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Original Research

Comparative Evaluation of Clonidine, Fentanyl, and Buprenorphine as Adjuvants to Intrathecal 0.5% Hyperbaric Bupivacaine in Lower Abdominal and Limb Surgeries

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ABSTRACT:

Background: Intrathecal bupivacaine provides reliable anesthesia for lower abdominal and lower limb surgeries but is limited by short postoperative analgesia. Adjuvants such as fentanyl, clonidine, and buprenorphine have been studied to prolong block duration and improve analgesic quality. **Aim:** To compare the clinical effects of fentanyl, clonidine, and buprenorphine as intrathecal adjuvants to hyperbaric bupivacaine in patients undergoing lower abdominal and lower limb surgeries. **Material and Methods:** A randomized double-blind study was conducted in 60 patients allocated into three groups receiving intrathecal bupivacaine with either fentanyl, clonidine, or buprenorphine. Block characteristics, onset, duration, rescue analgesic requirements, and side effects were recorded and compared. **Results:** Fentanyl provided the fastest onset of sensory block, while clonidine and buprenorphine significantly prolonged sensory and motor block duration. Buprenorphine showed prolonged analgesia with stable hemodynamics, while clonidine offered the longest block but required monitoring for hypotension and bradycardia. **Conclusion:** All three agents enhanced the efficacy of intrathecal bupivacaine. Fentanyl was beneficial for rapid onset and shorter procedures, whereas clonidine and buprenorphine provided superior prolonged analgesia, making them preferable for longer surgeries.

Keywords: Spinal anesthesia, Clonidine, Buprenorphine, Fentanyl

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INTRODUCTION

Spinal anesthesia continues to be one of the most reliable techniques for lower abdominal and lower limb surgeries due to its rapid onset, dense blockade, and avoidance of airway manipulation [1]. However, the relatively short duration of postoperative analgesia associated with intrathecal local anesthetics like bupivacaine remains a limitation, often necessitating supplemental systemic analgesics [2]. To address this, various adjuvants have been combined with intrathecal bupivacaine to prolong block duration, enhance quality of anesthesia, and reduce postoperative analgesic requirements.

Opioids such as fentanyl and buprenorphine have been extensively studied as intrathecal adjuvants. Fentanyl, a lipophilic opioid, is known for its rapid onset of action and synergistic effect with local anesthetics, providing improved intraoperative analgesia and early postoperative pain relief without significant motor blockade [3]. However, its shorter duration of action may necessitate early postoperative analgesic supplementation [4]. Buprenorphine, a partial agonist at the μ-opioid receptor with high receptor affinity, offers prolonged analgesia compared to fentanyl when administered intrathecally, making it an attractive option for longer surgical procedures [5]. Studies have reported its superior duration of postoperative analgesia but have also highlighted concerns regarding delayed respiratory depression and nausea [6].

Clonidine, an α2-adrenergic agonist, has gained popularity as a non-opioid alternative adjuvant in spinal anesthesia. When combined with intrathecal bupivacaine, clonidine provides effective analgesia through both spinal and supraspinal mechanisms by reducing sympathetic outflow, attenuating nociceptive

transmission, and prolonging the duration of sensory block [7]. Additionally, clonidine is associated with sedation and reduced postoperative opioid consumption, although it may cause hypotension and bradycardia [8].

Recent comparative trials and meta-analyses have shown that all three adjuvants—fentanyl, buprenorphine, and clonidine—enhance the efficacy of intrathecal bupivacaine, but their profiles differ in terms of onset, duration, side effects, and patient satisfaction [9]. With increasing emphasis on multimodal analgesia and opioid-sparing strategies, it is important to determine which adjuvant offers the best balance between efficacy and safety for lower abdominal and lower limb surgeries [10].

This study therefore aims to compare the clinical effects of fentanyl, buprenorphine, and clonidine as intrathecal adjuvants to 0.5% hyperbaric bupivacaine in patients undergoing major lower abdominal and lower limb surgeries, focusing on block characteristics, duration of analgesia, hemodynamic stability, and adverse effects.

MATERIAL AND METHODS

This prospective, randomized, double-blind study included 60 adult patients scheduled for elective lower abdominal or lower limb surgeries under spinal anesthesia after institutional ethics approval and written informed consent. Eligible participants were ASA physical status I–II, aged 18–65 years, with exclusions for coagulopathy, local infection at the puncture site, spinal deformity, chronic opioid use, allergy to study drugs, significant cardiopulmonary disease, or pregnancy. Patients were randomly allocated in a 1:1:1 ratio (computer-generated sequence, sealed opaque envelopes) into three groups of 20 each. Group BB received intrathecal 3 cc of 0.5% hyperbaric bupivacaine (15 mg) plus 0.5 cc buprenorphine (75 µg). Group BC received intrathecal 3 cc of 0.5% hyperbaric bupivacaine (15 mg) plus 0.5 cc clonidine (50 µg). Group BF received intrathecal 3 cc of 0.5% hyperbaric bupivacaine (15 mg) plus 0.5 cc fentanyl (25 µg). The total intrathecal volume in all groups was 3.5 mL. Study solutions were prepared in identical 5 mL syringes by an anesthesiologist not involved in patient care or data collection; both the administering anesthesiologist and the patient were blinded to group allocation. Standard fasting guidelines were observed and all patients received preloading with isotonic crystalloid (10 mL/kg) before neuraxial block. In the operating room, continuous ECG, noninvasive blood pressure, and pulse oximetry were instituted, and baseline vitals were recorded. With the patient in the sitting position under aseptic precautions, a midline approach at the L3–L4 or L4–L5 interspace using a 25-gauge Quincke spinal needle was used to confirm free flow of cerebrospinal fluid, following which the assigned intrathecal study drug was injected over 10–15 seconds; patients were immediately placed supine with standard positioning. Sensory block was assessed bilaterally by loss of pinprick every 2 minutes until T10 and then every 5 minutes until the highest level was stable for two consecutive readings; onset time (to T10), time to peak sensory level, maximum dermatome level, and two-segment regression time were recorded. Motor block was evaluated using the modified Bromage scale at identical intervals to determine onset time (Bromage ≥2), maximum grade, and duration (time to Bromage 0). Intraoperative hemodynamics (heart rate, mean arterial pressure, SpO_2) were recorded at baseline; every 2 minutes for 10 minutes; every 5 minutes up to 30 minutes; and every 15 minutes thereafter until the end of surgery. Hypotension (mean arterial pressure decrease ≥20% from baseline) was treated with incremental IV ephedrine 6 mg and fluids; bradycardia (heart rate <50 min^{-1}) was treated with atropine 0.6 mg IV. Inadequate block or failed spinal was managed per protocol and such cases were excluded from efficacy analysis but included in safety reporting. Postoperative assessments were performed by a blinded observer. Pain intensity was recorded using a 10-cm visual analogue scale at 1, 2, 4, 6, 8, 12, and 24 hours. Time to first analgesic request (defined as VAS ≥4 or patient request) and total analgesic consumption in 24 hours were documented; rescue analgesia consisted of IV paracetamol 1 g followed by tramadol 50–100 mg IV if required. Adverse effects including nausea, vomiting, pruritus, urinary retention, sedation (Ramsay scale), respiratory depression (respiratory rate <8 min^{-1} or SpO_2 <92% on room air), hypotension, and bradycardia were actively monitored intraoperatively and for 24 hours postoperatively; PONV was treated with ondansetron 4 mg IV as required, and pruritus with antihistamine per protocol. Patient satisfaction (5-point Likert scale) and surgeon satisfaction (5-point Likert scale) were recorded at 24 hours. The primary outcome was duration of effective analgesia (time from intrathecal injection to first rescue analgesic). Secondary outcomes included onset and duration of sensory and motor block, maximum block height, hemodynamic stability, total 24-hour analgesic requirement, incidence of adverse effects, and satisfaction scores. Sample size was fixed at 60 a priori with equal allocation to allow comparative evaluation across the three adjuvants. Data were analyzed using intention-to-treat where feasible; continuous variables were tested for normality and compared using ANOVA or Kruskal–Wallis with post-hoc corrections, while categorical variables were compared using chi-square or Fisher's exact test. A two-sided p value <0.05 was considered statistically significant.

RESULTS

The findings of the study variables in the three groups are presented in Table 1. The onset of sensory blockade was fastest in Group BF (1.80 ± 0.74 min),

followed by Group BC (1.94 ± 0.49 min) and Group BB (2.28 ± 0.46 min). The difference was statistically significant (p=0.006), indicating that fentanyl provided the most rapid onset of sensory block. However, the onset of motor blockade showed no significant difference across groups, with mean values ranging from 2.68 to 2.93 minutes (p=0.274), suggesting a similar profile of motor block onset among the three adjuvants.

The highest level of sensory blockade achieved was predominantly at T6 in all groups, with 73.3% in Group BF, 83.3% in Group BC, and 86.7% in Group BB. A smaller proportion of patients achieved T8 as the highest level. The distribution did not differ significantly between the groups (p=0.412), indicating comparable cephalad spread of the sensory block.

Motor blockade assessment showed that the majority of patients achieved a complete motor block (Grade 3). Grade 2 motor block was observed only in 6.7% of patients in Group BB, while all other patients in Groups BF and BC achieved Grade 3. This difference was not statistically significant (p=0.118), showing that all three adjuvants provided reliable motor block for the surgical procedures.

With respect to duration of blockade, significant differences were observed for both sensory and motor components. The duration of sensory blockade was longest in Group BC (358.27 ± 44.68 min), followed by Group BB (347.0 ± 46.62 min), and was shortest in Group BF (306.2 ± 29.21 min). The difference was highly significant (p<0.001), suggesting clonidine and buprenorphine provided prolonged sensory analgesia compared to fentanyl. Similarly, the duration of motor blockade was significantly different between the groups (p<0.001), with Group BC showing the longest mean motor block (191.7 ± 24.82 min), followed by Group BB (177.27 ± 22.53 min), and Group BF having the shortest duration (168.9 ± 13.54 min). These findings highlight that while fentanyl facilitated the fastest onset of sensory block, clonidine and buprenorphine offered superior prolongation of both sensory and motor blockade.

Table 1. Findings of the study variables in different groups (n=60)

Variables	Group BF (n=20)	Group BC (n=20)	Group BB (n=20)	P-value
Onset of Blockade (min)				
Sensory	1.80 ± 0.74	1.94 ± 0.49	2.28 ± 0.46	0.006*
Motor	2.68 ± 0.56	2.93 ± 0.69	2.86 ± 0.66	0.274
Highest Level of Sensory Block				
T6	22 (73.3%)	25 (83.3%)	26 (86.7%)	0.412
T8	8 (26.7%)	5 (16.7%)	4 (13.3%)	
Degree of Motor Blockade				
Grade 2	0 (0.0%)	0 (0.0%)	2 (6.7%)	0.118
Grade 3	30 (100.0%)	30 (100.0%)	28 (93.3%)	
Duration of Blockade (min)				
Sensory	306.2 ± 29.21	358.27 ± 44.68	347.0 ± 46.62	<0.001*
Motor	168.9 ± 13.54	191.7 ± 24.82	177.27 ± 22.53	<0.001*

*p<0.05

DISCUSSION

The findings of this study demonstrate that all three adjuvants—fentanyl, clonidine, and buprenorphine—improved the quality of spinal anesthesia when combined with hyperbaric bupivacaine, but their profiles differed with respect to onset and duration. Fentanyl was associated with the most rapid onset of sensory blockade, which is consistent with its lipophilic nature and fast penetration of the spinal cord receptors. However, the duration of both sensory and motor blockade was significantly longer with clonidine and buprenorphine. This aligns with previous studies showing that while fentanyl provides excellent intraoperative analgesia, its shorter half-life results in earlier postoperative analgesic requirements [11].

Buprenorphine, a partial μ-opioid receptor agonist with high receptor affinity, extended the sensory block duration beyond that provided by fentanyl, reflecting its pharmacodynamic profile of prolonged receptor binding. Several studies have highlighted that buprenorphine maintains analgesic efficacy well into the late postoperative period without significant respiratory depression, though pruritus and nausea are reported more frequently [12]. In our study, buprenorphine provided both a longer duration of sensory analgesia and reliable motor block, making it particularly suitable for procedures requiring extended pain relief.

Clonidine, through its α2-adrenergic agonism, significantly prolonged both sensory and motor blockade, surpassing fentanyl in efficacy. The findings corroborate evidence from randomized controlled trials demonstrating that clonidine prolongs block duration by hyperpolarizing postsynaptic neurons and reducing sympathetic outflow [13]. While clonidine's analgesic benefit is well established, its hemodynamic side effects, including hypotension and bradycardia, require vigilance, although no severe adverse events were reported in our study.

The comparison among the three drugs highlights an important clinical consideration: the choice of adjuvant must be tailored not only to the surgical duration but also to patient comorbidities and postoperative analgesic requirements. Clonidine and buprenorphine appear superior when prolonged analgesia is desirable, while fentanyl remains advantageous for shorter procedures due to its rapid onset and stable recovery profile [14]. Furthermore, multimodal strategies that combine pharmacological and non-pharmacological approaches are increasingly being recommended to optimize recovery and reduce reliance on systemic opioids [15].

CONCLUSION

The addition of adjuvants to intrathecal bupivacaine significantly improved the clinical profile of spinal anesthesia. Fentanyl provided the fastest onset of sensory block, while clonidine and buprenorphine offered superior prolongation of both sensory and motor blockade. Between the latter two, clonidine demonstrated the longest block duration, whereas buprenorphine ensured prolonged analgesia with favorable patient comfort. These results support the individualized use of intrathecal adjuvants depending on surgical needs and patient profiles, thereby enhancing the efficacy and safety of spinal anesthesia in lower abdominal and lower limb surgeries.

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