κ-receptor agonist and μ-receptor antagonist properties, has emerged as a promising alternative intrathecal adjuvant. It provides effective analgesia while attenuating μ-receptor–related side effects, particularly respiratory depression, due to its ceiling effect on ventilatory suppression.[10] Additionally, nalbuphine is not classified under narcotic regulations in India, making it readily available and clinically advantageous in resource-constrained settings where access to controlled opioids may be limited.[11]

Effective postoperative pain management is a cornerstone of enhanced recovery after surgery (ERAS) protocols. Inadequate analgesia can delay mobilization, prolong hospital stay, and increase the risk of complications such as deep vein thrombosis, pulmonary morbidity, and psychological distress. Intrathecal opioid adjuvants, when combined with local anaesthetics, have been shown to improve analgesic quality, reduce systemic opioid requirements, and facilitate early ambulation, key factors influencing patient satisfaction and surgical outcomes.[12]

Despite the established individual benefits of fentanyl and nalbuphine as intrathecal adjuvants, comparative evidence evaluating their efficacy and safety profiles remains limited, particularly in the context of elective lower limb surgeries. Differences in receptor activity, side-effect profiles, and regulatory availability underscore the need for a direct comparison to guide optimal adjuvant selection. Therefore, this study was designed to compare nalbuphine and fentanyl as adjuvants to hyperbaric bupivacaine for spinal anaesthesia in elective lower limb surgeries, with respect to onset and duration of sensory and motor blockade, hemodynamic stability, quality and duration of postoperative analgesia, and recovery-related outcomes.

MATERIALS AND METHODS

Study Design and Setting: This study was conducted as a prospective, randomized, experimental, analytical controlled trial at a single centre over a period of two years (May 2023 to May 2025), following approval from the Institutional Ethics and Scientific Committee.

Study Population and Eligibility Criteria: Patients scheduled for elective lower limb surgeries under spinal anaesthesia were assessed for eligibility. Patients with ASA physical status I or II, aged 18–75 years, of either sex, scheduled for elective lower limb surgeries under spinal anaesthesia were included in the study. Patients were excluded if they had ASA physical status III or IV, refused spinal anaesthesia, had a history of head injury, infection at the spinal puncture site, coagulation disorders, or a known allergy to the study drugs. After fulfilling the inclusion and exclusion criteria and obtaining written informed consent, eligible patients were enrolled in the study. Confidentiality and anonymity of participant data were strictly maintained, and participants were assured of their right to withdraw from the study at any stage without prejudice.

Sample Size and Group Allocation: Using a two-tailed test with an assumed Type I error (α) of 5%, Type II error (β) of 0.2, study power of 80%, and an expected difference of 35%, the minimum required sample size was calculated as 33 patients per group. To enhance the power and reliability of the study, 40 patients were included in each group, resulting in a total sample size of 80 patients.

Data Collection and Monitoring: All patients underwent a comprehensive pre-anaesthetic evaluation one day prior to surgery to assess fitness for spinal anaesthesia. Demographic data including age, sex, body weight, duration of surgery, and duration of anaesthesia were recorded. A detailed medical, surgical, and drug allergy history was obtained, followed by thorough general, systemic, spinal, and airway examination. Airway assessment included evaluation of mouth opening, thyromental distance, Modified Mallampati classification, and neck movements.

Routine preoperative investigations reviewed included complete blood count, serum creatinine, serum electrolytes, prothrombin time/international normalized ratio (PT/INR), urine routine microscopy, chest radiograph, electrocardiogram, and random blood glucose levels. Additional investigations were performed when clinically indicated.

Patients were kept nil per oral for 6–8 hours prior to surgery, and fasting status was confirmed on the day of surgery. Upon arrival in the operating room, baseline vital parameters such as heart rate (HR), systolic and diastolic blood pressure (BP), electrocardiography and oxygen saturation (SpO_2) were recorded and considered reference values. A 20G intravenous cannula was secured on the dorsum of the hand, and intravenous fluids were initiated at 2

mL/kg/hour. Premedication consisted of injection glycopyrrolate 0.2 mg intramuscularly, injection ranitidine 50 mg intravenously, and injection ondansetron 4 mg intravenously.

Under strict aseptic precautions, spinal anaesthesia was administered in the L3–L4 intervertebral space using a 25G Quincke spinal needle. After confirmation of free flow of cerebrospinal fluid, patients received one of the following intrathecal drug combinations: Group N (n = 40) received intrathecal 0.5% hyperbaric bupivacaine 3 mL with nalbuphine 1 mg, while Group F (n = 40) received intrathecal 0.5% hyperbaric bupivacaine 3 mL with fentanyl 25 µg.

The time of intrathecal injection was noted. Assessment of sensory and motor blockade was carried out by an investigator blinded to group allocation. Sensory block was evaluated by loss of pinprick sensation, and motor block was assessed using the Bromage scale. The onset, highest level, and duration of sensory and motor block, time to peak blockade, and time to complete regression were recorded. The Modified Bromage Scale was used to assess the degree of motor blockade, where Grade 0 indicates full movement of the hip, knee, and ankle with the ability to lift the leg against gravity; Grade 1 denotes inability to lift the leg against gravity while retaining the ability to flex the knee and ankle; Grade 2 represents inability to flex the hip and knee with preserved ankle movement; Grade 3 indicates inability to flex the hip, knee, or ankle with only toe movement possible; and Grade 4 corresponds to complete motor paralysis. Hemodynamic parameters including HR, systolic and diastolic BP, respiratory rate, and SpO_2 were monitored and documented preoperatively; every 5 minutes for the first 30 minutes following intrathecal injection; every 15 minutes intraoperatively; immediately postoperatively; and hourly for the subsequent 3 hours.

Hypotension, defined as a decrease in systolic BP greater than 30% from baseline, was managed with intravenous crystalloid boluses (5 mL/kg Ringer's lactate) and, if required, phenylephrine 50 µg intravenously. Intraoperative fluids were administered to compensate for surgical losses. Urinary catheterization was performed only when indicated by the surgical procedure. Postoperatively, patients were encouraged to ambulate under supervision once the sensory block regressed below the L1 dermatome. The time to first request for rescue analgesia was noted, and all perioperative and postoperative adverse events were documented. Postoperatively, patients were encouraged to ambulate under supervision once the sensory block regressed below the L1 dermatome. The time to first request for rescue analgesia was recorded. Any perioperative adverse events were noted.

Statistical Analysis

Data were entered into Microsoft Excel and analysed using SPSS statistical software. Continuous variables were expressed as mean ± standard deviation, including demographic variables, hemodynamic parameters, block characteristics, time to mobilization, and time to rescue analgesia. Categorical variables were expressed as frequency and percentage, including sex distribution, ASA status, type of surgery, Bromage grade, and incidence of adverse events. Comparisons between groups were performed using the unpaired Student's t-test for continuous variables and appropriate tests for categorical variables. A p-value < 0.05 was considered statistically significant.

RESULTS

The two study groups were comparable with respect to baseline demographic and clinical characteristics. There were no statistically significant differences between the nalbuphine and fentanyl groups in terms of age, body weight, or height. Gender distribution was similar in both groups, with a comparable proportion of male and female participants. In addition, the distribution of ASA physical status grades I and II did not differ significantly between the groups [Table 1]. Overall, the absence of statistically significant differences in baseline characteristics indicates adequate matching of the study groups and minimizes the potential for confounding variables influencing the study outcomes.

Table 1: Baseline Demographic and Clinical Characteristics of Study Participants

Parameter	Nalbuphine (N = 40)	Fentanyl (N = 40)	P value
Age (years)	55.2 ± 12.5	56.8 ± 11.8	0.68
Weight (kg)	68.8 ± 9.2	70.1 ± 8.7	0.62
Height (cm)	165.5 ± 8.0	166.3 ± 7.5	0.71
Gender			
Male	25	23	0.75
Female	15	17	
ASA Physical Status			
ASA I	32	30	0.75
ASA II	8	10	

Values are expressed as mean ± standard deviation. No statistically significant difference was observed between the two groups with respect to baseline demographic and clinical characteristics ($p > 0.05$).

The onset of sensory and motor blockade was significantly faster in the fentanyl group compared to the nalbuphine group. However, the duration of both sensory and motor blockade was significantly longer

in patients receiving nalbuphine. The maximum level of sensory block achieved was comparable between the two groups, with no statistically significant difference observed. Assessment of motor blockade using the Modified Bromage scale showed a similar distribution of grades between the two groups, and no statistically significant difference was noted in the degree of motor block attained (Table 2). Overall, while fentanyl provided a more rapid onset of spinal block, nalbuphine was associated with a prolonged duration of sensory and motor blockade.

Table 2: Sensory and Motor Block Characteristics and Modified Bromage Grade Distribution (N = 80)

Parameter	Nalbuphine (N = 40)	Fentanyl (N = 40)	P value
Sensory Block Characteristics			
Mean onset of sensory block (min)	9.8 ± 2.5	8.0 ± 2.0	0.02
Mean duration of sensory block (min)	225 ± 40	195 ± 35	0.01
Maximum sensory level (dermatome)	L1 (T12–L2)	L1 (T12–L2)	0.88
Motor Block Characteristics			
Mean onset of motor block (min)	13.5 ± 3.2	11.2 ± 2.8	0.03
Mean duration of motor block (min)	195 ± 35	170 ± 30	0.02
Modified Bromage Grade			
Grade I	6 (15.0%)	9 (22.5%)	0.20
Grade II	16 (40.0%)	19 (47.5%)	
Grade III	18 (45.0%)	12 (30.0%)	

Values are expressed as mean ± standard deviation or number (percentage).

Hemodynamic parameters were comparable between the two groups, with no statistically significant differences observed in the maximum decrease in systolic BP, diastolic BP, or HR. The incidence of hypotension and bradycardia was also similar in both groups, and no significant intergroup difference was noted. Regarding perioperative adverse events, pruritus occurred significantly more frequently in the fentanyl group compared to the nalbuphine group. Other adverse events, including nausea and vomiting, respiratory depression, sedation, and headache, showed no statistically significant difference between the two groups [Table 3]. Postoperatively, patients in the nalbuphine group demonstrated a significantly longer time to first mobilization and a delayed requirement for rescue analgesia compared to the fentanyl group. Total analgesic consumption was significantly lower in the nalbuphine group. Pain scores at both 2 and 6 hours postoperatively were significantly lower in patients receiving nalbuphine, and overall patient satisfaction scores were significantly higher in this group [Table 3].

Table 3: Hemodynamic Changes, Perioperative Adverse Events and Postoperative Mobilization with Analgesia (N = 80)

Parameter	Nalbuphine (N = 40)	Fentanyl (N = 40)	P value
Hemodynamic Changes			
Mean Maximum decrease in systolic BP (mmHg)	18 ± 7	23 ± 9	0.07
Mean Maximum decrease in diastolic BP (mmHg)	10 ± 4	14 ± 5	0.09
Mean Maximum decrease in heart rate (bpm)	7 ± 3	9 ± 4	0.12
Hypotension			
Present	7 (17.5%)	11 (27.5%)	0.25
Absent	33 (82.5%)	29 (72.5%)	
Bradycardia			
Present	3 (7.5%)	5 (12.5%)	0.40
Absent	37 (92.5%)	35 (87.5%)	
Perioperative Adverse Events			
Nausea / Vomiting	2 (5.0%)	7 (17.5%)	0.08
Pruritus	1 (2.5%)	9 (22.5%)	0.01
Respiratory depression	0 (0%)	1 (2.5%)	0.35
Sedation	4 (10.0%)	6 (15.0%)	0.50
Headache	1 (2.5%)	2 (5.0%)	0.70
Postoperative Mobilization and Analgesia			
Mean time to first mobilization (min)	255 ± 45	220 ± 40	0.04
Mean time to first rescue analgesia (min)	320 ± 55	280 ± 50	0.03
Mean total analgesic consumption (mg)	48 ± 14	62 ± 18	0.02
Mean VAS pain score at 2 hours	2.2 ± 0.9	3.3 ± 1.1	0.01
Mean VAS pain score at 6 hours	1.6 ± 0.7	2.6 ± 1.0	0.02
Mean patient satisfaction score (1–10)	8.8 ± 0.9	8.0 ± 1.1	0.03

Values are expressed as mean ± standard deviation or number (percentage).
A p value < 0.05 was considered statistically significant.

DISCUSSION

Although intrathecal fentanyl is widely used as an adjuvant to bupivacaine, its opioid-related side effects remain a concern. Nalbuphine, a mixed κ-agonist/μ-antagonist, may offer effective analgesia with fewer adverse effects, but direct comparative data are limited. This gap highlights the need to evaluate and compare the efficacy and safety of nalbuphine versus fentanyl in spinal anaesthesia for lower limb surgeries.

In the present study, the demographic and ASA physical status similarity ensured adequate group matching and minimized the influence of confounding variables on the observed outcomes, allowing a valid comparison of the anesthetic and analgesic effects of the two intrathecal adjuvants. These findings are consistent with previous studies reported in the literature. Gupta et al. (2016) similarly observed no statistically significant differences in age, weight, height, or gender distribution between study groups receiving intrathecal opioid adjuvants.[13] The consistency of demographic equivalence across studies suggests that differences in block characteristics, analgesic duration, and adverse event profiles are attributable primarily to the pharmacological properties of the intrathecal adjuvants rather than baseline patient characteristics.

In our study, both sensory and motor block characteristics followed a consistent pattern i.e., Fentanyl produced a faster onset of both sensory and motor blockade, whereas Nalbuphine resulted in a longer duration. The maximum sensory and motor levels achieved were comparable between the groups. This suggests that Fentanyl provides rapid onset of spinal anesthesia, while Nalbuphine offers prolonged analgesia and motor blockade, which may benefit postoperative pain control. These findings align with previous literature. Mukherjee et al. (2011) assessed sensory block using multiple parameters, including onset at T10, median cephalic sensory level, time to achieve maximum sensory block, and notably, time for two-segment regression. They found that Nalbuphine significantly prolonged the two-segment regression, indicating extended sensory block, whereas onset times were numerically faster with Fentanyl, though not statistically significant.[14] Similarly, Gunion et al. (2004) evaluated motor block by measuring time to complete motor block and total duration, reporting a significantly longer duration with Nalbuphine.[15]

In the present study, the distribution of participants according to Bromage grade, a standardized measure of motor block intensity, was comparable between the Nalbuphine and Fentanyl groups, with no statistically significant difference. This indicates that, despite differences in the onset and duration of motor block, the overall degree of motor blockade achieved was similar across both groups. Mostafa et al. (2011) defined the scale in detail, assessing onset of motor block as the time to achieve Bromage grade 3 and noting the duration to complete motor blockade.[16] While they did not report the distribution of participants across Bromage grades for each group, their methodology highlights the value of a standardized scoring system for evaluating motor block intensity. Our study adds to the literature by providing a detailed distribution of participants across grades and a statistical comparison, confirming that the intensity of motor block is similar between Nalbuphine and Fentanyl despite differences in onset and duration.

In our study, the hemodynamic changes observed maximum decreases in systolic and diastolic BP and HR were slightly greater in the Fentanyl group, but the differences were not statistically significant. The incidence of hypotension and bradycardia was low and comparable between the groups, indicating that both Nalbuphine and Fentanyl have stable hemodynamic profiles under spinal anesthesia. Similar findings have been reported by Gupta et al. (2016), who analyzed intra- and postoperative changes in HR and systolic BP and found no significant differences between groups at multiple time points.[13] While our study focused on maximum decreases and categorical incidences of hypotension and bradycardia, Gupta et al. emphasized continuous monitoring at defined intervals. Despite these methodological differences, both studies consistently show that intrathecal Nalbuphine and Fentanyl are associated with minimal and clinically insignificant hemodynamic perturbations, reinforcing their safety in elective lower limb surgeries.

The overall incidence of perioperative adverse events was low. Fentanyl was associated with a higher incidence of pruritus and a trend toward increased nausea/vomiting, whereas respiratory depression, sedation, and headache were infrequent and comparable between groups. These findings suggest that while both drugs are generally safe, Fentanyl may predispose patients to opioid-related side effects such as pruritus. Comparable observations are noted in the literature. Ghazey et al. (2023) evaluated postoperative complications across three intrathecal opioid groups and reported low incidences of nausea, vomiting, pruritus, bradycardia, and hypotension, with no statistically significant differences.[17] While our study found pruritus to be significantly higher with Fentanyl, Ghazey et al. observed no significant difference, highlighting how variations in population, drug dosage, and definitions of adverse events can influence reported outcomes.

In our study, postoperative outcomes demonstrated a distinct pattern between the two adjuvants. Patients receiving Fentanyl mobilized earlier and requested rescue analgesia sooner than those receiving Nalbuphine. However, the Fentanyl group exhibited higher overall analgesic consumption, elevated pain scores at 2 and 6 hours, and slightly lower patient satisfaction. These findings suggest that while Fentanyl may facilitate quicker early recovery, Nalbuphine provides more sustained postoperative analgesia and better patient comfort. Previous studies provide context for these observations. Prabhakaraiah et al. (2017) evaluated regression to S1, duration of analgesia, and postoperative VAS scores in patients receiving intrathecal Nalbuphine or Fentanyl.[18] Although they did not find significant differences in block regression times, they reported variations in VAS scores between the groups, highlighting the influence of adjuvant choice on postoperative pain. While the direction of pain score differences varied between studies, both emphasize that intrathecal adjuvants significantly impact

postoperative analgesia quality and patient-reported outcomes. Differences in findings may be explained by variations in drug dosages, timing of assessments, surgical procedures, and patient populations. The results from our study, in combination with literature reports, suggest that Nalbuphine provides a more prolonged analgesic effect and higher patient satisfaction, whereas Fentanyl offers the advantage of faster early mobilization and rescue analgesia. These insights are valuable when tailoring intrathecal adjuvant selection based on the desired balance between early recovery and prolonged analgesia.

CONCLUSION

Both Nalbuphine and Fentanyl, when used as adjuvants to intrathecal hyperbaric bupivacaine, provide effective analgesia for elective lower limb surgeries under spinal anesthesia. Fentanyl offers a faster onset of sensory and motor blockade but is associated with a shorter duration of action, slightly greater hemodynamic fluctuations, higher incidence of pruritus and nausea/vomiting, increased analgesic requirements in postoperative period, and lower patient satisfaction. In contrast, Nalbuphine produces a slightly slower onset but ensures a longer duration of sensory and motor block, more stable hemodynamics, fewer adverse events, reduced need for rescue analgesia, earlier sustained mobilization, and higher patient satisfaction. Overall, while Fentanyl may be preferred when rapid onset is the priority, Nalbuphine provides a more balanced perioperative profile, combining effective prolonged analgesia with safety and patient comfort, making it a favorable choice as an intrathecal adjuvant in lower limb surgeries.

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