International Journal of Medical and Pharmaceutical Research

Online ISSN-2958-3683 | Print ISSN-2958-3675
Frequency: Bi-Monthly
Available online on: https://ijmpr.in/

Original Article

A Comparative Study of Fentanyl Versus Clonidine as an Adjuvant to Hyperbaric Bupivacaine in Spinal Anaesthesia for Different Lower Limb Surgeries

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Received: 12-05-2026
Accepted: 20-06-2026
Available online:31-07-2026

ABSTRACT

Introduction: Spinal anaesthesia with hyperbaric bupivacaine is commonly used for lower limb surgery, but its duration of analgesia may be limited. Intrathecal adjuvants can improve block quality and prolong postoperative pain relief. This study compared clonidine and fentanyl as adjuvants to hyperbaric bupivacaine in patients undergoing lower limb surgery.

Materials and Methods: This randomized prospective comparative study included 60 patients aged 18 to 60 years with American Society of Anesthesiologists (ASA) physical status I or II who underwent lower limb surgery under spinal anaesthesia. Patients were randomly divided into two groups of 30 each. Group BC received 3 mL of 0.5% hyperbaric bupivacaine with clonidine 45 µg, while Group BF received 3 mL of 0.5% hyperbaric bupivacaine with fentanyl 25 µg. Sensory and motor block characteristics, duration of analgesia, rescue analgesic requirement, hemodynamic changes, and complications were assessed.

Results: The mean onset of sensory block was slower in Group BC than in Group BF, 1.36 ± 0.10 minutes versus 1.18 ± 0.13 minutes, respectively, with a statistically significant difference. The mean time to achieve sensory blockade at the T10 dermatome was also longer in Group BC, 5.40 ± 0.40 minutes versus 5.14 ± 0.52 minutes. The duration of analgesia was significantly longer with clonidine than with fentanyl, 512.33 ± 74.71 minutes versus 270.37 ± 34.41 minutes. The mean rescue analgesic requirement during the first 24 hours was significantly lower in Group BC, 1.60 ± 0.72 doses, compared with 2.43 ± 0.57 doses in Group BF. Intraoperative bradycardia, hypotension, and drowsiness were more frequent with clonidine, although the overall difference in intraoperative complications was not statistically significant. Postoperative drowsiness occurred in 13.3% of patients receiving clonidine and in none receiving fentanyl.

Conclusion: Intrathecal clonidine provided markedly longer postoperative analgesia and reduced the requirement for rescue analgesics compared with fentanyl. However, clonidine was associated with a higher occurrence of hypotension, bradycardia, and drowsiness. Clonidine may be a more effective adjuvant to hyperbaric bupivacaine when prolonged analgesia is desired.

Keywords*: Clonidine, Fentanyl, Hyperbaric bupivacaine, Spinal anaesthesia, Lower limb surgery, Postoperative analgesia.*

INTRODUCTION

Spinal anaesthesia is widely used for lower limb surgery because it provides rapid onset, effective sensory and motor blockade, good muscle relaxation and avoidance of airway manipulation. Hyperbaric bupivacaine is commonly selected because of its reliable action and relatively long duration. However, postoperative analgesia after a single intrathecal dose may be inadequate, while increasing the bupivacaine dose may prolong motor blockade and increase haemodynamic

adverse effects. Intrathecal adjuvants are therefore added to improve block quality, prolong analgesia, and reduce the need for additional analgesics.[1,2]

Fentanyl is a highly lipophilic synthetic opioid that acts mainly on mu opioid receptors in the substantia gelatinosa of the spinal cord. When administered intrathecally with bupivacaine, it enhances intraoperative analgesia and may prolong postoperative pain relief without markedly delaying recovery from motor blockade. Its high lipid solubility results in rapid onset and limited movement towards the brain. However, fentanyl may cause pruritus, nausea, vomiting, urinary retention, and respiratory depression.[2,3]

Clonidine is α2 adrenergic receptor agonist that produces analgesia by reducing the release of nociceptive neurotransmitters and suppressing pain transmission in the dorsal horn of the spinal cord. When added to intrathecal bupivacaine, clonidine may prolong sensory blockade, motor blockade, and postoperative analgesia. Unlike intrathecal opioids, it is not commonly associated with pruritus or clinically important respiratory depression. However, sedation, hypotension, and bradycardia may occur, particularly with higher doses.[3,4]

Previous studies comparing intrathecal clonidine and fentanyl have reported variations in the onset and duration of blockade, postoperative analgesia, sedation, and hemodynamic effects. These differences may be related to the adjuvant dose, the bupivacaine dose, the surgical procedure, and the study population. Some studies have reported longer postoperative analgesia with clonidine, while others have found comparable block characteristics between the two drugs.[2-6]

Therefore, the present study was conducted to compare intrathecal clonidine 45 µg and fentanyl 25 µg as adjuvants to 3 mL of 0.5% hyperbaric bupivacaine in patients undergoing lower limb surgery. The study compared the onset and duration of sensory and motor blockade, duration of postoperative analgesia, rescue analgesic requirement, hemodynamic changes, and adverse effects.

MATERIALS AND METHODS

Study Design and Setting

This randomized, prospective, comparative study was conducted at L.G. Hospital, Maninagar, Ahmedabad, from June 2019 to June 2021, with approval from the Institutional Ethics Committee. Written informed consent was obtained from all participants.

Study Population

A total of 60 patients of either sex, aged 18 to 60 years, with American Society of Anesthesiologists (ASA) physical status I or II and scheduled for lower limb surgery under spinal anaesthesia were included. Patients who refused participation, had American Society of Anesthesiologists physical status III or higher, allergy to local anaesthetics, local infection, bleeding disorder, or altered coagulation profile were excluded.

Anaesthetic Procedure

Patients were randomly allocated into two groups of 30 each. Group BF received 3 mL of 0.5% hyperbaric bupivacaine with fentanyl 25 µg, while Group BC received 3 mL of 0.5% hyperbaric bupivacaine with clonidine 45 µg intrathecally. Spinal anaesthesia was administered at the L2 to L3 or L3 to L4 intervertebral space using a 23 G spinal needle under aseptic precautions.

Outcome Assessment

Sensory block was assessed by the pinprick method, while motor block was evaluated using the modified Bromage scale. The onset and duration of sensory and motor blockade, the duration of postoperative analgesia, the requirement for rescue analgesia during the first 24 hours, hemodynamic parameters, and adverse effects were recorded.

Statistical Analysis

Data were analyzed using SPSS version 27.0 and GraphPad Prism version 5. Continuous variables were expressed as the mean and standard deviation, while categorical variables were presented as frequencies and percentages. The student's t test, chi-square test, and Fisher's exact test were applied as appropriate. A P value below 0.05 was considered statistically significant.

RESULTS

A total of 60 patients were included, with 30 patients each in Group BC and Group BF. The mean age was significantly lower in Group BC than in Group BF, 35.30 ± 8.55 years versus 43.47 ± 11.04 years, respectively. Sex distribution and American Society of Anesthesiologists physical status were comparable between the groups.

Table 1: Baseline Characteristics of the Study Groups

Characteristic	Group BC	Group BF	P value

	(n = 30)	(n = 30)	
Age, years	35.30 ± 8.55	43.47 ± 11.04	0.0022
Male	17 (56.7%)	24 (80.0%)	0.0520
Female	13 (43.3%)	6 (20.0%)	
ASA physical status I	18 (60.0%)	14 (46.7%)	0.3006
ASA physical status II	12 (40.0%)	16 (53.3%)	
Preoperative systolic blood pressure, mmHg	123.80 ± 6.21	120.20 ± 4.76	0.0145
Preoperative diastolic blood pressure, mmHg	77.57 ± 5.43	76.93 ± 4.64	0.6290
Preoperative respiratory rate, per minute	15.41 ± 1.11	18.80 ± 0.80	<0.0001
Preoperative oxygen saturation, %	98.93 ± 1.01	98.40 ± 1.00	0.0452

Values are presented as mean ± standard deviation or as numbers with percentages.

Sensory and Motor Block Characteristics

The onset of sensory block was significantly faster in Group BF than in Group BC, with mean values of 1.18 ± 0.13 minutes and 1.36 ± 0.10 minutes, respectively. The time required to achieve sensory block at the T10 dermatome was also shorter in Group BF.

In contrast, the onset of motor block was significantly faster in Group BC than in Group BF, 1.79 ± 0.15 minutes versus 2.56 ± 0.51 minutes. The time required to achieve motor block to scale 3 was also significantly shorter in Group BC, 3.58 ± 0.32 minutes versus 4.08 ± 0.32 minutes.

Table 2: Comparison of Block Characteristics and Analgesic Outcomes

Outcome	Group BC	Group BF	P value
Onset of sensory block, minutes	1.36 ± 0.10	1.18 ± 0.13	<0.0001
Time to sensory block at T10, minutes	5.40 ± 0.40, n = 30	5.14 ± 0.52, n = 29	0.0334
Onset of motor block, minutes	1.79 ± 0.15	2.56 ± 0.51	<0.0001
Time to achieve motor block to scale 3, minutes	3.58 ± 0.32	4.08 ± 0.32	<0.0001
Duration of surgery, minutes	121.83 ± 17.44	145.67 ± 37.48	0.0025
Duration of analgesia, minutes	512.33 ± 74.71	270.37 ± 34.41	<0.0001
Rescue analgesic doses in 24 hours	1.60 ± 0.72	2.43 ± 0.57	<0.0001

Values are presented as mean ± standard deviation. Data for the time to sensory block at the T10 dermatome were available for 29 patients in Group BF.

Duration of Analgesia and Rescue Analgesic Requirement

The mean duration of analgesia was significantly longer in Group BC than in Group BF, 512.33 ± 74.71 minutes versus 270.37 ± 34.41 minutes. The mean number of rescue analgesic doses required during the first 24 hours was significantly lower in Group BC, 1.60 ± 0.72 doses, compared with 2.43 ± 0.57 doses in Group BF.

In Group BC, 16 patients required 1 rescue analgesic dose, 10 required 2 doses, and 4 required 3 doses. In Group BF, 18 patients required two doses, 11 required three, and 1 required four.

Adverse Effects

Intraoperative complications were observed in 12 patients in Group BC and 5 patients in Group BF. The overall difference in intraoperative complications was not statistically significant. Postoperative drowsiness occurred in four patients in Group BC and none in Group BF, with a statistically significant difference.

Table 3: Intraoperative and Postoperative Adverse Effects

Adverse effect	Group BC (n = 30)	Group BF (n = 30)
Bradycardia	3 (10.0%)	2 (6.7%)
Hypotension	6 (20.0%)	1 (3.3%)
Intraoperative drowsiness	3 (10.0%)	0
Nausea	0	1 (3.3%)
Shivering	0	1 (3.3%)
No intraoperative complication	18 (60.0%)	25 (83.3%)
Postoperative drowsiness	4 (13.3%)	0

The P value for the overall comparison of intraoperative complications was 0.0778. The P value for postoperative drowsiness was 0.0384.

DISCUSSION

The present study compared intrathecal clonidine 45 µg and fentanyl 25 µg as adjuvants to hyperbaric bupivacaine in patients undergoing lower limb surgery. The main finding was that clonidine provided a markedly longer duration of postoperative analgesia and reduced the need for rescue analgesics. However, the onset of sensory and motor block was faster with fentanyl, while hypotension, bradycardia, and drowsiness were more frequent with clonidine.

The onset of sensory block was significantly faster in the fentanyl group than in the clonidine group. The time required to achieve sensory block at the T10 dermatome was also shorter with fentanyl. Similar findings were reported by Routray et al., who observed a faster onset of sensory block with fentanyl than with clonidine.[3] Bajwa et al. also reported a slightly faster sensory block onset with fentanyl, although the difference was not statistically significant.[5]

The onset of motor block and the time required to achieve complete motor block were also shorter in the fentanyl group. These findings may be related to the high lipid solubility and rapid spinal action of fentanyl. However, Singh et al. reported an earlier onset of sensory and motor block with clonidine.[4] Differences in clonidine and bupivacaine doses, total intrathecal volume, and block assessment method may explain these variations.

The mean duration of analgesia was significantly longer in the clonidine group than in the fentanyl group, 512.33 ± 74.71 minutes versus 270.37 ± 34.41 minutes. This was the most important finding of the present study.

Routray et al. reported a longer duration of analgesia with clonidine than with fentanyl, 510.84 minutes versus 434.95 minutes.[3] Bajwa et al. also found that clonidine prolonged postoperative analgesia compared with fentanyl.[5] Datta et al. observed a mean duration of analgesia of 325 minutes with clonidine and 240 minutes with fentanyl.[7] These findings support the superior analgesic duration of intrathecal clonidine.

Clonidine produces analgesia by stimulating spinal alpha 2 adrenergic receptors. This decreases the release of nociceptive neurotransmitters and suppresses pain transmission in the dorsal horn of the spinal cord. Fentanyl acts through spinal opioid receptors and provides rapid analgesia, but its high lipid solubility results in shorter retention in the cerebrospinal fluid.[2,3] The mean rescue analgesic requirement during the first 24 hours was significantly lower in the clonidine group than in the fentanyl group, 1.60 ± 0.72 doses versus 2.43 ± 0.57 doses. More than half of the patients in the clonidine group required only one rescue analgesic dose, whereas most patients in the fentanyl group required two or three doses.

Singh et al. similarly reported lower postoperative analgesic requirements in patients receiving clonidine.[4] Shah and Diwan also observed that postoperative analgesic consumption was greater in the fentanyl group than in groups receiving clonidine.[8] Reduced rescue analgesic requirement is clinically useful because it improves patient comfort and decreases exposure to additional analgesic drugs.

Hypotension, bradycardia, and drowsiness were more frequent in the clonidine group. Hypotension occurred in 20.0% of patients receiving clonidine compared with 3.3% receiving fentanyl. Postoperative drowsiness occurred only in the clonidine group. These effects are expected because clonidine reduces central sympathetic outflow and produces sedation.[3,5]

Routray et al. reported greater sedation with clonidine than with fentanyl.[3] Bajwa et al. also observed higher sedation scores in the clonidine group.[5] Mahendru et al. reported that clonidine prolonged sensory and motor block while maintaining acceptable hemodynamic stability.[2] Agarwal et al. found that low-dose intrathecal clonidine prolonged spinal block and analgesia without causing major hemodynamic instability in elderly patients.[6]

The results indicate that clonidine is more effective when prolonged postoperative analgesia is required. Fentanyl may be preferred when a faster onset and lower sedation are important. The selection of an intrathecal adjuvant should therefore consider the expected duration of surgery, postoperative analgesic requirement, and the patient's hemodynamic condition. The present study had certain limitations. It was conducted at a single center with a small sample size. Differences in age, baseline respiratory rate, systolic blood pressure, oxygen saturation, and duration of surgery were present between the groups. Various types of lower-limb surgeries were included, which may have influenced postoperative pain. Pain scores and total rescue analgesic dose in milligrams were not recorded. Larger randomized, double-blind studies with standardized surgical procedures are required to confirm these findings.

CONCLUSION

Intrathecal clonidine 45 µg as an adjuvant to hyperbaric bupivacaine provided significantly longer postoperative analgesia and reduced rescue analgesic requirements compared with fentanyl 25 µg in patients undergoing lower limb surgery. Fentanyl produced a faster onset of sensory and motor block, while clonidine was associated with more hypotension, bradycardia, and drowsiness. Thus, clonidine may be preferred when prolonged postoperative analgesia is required, provided adequate hemodynamic monitoring is available.

Conflict of Interest
The authors declare no conflicts of interest regarding the publication of this study.

Funding
This research did not receive any specific funding from public, commercial, or not-for-profit organizations.

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