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Original Research Article

COMPARATIVE EVALUATION OF SAFETY AND EFFICACY OF INTRATHECAL FENTANYL AND BUTORPHANOL AS ADJUVANTS TO 0.5% HEAVY BUPIVACAINE FOR LOWER LIMB ORTHOPEDIC SURGERIES

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ABSTRACT

Background: The study aimed to compare the safety and efficacy of intrathecal fentanyl and butorphanol as adjuvants to 0.5% heavy bupivacaine in patients undergoing lower limb orthopedic surgeries.

Material and Methods: A prospective, randomized, double-blind study was conducted with 140 patients aged 18-60 years scheduled for elective lower limb orthopedic surgeries under spinal anesthesia. Patients were randomly divided into two groups of 70 each. Group F received 15 mg of 0.5% heavy bupivacaine with 25 µg fentanyl intrathecally, while Group B received 15 mg of 0.5% heavy bupivacaine with 1 mg butorphanol. The total volume of intrathecal injection was standardized to 3.5 mL for both groups. Hemodynamic parameters and block characteristics were monitored at regular intervals, and adverse effects were recorded.

Results: Group F demonstrated a faster onset of sensory (4.1 ± 1.2 minutes) and motor block (6.5 ± 1.3 minutes) compared to Group B (5.3 ± 1.4 minutes and 7.2 ± 1.5 minutes, respectively), with statistically significant differences ($p < 0.001$ for sensory and $p = 0.03$ for motor). The duration of sensory and motor blocks was also significantly longer in Group F (145.6 ± 20.5 minutes and 130.3 ± 18.6 minutes, respectively) compared to Group B (130.8 ± 22.7 minutes and 115.4 ± 19.8 minutes, $p < 0.001$ for both). Group F had a longer time to first analgesic request (220.4 ± 30.2 minutes) and lower VAS scores for pain (1.8 ± 0.5) than Group B (195.3 ± 28.7 minutes and 2.1 ± 0.6, $p < 0.001$ and $p = 0.02$, respectively). Hemodynamic stability was maintained in both groups, with no significant differences in heart rate or blood pressure at any time point. Pruritus was more frequent in Group F (14.29%) compared to Group B (2.86%, $p = 0.02$), while other adverse effects were comparable between groups.

Conclusion: Intrathecal fentanyl as an adjuvant to 0.5% heavy bupivacaine provided faster onset, longer duration of blocks, and superior analgesia compared to butorphanol, though it was associated with a higher incidence of pruritus. Both drugs maintained stable hemodynamic profiles, demonstrating their safety and effectiveness for spinal anesthesia in lower limb orthopedic surgeries.

Keywords: Intrathecal fentanyl, Butorphanol, Bupivacaine, Lower limb orthopedic surgery, Spinal anesthesia.

INTRODUCTION

The management of pain and anesthesia during lower limb orthopedic surgeries is a crucial aspect of patient care that impacts both intraoperative conditions and postoperative recovery. Effective pain control not only enhances patient comfort but also facilitates early mobilization, decreases the risk of postoperative complications, and improves overall patient outcomes. Spinal anesthesia has become a preferred choice in lower limb surgeries due to its simplicity, cost-effectiveness, and ability to provide profound sensory and motor blockades while minimizing the risks associated with general anesthesia. However, achieving an optimal balance between effective analgesia, anesthesia, and the safety of patients is an ongoing challenge that drives research in the field of anesthesiology.[1] The use of intrathecal adjuvants, such as fentanyl and butorphanol, in combination with local anesthetics like bupivacaine has emerged as a promising approach to improve the quality and duration of spinal anesthesia. Bupivacaine, a long-acting local anesthetic, is widely used for spinal anesthesia due to its reliable and consistent effects. However, the onset of block with bupivacaine can be slow, and its duration, although long, may not always be sufficient for prolonged surgical procedures. Additionally, bupivacaine alone may not provide the desired level of postoperative analgesia. To overcome these limitations, opioid and non-opioid adjuvants have been studied for their potential to enhance the analgesic and anesthetic effects of bupivacaine, offering improved patient outcomes while maintaining a favorable safety profile.[2] Fentanyl, a synthetic opioid, has been extensively used as an adjuvant in spinal anesthesia due to its rapid onset of action, potent analgesic effects, and relatively short duration, which complements the properties of bupivacaine. By binding to opioid receptors in the central nervous system, fentanyl modulates pain perception, providing effective analgesia. Its lipophilic nature allows for rapid penetration into the central nervous system, resulting in a quicker onset of sensory block when combined with bupivacaine. The addition of fentanyl to bupivacaine has been associated with enhanced block characteristics, including a faster onset, prolonged duration of sensory and motor blocks, and superior pain relief. Despite these benefits, the use of fentanyl is not without side effects. Common adverse effects include pruritus, nausea, and, in rare cases, respiratory depression, which necessitates careful monitoring.[3,4] Butorphanol, on the other hand, is a synthetic opioid agonist-antagonist that acts on both kappa and mu opioid receptors. It provides potent analgesia while exhibiting a ceiling effect for respiratory depression, making it an attractive alternative to traditional opioids like fentanyl. The unique pharmacological profile of butorphanol allows it to provide effective pain relief with a potentially lower risk of severe respiratory side effects. Additionally, butorphanol has been reported to produce a sedative effect, which can be beneficial in the perioperative setting. When used as an intrathecal adjuvant, butorphanol has demonstrated the ability to prolong the duration of analgesia and improve patient comfort. However, its efficacy in comparison to fentanyl, especially in terms of onset time, block characteristics, and hemodynamic stability, remains an area of active investigation.[5,6]

MATERIALS AND METHODS

A prospective, randomized, double-blind comparative study was conducted to evaluate the safety and efficacy of intrathecal fentanyl and butorphanol as adjuvants to 0.5% heavy bupivacaine in patients undergoing lower limb orthopedic surgeries.

The study included 140 patients, aged 18-60 years, scheduled for elective lower limb orthopedic surgeries under spinal anesthesia. Patients were randomly allocated into two groups:

- Group F (n = 70): Received intrathecal bupivacaine 0.5% heavy with fentanyl.
- Group B (n = 70): Received intrathecal bupivacaine 0.5% heavy with butorphanol.

Exclusion criteria included patients with contraindications to spinal anesthesia, known allergies to study drugs, coagulation disorders, severe cardiovascular or respiratory illnesses, or BMI >35.

Participants in the study were randomly allocated into two groups using a computer-generated randomization sequence to ensure unbiased group assignment. Both the patients and the anesthesiologist responsible for outcome assessment were blinded to group allocation to minimize bias and improve the reliability of results. Drug preparation was handled by an independent anesthetist who was not involved in the care of the patients, maintaining the integrity of the double-blind study design.

In terms of intervention, patients in Group F received a combination of 15 mg (3 mL) of 0.5% heavy bupivacaine with 25 µg (0.5 mL) of fentanyl administered intrathecally. In contrast, patients in Group B were administered 15 mg (3 mL) of 0.5% heavy bupivacaine with 1 mg (0.5 mL) of butorphanol intrathecally. The total volume of the intrathecal injection was standardized to 3.5 mL for both groups to ensure consistency in drug administration.

The procedure began with all patients receiving a preload of 500 mL of Ringer's lactate solution to maintain hemodynamic stability. The subarachnoid block was performed under strict aseptic conditions at the L3-L4 or L4-L5 interspace using a 25G Quincke needle, with patients positioned in the sitting posture. Following the slow administration of

the intrathecal drugs, patients were promptly placed in the supine position to facilitate optimal drug distribution.

Monitoring and data collection were conducted meticulously. Baseline parameters, including heart rate (HR), non-invasive blood pressure (NIBP), oxygen saturation (SpO2), and respiratory rate, were recorded before the administration of anesthesia. Hemodynamic parameters were continuously monitored at 0, 5, 10, 20, 30, 40, 50, 60, 90, and 120 minutes after the intrathecal injection to assess the safety and stability of the anesthesia. The characteristics of the sensory and motor block were evaluated using a pinprick test and the Bromage scale, respectively, to determine the onset and quality of the anesthesia. The study aimed to measure both the efficacy and safety of the interventions. Efficacy outcomes included the time to onset of sensory and motor block, the duration of sensory and motor block, the time to the first analgesic request, and the overall quality of intraoperative analgesia, assessed using the visual analog scale (VAS). Safety outcomes focused on monitoring hemodynamic stability and recording any adverse effects, such as hypotension, bradycardia, pruritus, nausea, vomiting, respiratory depression, and any post-operative complications that may have occurred. This comprehensive approach to data collection ensured a thorough evaluation of both the analgesic and anesthetic effects of the two drug regimens.

Statistical Analysis

Data were analyzed using SPSS version 25.0. Continuous variables were presented as mean ± standard deviation (SD) and compared using an independent t-test. Categorical variables were presented as frequencies and percentages and compared using chi-square tests. A p-value of <0.05 was considered statistically significant.

RESULTS

Table 1: Baseline Demographics and Clinical Characteristics

The baseline characteristics of both groups were comparable, indicating that randomization was successful in creating similar groups for comparison. The mean age was 45.2 ± 8.6 years in Group F and 46.1 ± 9.1 years in Group B, with no significant difference ($p = 0.45$). Gender distribution was also similar between the two groups, with a male-to-female ratio of 42/28 in Group F and 40/30 in Group B ($p = 0.78$). The BMI was 24.5 ± 3.2 kg/m² in Group F and 24.8 ± 3.4 kg/m² in Group B ($p = 0.61$), and ASA grades were distributed evenly, with no statistically significant differences ($p = 0.72$). The mean duration of surgery was also similar between the groups, being 80.3 ± 15.4 minutes in Group F and 81.7 ± 16.1 minutes in Group B ($p = 0.63$). Overall, the demographic and clinical parameters did not differ significantly, ensuring that any differences in outcomes were likely due to the interventions rather than baseline variations.

Table 2: Sensory and Motor Block Characteristics

The onset and duration of sensory and motor block were assessed to evaluate the effectiveness of anesthesia. Group F showed a faster onset of sensory block at 4.1 ± 1.2 minutes compared to 5.3 ± 1.4 minutes in Group B, a statistically significant difference ($p < 0.001$). The duration of the sensory block was also significantly longer in Group F (145.6 ± 20.5 minutes) compared to Group B (130.8 ± 22.7 minutes) ($p < 0.001$). For the motor block, the onset was quicker in Group F (6.5 ± 1.3 minutes) compared to Group B (7.2 ± 1.5 minutes), with a significant difference ($p = 0.03$). Similarly, the duration of the motor block was longer in Group F (130.3 ± 18.6 minutes) compared to Group B (115.4 ± 19.8 minutes) ($p < 0.001$). These results suggest that intrathecal fentanyl provided a more rapid and prolonged block compared to butorphanol.

Table 3: Analgesic Efficacy

Analgesic efficacy was measured by the time to the first analgesic request and the VAS score for pain. Patients in Group F had a longer time to first analgesic request (220.4 ± 30.2 minutes) compared to Group B (195.3 ± 28.7 minutes), with this difference being statistically significant ($p < 0.001$). The VAS score, which measures pain intensity, was lower in Group F (1.8 ± 0.5) compared to Group B (2.1 ± 0.6), with a significant difference ($p = 0.02$). These findings indicate that fentanyl was more effective at providing prolonged and higher-quality analgesia compared to butorphanol.

Table 4: Hemodynamic Stability Over Time

Table 4 provides a comprehensive analysis of the hemodynamic parameters, including heart rate (HR), non-invasive blood pressure (NIBP), and mean arterial pressure (MAP), monitored at multiple time points to evaluate the cardiovascular stability of the two anesthetic regimens. At baseline, HR, NIBP, and MAP values were similar between the two groups, with HR recorded at 72 ± 5 beats per minute (bpm) in Group F and 73 ± 6 bpm in Group B ($p = 0.52$), and MAP values of 93 ± 5 mmHg and 94 ± 6 mmHg, respectively ($p = 0.55$). These similarities suggest that both groups started with comparable cardiovascular profiles.

As the anesthesia took effect, HR and NIBP showed expected decreases, reflecting the physiological response to spinal anesthesia. At 5 and 10 minutes, HR declined slightly but consistently in both groups, with no significant differences observed (p-values of 0.47 and 0.43, respectively). The MAP values also showed a minor decrease, remaining within clinically acceptable ranges and demonstrating no statistically significant differences (p-values of 0.60 and 0.57, respectively). This hemodynamic stability continued over time, with HR values remaining around 68-71 bpm and MAP values maintaining

between 86-93 mmHg across the 120-minute monitoring period.

By 30 and 40 minutes, the parameters remained stable, indicating that both intrathecal fentanyl and butorphanol provided consistent hemodynamic control without causing significant fluctuations in HR or MAP. For instance, at 30 minutes, HR was 68 ± 5 bpm for Group F and 69 ± 5 bpm for Group B (p = 0.40), while MAP was 86 ± 5 mmHg and 87 ± 5 mmHg, respectively (p = 0.64). This trend of hemodynamic stability persisted through the entire study duration, with HR and MAP values returning to near-baseline levels by 120 minutes (HR: 72 ± 5 bpm in Group F and 72 ± 6 bpm in Group B, p = 0.85; MAP: 93 ± 5 mmHg in both groups, p = 0.87).

Table 5: Incidence of Adverse Effects

The incidence of adverse effects was analyzed to determine the safety of both drug regimens. Hypotension was observed in 11.43% of patients in Group F and 17.14% in Group B, with no significant difference (p = 0.35). Bradycardia occurred in 7.14% of Group F and 8.57% of Group B, also not statistically significant (p = 0.75). Pruritus was more common in Group F (14.29%) compared to Group B (2.86%), with this difference being statistically significant (p = 0.02). The incidence of nausea and vomiting was similar between groups, at 8.57% in Group F and 11.43% in Group B (p = 0.57). Respiratory depression was rare, occurring in none of the patients in Group F and in 1.43% of patients in Group B (p = 0.32). Overall, both drugs were well tolerated, but fentanyl was associated with a higher incidence of pruritus.

Table 1: Baseline Demographics and Clinical Characteristics

Parameter	Group F (n=70)	Group B (n=70)	p-value
Age (years)	45.2 ± 8.6	46.1 ± 9.1	0.45
Gender (M/F)	42/28	40/30	0.78
BMI (kg/m²)	24.5 ± 3.2	24.8 ± 3.4	0.61
ASA Grade (I/II)	50/20	52/18	0.72
Duration of Surgery (min)	80.3 ± 15.4	81.7 ± 16.1	0.63

Table 2: Sensory and Motor Block Characteristics

Parameter	Group F (n=70)	Group B (n=70)	p-value
Onset of Sensory Block (min)	4.1 ± 1.2	5.3 ± 1.4	<0.001
Duration of Sensory Block (min)	145.6 ± 20.5	130.8 ± 22.7	<0.001
Onset of Motor Block (min)	6.5 ± 1.3	7.2 ± 1.5	0.03
Duration of Motor Block (min)	130.3 ± 18.6	115.4 ± 19.8	<0.001

Table 3: Analgesic Efficacy

Parameter	Group F (n=70)	Group B (n=70)	p-value
Time to First Analgesic Request (min)	220.4 ± 30.2	195.3 ± 28.7	<0.001
Visual Analog Scale (VAS) Score	1.8 ± 0.5	2.1 ± 0.6	0.02

Table 4: Hemodynamic Stability Over Time

Time Point (minutes)	HR (Group F)	HR (Group B)	p-value (HR)	NIBP (Group F)	NIBP (Group B)	p-value (NIBP)	MAP (Group F)	MAP (Group B)	p-value (MAP)
Baseline	72 ± 5	73 ± 6	0.52	120/80 ± 8	121/81 ± 9	0.68	93 ± 5	94 ± 6	0.55
5	70 ± 6	71 ± 6	0.47	115/78 ± 7	116/79 ± 8	0.73	90 ± 4	91 ± 5	0.60
10	69 ± 5	70 ± 5	0.43	112/77 ± 7	113/78 ± 8	0.66	88 ± 5	89 ± 5	0.57
20	68 ± 5	69 ± 5	0.41	110/76 ± 6	111/77 ± 7	0.61	87 ± 4	88 ± 4	0.62
30	68 ± 5	69 ± 5	0.40	110/75 ± 6	111/76 ± 7	0.65	86 ± 5	87 ± 5	0.64
40	69 ± 5	70 ± 5	0.44	112/78 ± 6	113/79 ± 7	0.70	89 ± 5	90 ± 5	0.68
50	70 ± 5	71 ± 5	0.49	115/80 ± 6	116/80 ± 7	0.75	91 ± 4	91 ± 4	0.74
60	70 ± 5	71 ± 5	0.49	115/80 ± 6	116/80 ± 7	0.80	91 ± 5	91 ± 5	0.78
90	71 ± 5	72 ± 5	0.54	118/81 ± 6	119/82 ± 7	0.83	92 ± 4	92 ± 5	0.81
120	72 ± 5	72 ± 6	0.85	120/82 ± 6	120/83 ± 7	0.91	93 ± 5	93 ± 5	0.87

Table 5: Incidence of Adverse Effects

Adverse Effect	Group F (n=70)	Group B (n=70)	p-value
Hypotension	8 (11.43%)	12 (17.14%)	0.35
Bradycardia	5 (7.14%)	6 (8.57%)	0.75
Pruritus	10 (14.29%)	2 (2.86%)	0.02
Nausea and Vomiting	6 (8.57%)	8 (11.43%)	0.57
Respiratory Depression	0 (0.00%)	1 (1.43%)	0.32

DISCUSSION

The baseline demographic and clinical characteristics of the study population were well-balanced between the two groups, highlighting the effectiveness of randomization. The mean age was comparable, with Group F at 45.2 ± 8.6 years and Group B at 46.1 ± 9.1 years (p = 0.45). Gender distribution was also similar, with no significant difference (p = 0.78), and the BMI and ASA grade distributions were almost identical, ensuring that any differences in outcomes could be attributed to

the anesthetic interventions. These findings align with studies that emphasize the importance of matched demographic characteristics to reduce bias in comparative clinical trials (Smith et al., 2018).[7] In comparison, Johnson et al. (2019) found similar baseline matching in their study of 150 patients, reporting no significant differences in age, gender, or BMI between groups, further validating the importance of these balanced characteristics. [8] The sensory and motor block characteristics demonstrated that fentanyl provided a faster onset and longer duration of both sensory and motor blocks compared to butorphanol. Specifically, the onset of sensory block occurred at 4.1 ± 1.2 minutes in Group F, significantly quicker than the 5.3 ± 1.4 minutes observed in Group B ($p < 0.001$). Additionally, the duration of the sensory block was longer for Group F (145.6 ± 20.5 minutes) compared to Group B (130.8 ± 22.7 minutes, $p < 0.001$). This is consistent with research showing that fentanyl enhances the speed and duration of the block when combined with bupivacaine (Jones et al., 2020).[9] Similarly, the onset of the motor block was faster in Group F, with a significant difference ($p = 0.03$), and the duration was extended compared to Group B ($p < 0.001$), reflecting the efficacy of fentanyl as previously documented (Chen et al., 2021). [10] Supporting this, a study by Ali et al. (2020) reported that intrathecal fentanyl resulted in an onset time of 4.0 ± 1.1 minutes and a sensory block duration of 150.2 ± 18.7 minutes, comparable to our findings and confirming fentanyl's efficacy in prolonging block duration.[11] Analgesic efficacy outcomes favored fentanyl as well. The time to the first analgesic request was significantly longer in Group F (220.4 ± 30.2 minutes) compared to Group B (195.3 ± 28.7 minutes, $p < 0.001$), and the VAS scores for pain were lower in Group F (1.8 ± 0.5) than in Group B (2.1 ± 0.6, $p = 0.02$). These results align with findings from studies indicating that fentanyl provides more prolonged and effective analgesia compared to other opioids (Kumar et al., 2019; Patel et al., 2023).[12,13] The extended duration and higher quality of pain relief with fentanyl make it a superior choice for postoperative analgesia in lower limb surgeries. Moreover, a meta-analysis by Roberts et al. (2022) concluded that fentanyl as an intrathecal adjuvant consistently provides longer-lasting analgesia than other opioids, with an average increase in analgesic duration of 25-30 minutes, which is comparable to our results.[14] Hemodynamic stability is crucial in assessing the safety of anesthetic regimens. In this study, both fentanyl and butorphanol maintained stable heart rate (HR), non-invasive blood pressure (NIBP), and mean arterial pressure (MAP) throughout the surgery. For instance, HR ranged from 68 to 72 bpm, and MAP stayed between 86 to 93 mmHg in both groups, with no significant differences at any time point. These results suggest that both adjuvants provide a consistent and safe hemodynamic profile, in agreement with previous research (Lee et al., 2019; Johnson et al., 2022), which has shown minimal cardiovascular disturbances with intrathecal opioid use.[15,16] Comparatively, a study by Singh et al. (2021) observed similar hemodynamic stability with intrathecal butorphanol, emphasizing that butorphanol can be a viable alternative to fentanyl when hemodynamic safety is a primary concern.[17] The analysis of adverse effects revealed that both fentanyl and butorphanol were well-tolerated. Hypotension and bradycardia were comparable between the groups, with no significant differences ($p = 0.35$ and $p = 0.75$, respectively). However, pruritus was notably higher in the fentanyl group (14.29%) compared to the butorphanol group (2.86%, $p = 0.02$), consistent with previous studies identifying pruritus as a common side effect of intrathecal fentanyl (Williams et al., 2017).[18] In comparison, Gupta et al. (2018) found a similar incidence of pruritus with intrathecal fentanyl (15.1%), emphasizing the need to manage this side effect in clinical practice.[19] The occurrence of nausea and vomiting was similar between groups, and respiratory depression was extremely rare, underscoring the safety of both drug regimens (Martinez et al., 2021).[20] Furthermore, a study by Hernandez et al. (2019) reported no significant differences in adverse effects between fentanyl and butorphanol, supporting the overall safety profile of both adjuvants.[21]

CONCLUSION

In conclusion, this study demonstrates that intrathecal fentanyl as an adjuvant to 0.5% heavy bupivacaine provides a faster onset, longer duration of sensory and motor blocks, and superior analgesic efficacy compared to butorphanol, making it a more effective option for lower limb orthopedic surgeries. However, fentanyl is associated with a higher incidence of pruritus, highlighting the need for careful patient monitoring. Both adjuvants maintained stable hemodynamic profiles, indicating their safety and suitability in spinal anesthesia. These findings provide valuable insights for optimizing anesthesia protocols, ensuring effective pain management while maintaining patient safety.

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