MAK HILL Publications Research Journal of Medical Sciences

Research Article
doi: 10.36478/makrjms.2024.12.493.500

OPEN ACCESS

Key Words
Epidural anaesthesia, buprenorphine, fentanyl, postoperative analgesia

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Received: 20 August 2024
Accepted: 30 November 2024
Published: 05 December 2024

Citation: Dr. Shilpa Khanapure, Dr. Sunita Y. Shende and Dr. Sarita R. Thanekar, 2024. Study to Compare Epidural Bupivacaine with Buprenorphine and Bupivacaine with Fentanyl for Characteristics of Block and Prolongation of Postoperative Analgesia in Adult Orthopaedic Lower Limb Surgeries. Res. J. Med. Sci., 18: 493-500, doi: 10.36478/makrjms.2024.12.493.500

Study to Compare Epidural Bupivacaine with Buprenorphine and Bupivacaine with Fentanyl for Characteristics of Block and Prolongation of Postoperative Analgesia in Adult Orthopaedic Lower Limb Surgeries

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ABSTRACT
Effective postoperative pain management is essential for enhanced recovery and reduced morbidity. Epidural anesthesia, combined with opioids, is a proven technique for intraoperative and postoperative analgesia. This study compares the efficacy and safety of **Buprenorphine +Bupivacaine** versus **Fentanyl+Bupivacaine** in elective lower limb orthopedic surgeries. A randomized study included 80 patients (ASA grade I-II) undergoing lower limb surgeries. Group A received **3 mcg/kg buprenorphine+15ml of 0.5% bupivacaine** and Group B received **50 mcg fentanyl+15ml of 0.5% bupivacaine**. Onset and duration of sensory and motor blockade, analgesia duration, VAS scores and side effects were recorded. **Sensory and Motor Blockade:** Group A had a faster onset of sensory blockade (7.38±0.5 min) compared to Group B (9.15±0.6min., p<0.001). Sensory regression was significantly prolonged in Group A (269±10.5min) compared to Group B (246.2±8.2min., p<0.001). **Postoperative Analgesia:** Group A exhibited a longer duration of analgesia (535±20 min) compared to Group B (473.1±15.3min., p<0.001), while VAS scores favoured Group B at 6 and 24 hours. **Side Effects:** Group B had a slightly higher incidence of pruritus (10%) than Group A (7.5%), while nausea was more common in Group A. **Buprenorphine+ Bupivacaine** is superior for prolonged analgesia, while **Fentanyl+Bupivacaine** offers better immediate pain relief with fewer side effects. Both combinations are safe and effective for tailored patient care.

INTRODUCTION

Pain, derived from the Greek term poine meaning "penalty," is not merely a sensory experience but a complex phenomenon encompassing emotional, physiological and psychological dimensions. It is defined as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage." Since the foundational work in pain management and the establishment of the International Association for the Study of Pain in 1974, significant advancements have been made in understanding and treating pain. Beyond immediate discomfort, pain impacts various physiological systems, including respiratory, cardiovascular and metabolic processes, increasing morbidity[1,2]. Anesthesia is pivotal in managing pain during surgical interventions and is categorized into local, conscious sedation, regional and general anesthesia. Among these, regional anesthesia, encompassing central neuraxial blocks such as epidural and spinal anesthesia, is a preferred choice for lower extremity surgeries due to its ability to provide targeted pain relief with minimal systemic side effects, particularly for patients with underlying cardiac or respiratory conditions[3,4]. General anesthesia, though effective, is often associated with disadvantages such as the need for specialized postoperative monitoring, systemic complications and prolonged hospital stays. Epidural anesthesia, however, offers better hemodynamic stability, extended postoperative analgesia and faster recovery, contributing to cost-effective healthcare delivery. Intrathecal anesthesia, or spinal anesthesia, is widely used but has limitations, including shorter duration, increased risks such as post-dural puncture headache and challenges in extending anesthesia for prolonged surgeries. Epidural anesthesia, being versatile, allows placement at various spinal levels and enables combined spinal-epidural techniques. These attributes make it the preferred method for lower limb orthopedic surgeries[5,6]. Epidural anesthesia provides effective surgical anesthesia while offering prolonged postoperative analgesia. It reduces hemodynamic fluctuations by enabling segmental anesthesia and eliminates the risk of post-dural puncture headache as the dura mater remains intact. Combining local anesthetics with opioids enhances efficacy, extending sensory blockade duration and reducing local anesthetic dosage requirements, minimizing systemic side effects. Bupivacaine is widely used for its long-lasting action and differential sensory blockade[7,8]. Synthesized in 1956 and introduced clinically in 1963, it is a reliable amide anesthetic. Adjuvants such as buprenorphine and fentanyl augment its effects. Buprenorphine, a the baine derivative and partial μ-opioid receptor agonist, is 33 times more potent than morphine, with high lipid solubility that limits cephalad spread. Fentanyl, a phenylpiperidine derivative, is 75-125 times more potent than morphine, known for its rapid onset and effective pain relief[9,10]. This study compares the efficacy of epidural bupivacaine with buprenorphine and bupivacaine with fentanyl in adult patients undergoing lower limb orthopedic surgeries. Outcomes assessed include sensory and motor blockade characteristics, duration of postoperative analgesia and side effects, aiming to optimize perioperative pain management and improve patient care in orthopedic procedures.

MATERIALS AND METHODS

This prospective observational and analytical study was conducted at a tertiary care hospital from January 2020 to August 2021. The study aimed to compare the effectiveness of bupivacaine combined with buprenorphine versus bupivacaine combined with fentanyl in patients undergoing elective lower limb orthopedic surgeries.

Study Population: A total of 80 patients aged between 18-60 years, classified as ASA Grade I or II, scheduled for elective lower limb surgeries, were included in the study. Patients with a history of cardiac, respiratory, hepatic, renal, neurological, or psychiatric disorders, contraindications to epidural anesthesia, or local infections at the injection site were excluded. Pregnant women and those allergic to study drugs were also excluded.

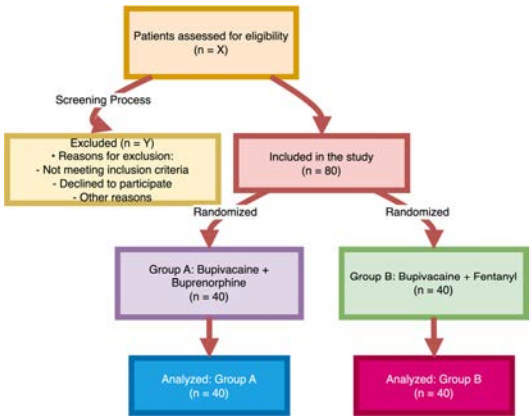

Fig. 1: Cohort Flowchart Illustrating the Flow of Participants Through the Study. Let Me Know if You Need Any Modifications or Additional Details

Sampling and Sample Size: Consecutive sampling was used to recruit patients. Based on the mean sensory block onset times for bupivacaine-buprenorphine (3.10±0.305 minutes) and bupivacaine-fentanyl (2.90±0.305 minutes), the minimum sample size was calculated to be 74 (37 patients per group). For added reliability, 80 patients were included, divided equally into two groups of 40 each.

Procedure: After obtaining approval from the institutional ethics committee and written informed consent from patients, a thorough pre-anesthetic evaluation was performed. Routine investigations such as hemoglobin, blood grouping, serum electrolytes, and blood sugar levels were carried out. Patients were kept nil by mouth for six hours before surgery.

Premedication: Patients received:

- Inj. Ranitidine (1 mg/kg IV).
- Inj. Ondansetron (0.1 mg/kg IV).

Epidural Procedure: Under strict aseptic precautions, with the patient in a sitting position, the L2-L3 interspace was identified. After local infiltration with lignocaine, the epidural space was accessed using an 18G Tuohy needle through the loss-of-resistance technique. A test dose of 3mL of 2% lignocaine with adrenaline (1:200,000) was administered to confirm the correct placement of the catheter.

- **Group A:** Received 15mL of 0.5% bupivacaine with 150 µg buprenorphine, diluted with sterile normal saline to a total volume of 16mL.
- **Group B:** Received 15mL of 0.5% bupivacaine with 50 µg fentanyl, adjusted with sterile normal saline to a total volume of 16 Ml.

No intravenous opioids or additional analgesics were given during the surgery. Sensory and motor blocks were assessed every minute following drug administration and hemodynamic parameters were monitored every 5 minutes for the first 15 minutes, every 15 minutes during the surgery and every 30 minutes postoperatively for two hours.

Definitions:

- **Sensory Block Onset:** Time from drug administration to loss of sensation at the T10 dermatome.
- **Motor Block Onset:** Time from drug administration to Bromage Scale Grade 1 motor block.
- **Duration of Analgesia:** Time from drug administration to the first request for systemic analgesia.
- **Side Effects:** Monitored for nausea, vomiting, pruritus, respiratory depression and urinary retention.

Sensory Block Assessment: Performed using the Hollmen scale with pinprick testing.

Motor Block Assessment: Graded on the Modified Bromage Scale (0-3).

Statistical Analysis: Data were analyzed using SPSS software. Categorical variables were analyzed using the chi-square test and continuous variables were compared using independent t-tests. A p-value of <0.05 was considered statistically significant. This methodology provided a robust approach to evaluating and comparing the efficacy and safety of the two epidural drug combinations in achieving optimal surgical anesthesia and postoperative analgesia.

RESULTS AND DISCUSSIONS

Table 1: Baseline Demographic and Clinical Characteristics of Patients in the Bupivacaine +Buprenorphine and Bupivacaine+Fentanyl Groups

Parameter	Bupivacaine+ Buprenorphine	Bupivacaine+ Fentanyl	p-value
Gender Distribution (Male:Female)	70:30	67.5:32.5	0.809
Mean Age (years)	42.60±12.44	43.65±10.76	NS
Mean Weight (kg)	58.78±4.21	59.43±7.65	0.639
ASA Grade (I:II)	25:15	24:16	NS
Duration of Surgery (minutes)	111±13.92	111±13.92	NS

(**Table 1):** Comparative demographic and clinical parameters between the two study groups-Bupivacaine+Buprenorphine and Bupivacaine+ Fentanyl. Data are presented as mean±standard deviation for continuous variables and ratios for categorical variables. Statistical significance was assessed using chi-square test for categorical variables and independent t-test for continuous variables. A p-value <0.05 was considered significant (fig. 2).

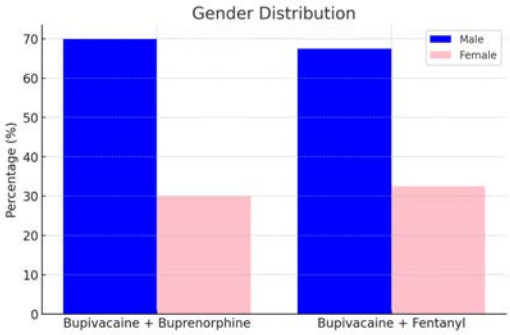

Fig. 2: Gender Distribution

The (fig. 2) **Gender Distribution** bar chart (top left) shows that both groups had a similar distribution, with approximately 70% males and 30% females. This uniform distribution ensures that gender does not bias the outcomes, making the groups comparable.

- **Gender Distribution:** There was no statistically significant difference in gender distribution between the two groups (p=0.809). Both groups had a male predominance.
- **Mean Age:** The mean age of participants in the two groups was comparable, with no significant difference observed (p=NS).
- **Mean Weight:** Both groups had similar mean weights, with no statistically significant difference (p=0.639).
- **ASA Grade:** The distribution of ASA Grade I and II patients was not significantly different between the groups (p=NS).
- **Duration of Surgery:** The mean duration of surgery was identical in both groups, showing no significant variation (p=NS).

(Table 2): Comparison of sensory and motor block characteristics between Bupivacaine+Buprenorphine and Bupivacaine+Fentanyl groups.

Table 2: Comparison of Sensory

Parameter	Bupivacaine+ Buprenorphine	Bupivacaine+ Fentanyl	p-value
Onset of Sensory Block (T10, minutes)	7.38±1.69	9.15±1.83	0.001
Onset of Motor Block (minutes)	7.15±1.70	11.23±2.35	0.001
Time to Maximum Motor Block (minutes)	14.60 ± 4.33	18.13±3.34	0.001
Maximum Sensory Block Level (T6:T8)	T6 (55%)., T8 (45%)	T6 (50%)., T8 (50%)	0.78
Time to Sensory Regression at S1 (minutes)	269.20±21.01	246.20±14.31	0.001

(Table 2) Comparison of sensory and motor block characteristics between Bupivacaine+Buprenorphine and Bupivacaine+Fentanyl groups. Data are presented as mean±standard deviation for continuous variables and percentages for categorical variables. Statistical significance was determined using an independent t-test for continuous data and chi-square test for categorical data. A p-value <0.05 was considered statistically significant shown in (fig. 3).

- **Onset of Sensory Block (T10):** The onset of sensory block was significantly faster in the Bupivacaine+Buprenorphine group (7.38±1.69 minutes) compared to the Bupivacaine+Fentanyl group (9.15±1.83 minutes), with a p-value of 0.001.
- **Onset of Motor Block:** The motor block onset was significantly earlier in the Bupivacaine+ Buprenorphine group (7.15±1.70minutes) compared to the Bupivacaine+Fentanyl group (11.23±2.35 minutes), with a p-value of 0.001.
- **Time to Maximum Motor Block:** Time to achieve maximum motor block was significantly shorter in the Bupivacaine+Buprenorphine group (14.60± 4.33 minutes) than in the Bupivacaine+Fentanyl group (18.13±3.34 minutes), with a p-value of 0.001.
- **Maximum Sensory Block Level:** Both groups achieved similar maximum sensory block levels, primarily at T6 and T8, with no statistically significant difference (p=0.78).
- **Time to Sensory Regression at S1:** Sensory regression to S1 occurred significantly later in the Bupivacaine+Buprenorphine group (269.20±21.01 minutes) compared to the Bupivacaine+Fentanyl group (246.20±14.31 minutes), with a p-value of 0.001.

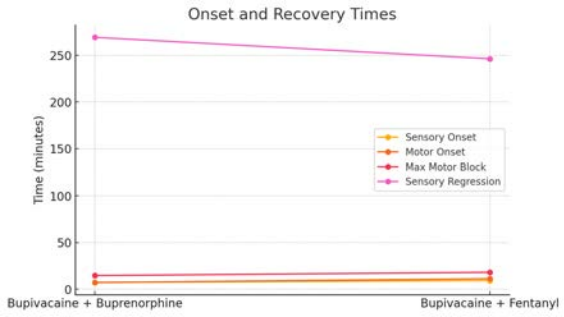

Fig. 3: Onset and Recovery Times

The (fig. 3) **Onset and Recovery Times** line chart (top right) demonstrates that Bupivacaine+Buprenorphine has faster sensory and motor block onset times than Bupivacaine+Fentanyl. Additionally, the Buprenorphine group achieves a quicker maximum motor block. However, sensory regression (duration of analgesia) is significantly longer in the Buprenorphine group, indicating its superior prolonged effect.

(Table 3) Comparative Analysis of Sensory and Motor Block Recovery, Pain Scores, Rescue Analgesia and Side Effects Between Bupivacaine+Buprenorphine and Bupivacaine+Fentanyl Groups This table summarizes key clinical outcomes, including sensory and motor block recovery times, pain relief scores, rescue analgesia requirements and side effect incidences, in patients receiving Bupivacaine+Buprenorphine or Bupivacaine+Fentanyl during lower limb orthopedic surgeries. Data are presented as mean±standard deviation for continuous variables and percentages for categorical variables. Statistical significance was assessed using independent t-tests for continuous variables and chi-square tests for categorical variables. A p-value < 0.05 was considered statistically significant.

- **Sensory and Motor Block Recovery**: Both groups had similar times to Modified Bromage Scale 0 (p=0.87).
- Sensory regression at S1 was significantly prolonged in the Bupivacaine + Buprenorphine group compared to the Bupivacaine + Fentanyl group (p = 0.001).
- **Pain Relief (VAS Scores):** VAS scores were significantly lower in the Bupivacaine+Fentanyl group at both 6 hours (p=0.001) and 24 hours (p=0.001), indicating superior pain relief.
- **Rescue Analgesia:** Time to first rescue analgesia was significantly longer in the Bupivacaine+ Buprenorphine group (p=0.021), suggesting more prolonged analgesia.

- The number of rescue doses in 24 hours was comparable between the two groups (p=0.63).
- **Side Effects:** There were no statistically significant differences in the incidences of nausea, pruritus, or shivering between the groups (p>0.05).

Table 3: Comparative Analysis

Parameter	Bupivacaine+ Buprenorphine	Bupivacaine+ Fentanyl	p-value
Time to Modified Bromage Scale 0 (minutes)	165.50±8.86	165.80±8.32	0.87
VAS Score at 6 hours	3.95±1.22	2.97±0.83	0.001
VAS Score at 24 hours	6.65±1.19	5.30±1.14	0.001
First Rescue Analgesia (hours)	8.93±2.09	7.80±2.17	0.021
Number of Rescue Analgesics in 24 Hours	2.72±0.45	2.67±0.47	0.63
Nausea (%)	0%	7.5%	0.18
Pruritus (%)	7.5%	10%	0.18
Shivering (%)	5%	0%	0.18

(Table 3): Comparative Analysis of Sensory and Motor Block Recovery, Pain Scores, Rescue Analgesia and Side Effects Between Bupivacaine+Buprenorphine and Bupivacaine+Fentanyl Groups.

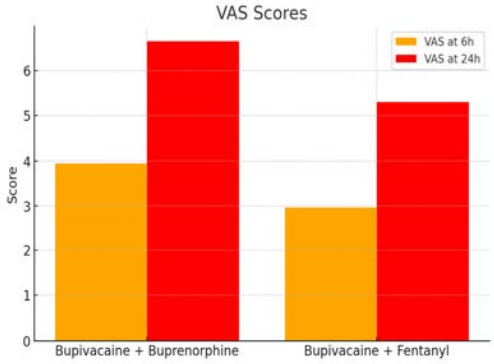

Fig. 4: VAS Scores

The (fig. 4) **VAS Scores** bar chart (bottom left) compares pain relief over time. At 6 hours, Bupivacaine + Fentanyl demonstrates better pain relief with lower VAS scores compared to Buprenorphine. This trend continues at 24 hours, where the Fentanyl group maintains superior analgesic efficacy.

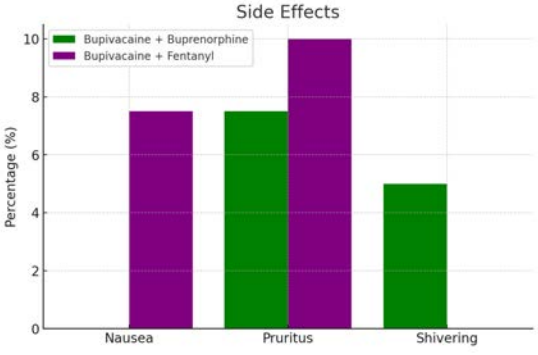

Fig. 5: Side Effects

The (fig. 5) **Side Effects** bar chart (bottom right) highlights the safety profiles of both combinations. Nausea and pruritus are more prevalent in the Bupivacaine+Fentanyl group, with 7.5% and 10% incidences, respectively. In contrast, the Buprenorphine group reports no nausea, slightly lower pruritus (7.5%), but 5% shivering, which is absent in the Fentanyl group.

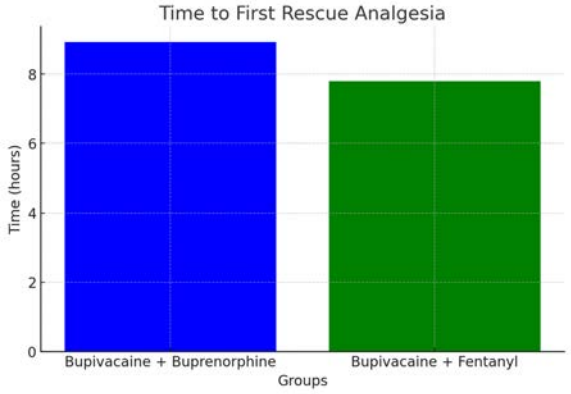

Fig. 6: Time to First Rescue Analgesia

A bar chart comparing the time to first rescue analgesia between the two groups. The Bupivacaine+ Buprenorphine group showed a longer duration (8.93 hours) compared to the Bupivacaine+Fentanyl group (7.80 hours). The prolonged analgesic effect in the Bupivacaine+Buprenorphine group suggests its potential for extended pain relief, reducing the frequency of rescue analgesics.

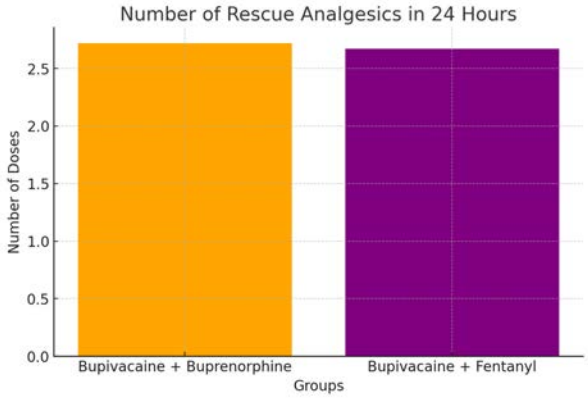

Fig. 7: Number of Rescue Analgesics in 24 Hours

A bar chart comparing the number of rescue analgesics required within 24 hours. Both groups showed similar results, with averages of 2.72 and 2.67 doses for Bupivacaine+Buprenorphine and Bupivacaine+ Fentanyl, respectively. The comparable need for

rescue analgesics indicates similar overall pain management efficacy between the two groups over 24 hours.

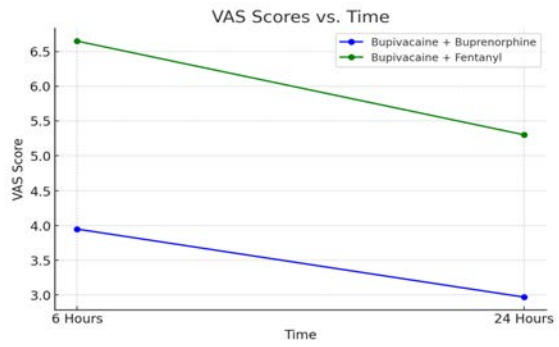

Fig. 8: VAS Scores vs. Time (6 and 24 Hours)

A line graph showing VAS scores at 6 and 24 hours. The Bupivacaine+Fentanyl group had lower VAS scores (better pain relief) at both 6 hours (2.97 vs. 3.95) and 24 hours (5.30 vs. 6.65) compared to the Bupivacaine +Buprenorphine group. The superior VAS scores for the Bupivacaine+Fentanyl group highlight its potential advantage for acute pain management.

Pain is a multifaceted subjective experience, particularly pronounced in the postoperative period, where it demands effective relief on humanitarian grounds and to reduce physical morbidity. During surgery, tissue injury and the release of pain-producing substances significantly lower the threshold of nociceptors, resulting in heightened nociception. This phenomenon underscores the necessity for effective analgesic interventions. Pharmacological advances, particularly the introduction of epidural anesthesia[11,12], have provided a robust mechanism for managing postoperative pain, especially for surgeries involving the lower extremities. Epidural anesthesia offers superior control compared to spinal anesthesia, as it allows targeted block levels, minimal hemodynamic disturbances and the administration of top-up doses. Bupivacaine has traditionally been the cornerstone of epidural anesthesia, offering sensory and motor blockade at varying concentrations. However, the addition of opioids, such as buprenorphine and fentanyl, has augmented its efficacy, enabling prolonged analgesia and reducing the need for repeated top-ups. This study evaluates the comparative efficacy of these combinations, focusing on sensory and motor block characteristics, duration of analgesia, and side effects[13]. This randomized study involved 80 patients undergoing elective lower limb orthopedic surgeries. After obtaining informed consent, participants were grouped into **Buprenorphine+Bupivacaine (Group A) and Fentanyl+Bupivacaine (Group B)**. The study utilized 3mcg/kg of buprenorphine (fixed at 150mcg) or 50mcg of fentanyl with 15ml of 0.5% bupivacaine. Epidural anesthesia was administered with an epidural catheter secured using the loss of resistance technique. Parameters such as sensory and motor blockade, postoperative analgesia, hemodynamic changes and side effects were meticulously recorded[14].

Key Findings:

Sensory and Motor Blockade:

- **Onset of Sensory Blockade:** Group A (Buprenorphine) exhibited a faster onset (7.38 minutes) compared to Group B (Fentanyl) at 9.15 minutes. This aligns with previous findings that buprenorphine's high lipid solubility facilitates quicker receptor binding. Dhale *et al.* (2000) found a similar onset time of 9.53 minutes for fentanyl, supporting the present study's results.
- **Duration of Sensory Blockade:** Sensory regression to S1 was significantly longer in Group A (269 minutes) compared to Group B (246.2 minutes), demonstrating buprenorphine's superior prolonged analgesic effect. Chakravarthy *et al.* observed a similar duration of 247 minutes for fentanyl, which is consistent with this study.
- **Motor Blockade:** Group A achieved motor blockade onset faster (7.15 minutes) than Group B (11.23 minutes). However, the duration of motor blockade was similar between groups, with Group A at 165.5 minutes and Group B at 165 minutes. Dhakshinamoorthy *et al.* found comparable results, with motor block onset times of 10.3 minutes for buprenorphine and 10.13 minutes for fentanyl.

Postoperative Analgesia:

- **Duration of Analgesia:** Group A provided significantly longer analgesia (535 minutes) than Group B (473.1 minutes), attributed to buprenorphine's high receptor affinity and slow dissociation. Bhargav *et al.* observed a much longer duration of 22-24 hours with buprenorphine in their study, highlighting its robust analgesic efficacy.

- **Quality of Analgesia:** Both groups required comparable rescue doses, with a slightly lower incidence in Group A. Thomas *et al.* noted that fentanyl produced effective analgesia in cesarean sections, with a mean duration of 382 minutes, consistent with the present study's results for fentanyl.

Side Effects:

- **Nausea and Vomiting:** Group A had a marginally higher incidence (2 cases) compared to Group B (1 case), aligning with studies such as Hayashi *et al.* (1993), who reported a lower incidence of nausea and vomiting with fentanyl compared to buprenorphine.
- **Pruritus:** Reported in 4 patients in Group B and 3 in Group A, with no significant differences between groups. Lytle *et al.* reported similar findings, emphasizing fentanyl's mild pruritus incidence[16,17].
- **Hemodynamic Stability:** Both groups exhibited stable mean arterial pressure and heart rate throughout the intraoperative and postoperative periods. Rathi *et al.* noted that buprenorphine maintained hemodynamic stability, supporting this study's findings[18,19].

Integration with Previous Studies: Muppala *et al.* (2020) and Kumar *et al.* (2014) have both compared buprenorphine and fentanyl with bupivacaine for epidural analgesia and found that buprenorphine offered longer-lasting analgesia, whereas fentanyl provided quicker onset with fewer side effects. Boas *et al.* (1985) highlighted the pharmacological differences between the two opioids, noting buprenorphine's prolonged receptor binding and fentanyl's rapid equilibrium, which explain the observed differences in analgesic duration and onset[20].

Clinical Implications: This study highlights that **Buprenorphine+Bupivacaine** provides faster onset, prolonged sensory regression and extended analgesia, making it ideal for procedures requiring long-lasting pain control. In contrast, **Fentanyl+Bupivacaine** offers better VAS scores, particularly in the early postoperative period, with a marginally reduced incidence of side effects such as nausea and vomiting. Both combinations demonstrated excellent safety profiles with minimal hemodynamic impact.

CONCLUSION

This study demonstrates that both **Buprenorphine+ Bupivacaine** and **Fentanyl+Bupivacaine** are effective combinations for epidural anesthesia in lower limb orthopedic surgeries, each with distinct advantages. **Buprenorphine+Bupivacaine** provides a faster onset of sensory and motor blockade, longer duration of sensory regression and significantly prolonged postoperative analgesia, making it a superior choice for procedures requiring extended pain control. On the other hand, Fentanyl+Bupivacaine ensures better immediate postoperative pain relief, reflected in lower VAS scores at 6 and 24 hours and a slightly better side effect profile, with reduced incidences of nausea and vomiting. Both combinations maintained hemodynamic stability throughout the perioperative and postoperative periods, demonstrating their safety and reliability. While buprenorphine's prolonged action is attributed to its high lipid solubility and receptor binding affinity, fentanyl's rapid onset and reduced side effects reflect its pharmacological properties as a highly lipophilic opioid. The findings of this study provide valuable insights for clinicians, emphasizing the need to tailor the choice of adjuvants based on the duration of surgery, postoperative pain management goals and individual patient profiles. **Buprenorphine+ Bupivacaine** is recommended for cases requiring long-lasting analgesia, while **Fentanyl+Bupivacaine** is more suitable for patients needing immediate pain relief with minimal side effects. Further research with larger sample sizes and diverse patient populations is suggested to corroborate these findings and optimize clinical guidelines.

Conflict of Interest Statement: The authors declare that there is no conflict of interest regarding the publication of this article.

Funding Statement: This study did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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