DOI: 10.7860/JCDR/2026/81416.22455

Original Article

Anaesthesia Section

Comparison of Two Different Doses of Intrathecal Clonidine as Adjuvant to Hyperbaric Levobupivacaine for Spinal Anaesthesia in Femur Fracture Surgeries: A Randomised Triple-blind Clinical Study

JATIN PATEL[1], RADHIKA JAIN[2], PRIYA KISHNANI[3], CHARMI SHAH[4]

ABSTRACT

Introduction: Femur fractures in elderly patients present unique challenges for anaesthetic management. Spinal anaesthesia with adjuvants has emerged as a preferred technique to enhance the quality of blockade while minimising local anaesthetic doses. Intrathecal clonidine, as an adjuvant to local anaesthetics, enhances the quality and duration of spinal anaesthesia. However, the optimal dose remains controversial due to dose-dependent side-effects.

Aim: To compare the efficacy and safety of two different doses of intrathecal clonidine (30 µg vs 50 µg) as an adjuvant to hyperbaric levobupivacaine for spinal anaesthesia in femur fracture surgeries.

Materials and Methods: This randomised triple-blind clinical study was conducted at the Department of Anaesthesiology at Shrimati Bhikhiben Kanjibhai Shah (SBKS) Medical Institute and Research Centre, Sumandeep Vidyapeeth, Piparia, Vadodara, Gujarat, India, from January 2022 to December 2024 after institutional ethics committee approval. A total of 62 American Society of Anaesthesiologists (ASA) I-II patients aged 18-65 years undergoing femur fracture surgeries were randomly allocated into two groups. Group LC30 (n=31) received 3 mL of 0.5% hyperbaric levobupivacaine with 30 µg clonidine and Group LC50 (n=31) received 3 mL of 0.5% hyperbaric levobupivacaine with 50 µg clonidine, both diluted to a total volume of 3.5 mL with normal saline. The onset and duration of sensory and motor blockade, along with the duration of absolute and effective analgesia, were assessed. Data analysis was performed using Jamovi software with independent t-tests for continuous variables and Chi-square tests for categorical variables. A p-value <0.05 was considered statistically significant.

Results: Demographic parameters, including age, gender, ASA grade and baseline haemodynamics, were comparable between the groups. No significant difference was observed in the onset of sensory or motor blockade between the two groups. The duration of sensory and motor blockade was longer in Group LC50 (263.30±9.2 and 359.20±18.1 min, respectively) compared to Group LC30 (215.78±7.7 and 300.27±10.6 min, respectively). The durations of absolute and effective analgesia were also longer in Group LC50 (300.50±18.2 and 451.70±18.2 min, respectively) compared to Group LC30 (289.90±11.9 and 315.10±37.6 min, respectively), with rescue analgesia required more frequently in the LC30 group. However, the LC50 group demonstrated a higher incidence of bradycardia (32.3% vs 12.9%), hypotension (45.2% vs 19.4%) and greater sedation compared to the LC30 group. Sedation scores were significantly higher in the LC50 group throughout the perioperative period.

Conclusion: Intrathecal clonidine 50 µg combined with hyperbaric levobupivacaine provides significantly prolonged sensory and motor blockade with extended postoperative analgesia compared to a 30 µg dose. However, the higher dose is associated with an increased incidence of haemodynamic side-effects, necessitating closer monitoring and prompt intervention.

Keywords: Analgesia, Bradycardia, Haemodynamics, Hypotension, Sedation

INTRODUCTION

Femur fractures represent a significant global healthcare burden, particularly in the elderly population, where the incidence continues to rise due to increasing life expectancy and age-related osteoporosis. Regional anaesthesia techniques, especially spinal anaesthesia, have become the preferred approach for lower limb orthopaedic surgeries because they provide excellent surgical conditions while avoiding the risks associated with general anaesthesia [1,2].

Spinal anaesthesia remains a cornerstone technique for lower limb orthopaedic procedures, including femur fracture surgeries, due to its reliability, cost-effectiveness and favourable safety profile [1]. The technique provides profound sensory and motor blockade while avoiding the complications associated with general anaesthesia, particularly in elderly patients presenting with femur fractures [2].

Levobupivacaine, the S(-)-enantiomer of racemic bupivacaine, has emerged as a safer alternative because it offers reduced cardiotoxicity and neurotoxicity while maintaining equivalent anaesthetic efficacy [3]. However, the duration of analgesia with local anaesthetics alone may be insufficient for complex orthopaedic procedures and postoperative pain management.

Adjuvants to spinal anaesthesia have gained popularity for enhancing the quality and duration of blockade while reducing local anaesthetic requirements. Among various adjuvants, clonidine, an α2-adrenergic agonist, has shown promising results due to its analgesic properties and favourable side-effect profile compared to opioids [4]. Clonidine acts by stimulating α2 receptors in the dorsal horn of the spinal cord, inhibiting substance P release and enhancing the hyperpolarisation effects of local anaesthetics [5].

Previous studies have demonstrated that intrathecal clonidine significantly prolongs sensory and motor blockade and provides extended postoperative analgesia [6-8]. However, the optimal dose remains controversial, as higher doses may lead to an increased incidence of haemodynamic side-effects, including hypotension, bradycardia and sedation [9,10]. Despite extensive research on intrathecal clonidine, there remains a gap in the literature specifically comparing 30 µg versus 50 µg doses with hyperbaric levobupivacaine in femur fracture surgeries. The present study addresses this gap by providing a direct comparison of these two clinically relevant doses.

The present study aimed to compare the efficacy and safety of two different doses of intrathecal clonidine as an adjuvant to hyperbaric levobupivacaine in patients undergoing femur fracture surgeries. The primary objectives were to assess the onset and duration of sensory and motor blockade and the duration of absolute and effective analgesia. The secondary objectives included evaluation of haemodynamic changes (heart rate, blood pressure), incidence of complications (hypotension, bradycardia, nausea/vomiting), sedation levels, 24-hour rescue analgesic requirements and patient satisfaction scores (1-10 scale).

MATERIALS AND METHODS

The present randomised triple-blind clinical study was conducted in the Department of Anaesthesiology at SBKS Medical Institute and Research Centre, Sumandeep Vidyapeeth, Piparia, Vadodara, Gujarat, India, from January 2022 to December 2024. The study was approved by the Institutional Ethics Committee (SVU/SBKS/IEC/2022-25) and registered with the Clinical Trials Registry of India (CTRI/2024/10/075804). Written informed consent was obtained from all participants.

Sample size calculation: The sample size was calculated using the formula for comparing two proportions:

$n = (Z\alpha/2 + Z\beta)^2 \times \{(p1(1-p1) + p2(1-p2))\}/(p1-p2)^2$

Where:

- $Z\alpha/2 = 1.96$ (critical value for 95% confidence level)
- $Z\beta = 0.84$ (critical value for 80% power)
- $\alpha = 0.05$ (significance level)
- $\beta = 0.20$ (type II error, power = 80%)
- p1 = 0.85 (estimated proportion of successful analgesia in LC50 group)
- p2 = 0.50 (estimated proportion of successful analgesia in LC30 group)

$n=(1.96+0.84)^2\times\{(0.85\times0.15+0.50\times0.50)\} / (0.85-0.50)^2$ $n=(2.80)^2\times(0.1275+0.25)/(0.35)^2$ $n=7.84\times0.3775/0.1225$ $n=24.15\approx25$ patients per group

Accounting for a 20% dropout rate: 25 × 1.2 = 31 patients per group.

Total sample size: 62 patients (31 per group).

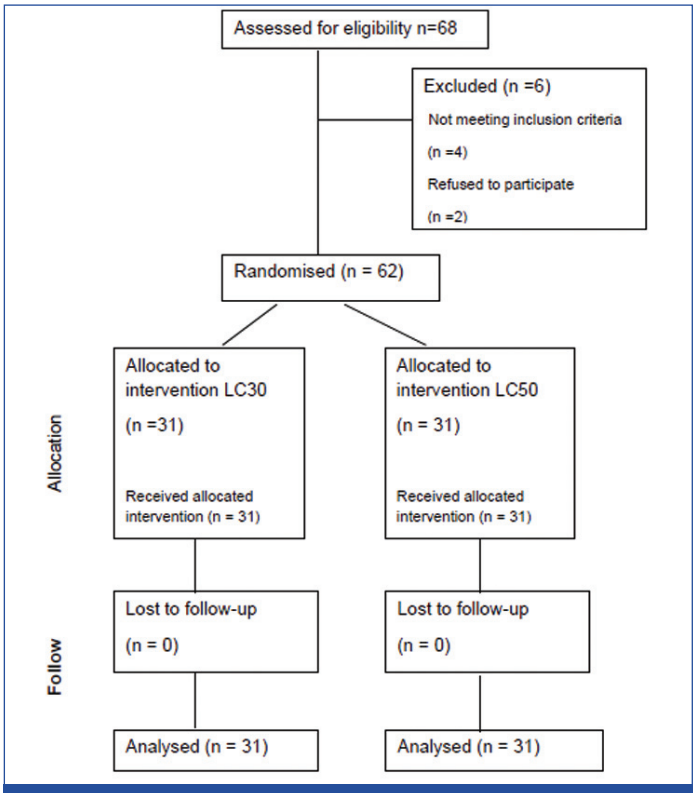
Based on previous literature suggesting a clinically meaningful difference of 45 minutes in the duration of analgesia between different clonidine doses, a total of 62 patients (31 per group) were enrolled [11].

Inclusion and Exclusion criteria: Inclusion criteria were ASA physical status I-II patients aged 18 to 65 years scheduled for elective femur fracture surgeries under spinal anaesthesia. Eligible participants had a body weight between 50 and 90 kg and a height ranging from 150 to 180 cm. Patients with no known history of allergy, sensitivity, or other reactions to local anaesthetics of the ester or amide type were included.

The exclusion criteria were as follows: contraindications to spinal anaesthesia such as coagulopathy, infection at the puncture site, or raised intracranial pressure; known allergies to the study drugs; a history of seizure disorders; current use of antihypertensive medications, particularly α2 agonists or antagonists; neurological disorders or peripheral neuropathy; ASA grade III-IV; pregnancy or lactation; and refusal to participate.

A total of 68 patients were assessed for eligibility, of whom 62 patients meeting the inclusion criteria were enrolled in the study. Six patients were excluded (4 due to ASA III status and 2 due to anticoagulant therapy).

Triple blinding was employed. Patients were randomly allocated into two groups using computer-generated randomisation with concealed allocation through sealed opaque envelopes. The randomisation sequence was generated by a statistician not involved in patient care. The study drugs were prepared by an anaesthesiologist not involved in patient assessment or data collection. Both the anaesthesiologist administering the block and the observer recording data were blinded to group allocation and patients were also blinded to their group assignment. The blinding code was broken only after completion of the statistical analysis. A total of 62 patients were randomised into two groups (LC30 and LC50, n=31 each) and all completed the study as per protocol, as shown in [Table/Fig-1]. There were no losses to follow-up or protocol violations.



[Table/Fig-1]: Consolidated Standards of Reporting Trials (CONSORT) flow diagram.

Study groups:

- **Group LC30 (n=31):** 3 mL of 0.5% hyperbaric levobupivacaine + 30 µg clonidine + 0.5 mL normal saline (total 3.5 mL)
- **Group LC50 (n=31):** 3 mL of 0.5% hyperbaric levobupivacaine + 50 µg clonidine + 0.3 mL normal saline (total 3.5 mL)

Study Procedure

The doses of clonidine were selected based on previous studies demonstrating their effectiveness while minimising side-effects [8-10].

Anaesthetic technique: All patients underwent standard preoperative assessment and overnight fasting. In the operating room, standard ASA monitoring was applied, including Electrocardiogram (ECG), non invasive blood pressure and pulse oximetry. An 18G intravenous cannula was secured and patients were preloaded with 10 mL/kg Ringer's lactate solution over 15 minutes.

Spinal anaesthesia was administered at the L3-L4 or L2-L3 interspace using a 23G Quincke spinal needle in the sitting position under strict aseptic precautions. After confirming free flow of cerebrospinal fluid, the study drug was injected slowly over 30-40 seconds with the bevel facing cephalad. Patients were then positioned supine with a 15-degree left lateral tilt.

Standardised protocols were implemented for perioperative complications. Hypotension (systolic BP <90 mmHg or >20% decrease from baseline) was treated with mephentermine 6 mg intravenous (i.v.) bolus and additional i.v. fluids. Bradycardia (<50 bpm) was managed with atropine 0.6 mg i.v.. Respiratory depression (SpO_2 <92%) was treated with supplemental oxygen via face mask.

Onset of sensory blockade was defined as the time from intrathecal injection to loss of pinprick sensation at the L1 level. Onset of motor blockade was defined as time to achieve Bromage Grade I (inability to raise the extended leg). Duration of sensory blockade was measured from injection to regression of sensory level to L1, while duration of motor blockade was the time to complete motor recovery (Bromage 0). Duration of absolute analgesia was defined as time from injection to first complaint of pain and duration of effective analgesia was time to first rescue analgesic requirement. Rescue analgesia consisted of diclofenac 75 mg IM when VAS ≥4.

Sensory blockade was assessed using the pinprick method every two minutes until peak level, then every 15 minutes. Motor blockade was evaluated using the modified Bromage scale [11] (Grade 0-3). Sedation was monitored using the Ramsay Sedation Scale [12] (score 1-6). Pain was assessed using the Visual Analogue Scale (VAS) (0-10).

Haemodynamic parameters were recorded at baseline and at predetermined intervals: 2, 4, 6, 8, 10, 15, 20, 25, 30, 45, 60, 90 and 120 minutes intraoperatively and 2 hours postoperatively. Patient satisfaction was measured using a 10-point scale (1=very unsatisfied, 10=very satisfied) at 24 hours postoperatively.

STATISTICAL ANALYSIS

Statistical analysis was performed using Jamovi version 2.0 software. Normality of the data was assessed using the Shapiro-Wilk test. Continuous variables were expressed as mean±standard deviation and compared using independent t-tests for normally distributed data and the Mann-Whitney U test for non parametric data. Categorical variables were presented as frequencies and percentages and compared using the Chi-square test or Fisher's-exact test, as appropriate. Repeated measures Analysis of Variance (ANOVA) was used to analyse haemodynamic parameters over time. A p-value <0.05 was considered statistically significant.

RESULTS

Both groups were comparable regarding demographic characteristics, with no significant differences observed in baseline haemodynamic parameters or distribution of co-morbidities [Table/Fig-2].

Parameters	LC30 group (n=31)	LC50 group (n=31)	t-value	p-value
Age (years)	52.11±14.20	54.12±13.77	0.57	0.58
Weight (kg)	70.03±13.03	62.97±11.22	1.08	0.28
Height (cm)	165.5±7.2	163.8±6.9	0.48	0.63
Gender (M/F)	17/14	13/18	χ^2=1.04	0.31
ASA Grade (I/II)	15/16	16/15	χ^2=0.06	0.81

[Table/Fig-2]: Demographic characteristics and baseline parameters.
Statistical test used: Independent t-test for continuous variables, Chi-square test for categorical variables

As shown in [Table/Fig-3], the LC50 group demonstrated a significantly faster onset of sensory blockade at the L1 level and motor blockade (Bromage Grade I) compared to the LC30 group. Time to achieve the highest sensory level was also significantly shorter in the LC50 group.

Parameters	LC30 group (n=31)	LC50 group (n=31)	t-value	p-value
Onset of sensory blockade at L1 level (min)	2.96±0.50	2.49±0.26	4.61	<0.001
Time to achieve sensory highest level (min)	12.24±1.29	11.78±1.31	1.40	0.03
Highest sensory level achieved (median)	T8 (T6-T10)	T6 (T4-T8)	-	0.02
Onset of motor blockade Grade I (min)	1.60±0.34	1.06±0.10	8.51	<0.001
Onset of motor blockade Grade III (min)	3.10±0.67	3.02±0.67	0.47	0.65

[Table/Fig-3]: Onset and characteristics of subarachnoid blockade.
Statistical test used: Independent t-test, Mann-Whitney U test for median values

The LC50 group showed a significantly longer duration of all measured parameters compared to the LC30 group. The most notable difference was observed in the duration of effective analgesia, which was approximately 136 minutes longer in the LC50 group [Table/Fig-4].

Parameters	LC30 group (n=31)	LC50 group (n=31)	t-value	p-value
Two segment regression (min)	102.50±6.8	148.10±8.18	23.7	<0.001
Duration of sensory blockade (min)	215.78±7.7	263.30±9.2	22.0	<0.001
Duration of motor blockade (min)	300.27±10.6	359.20±18.1	15.6	<0.001
Duration of absolute analgesia (min)	289.90±11.9	300.50±18.2	2.70	0.008
Duration of effective analgesia (min)	315.10±37.6	451.70±18.2	18.4	<0.001
Rescue analgesia in 24 hours (doses)	1.55±0.51	1.39±0.50	1.24	0.02

[Table/Fig-4]: Duration of blockade and analgesia.
Statistical test used: Independent t-test

As shown in [Table/Fig-5], the LC50 group exhibited significantly greater haemodynamic changes during the intraoperative period, with more pronounced decreases in heart rate and blood pressure from 15 minutes onwards compared to the LC30 group.

The LC50 group had a significantly higher incidence of bradycardia, hypotension and excessive sedation compared to the LC30 group. No cases of respiratory depression were observed in either group [Table/Fig-6].

The LC50 group required significantly less rescue analgesia during the first 24 hours postoperatively and reported higher patient satisfaction scores. No significant differences were observed in postoperative complications between the groups [Table/Fig-7]. Sedation scores were significantly higher in the LC50 group during the intraoperative period, particularly at 30 and 60 minutes after block administration [Table/Fig-8].

As shown in [Table/Fig-9], VAS scores showed significantly lower values at 2,4,6,8 hour post op times in LC50 group as compared to LC30 group.

DISCUSSION

The present study demonstrated that intrathecal clonidine, at both 30 µg and 50 µg doses, effectively augments hyperbaric levobupivacaine for spinal anaesthesia in femur fracture surgeries. The 50 µg dose provided superior blockade characteristics, with significantly prolonged sensory and motor blockade and extended postoperative analgesia, although at the cost of increased haemodynamic side-effects. These findings provide valuable evidence for optimising intrathecal clonidine dosing in orthopaedic anaesthesia.

The study found a significantly faster onset of sensory blockade with 50 µg clonidine compared to 30 µg (2.49±0.26 vs. 2.96±0.50

Time	Heart rate (bpm)			Systolic BP (mmHg)			Diastolic BP (mmHg)		
	LC30	LC50	p-value	LC30	LC50	p-value	LC30	LC50	p-value
0 min	82.45±6.12	79.87±5.98	0.09	125.32±5.87	123.68±6.21	0.28	77.84±4.95	76.23±5.12	0.21
2 min	80.45±6.90	78.94±5.32	0.31	122.45±8.90	119.94±8.32	0.24	75.45±5.90	73.94±5.32	0.28
4 min	79.51±7.21	78.45±5.13	0.48	118.51±9.21	115.45±9.13	0.18	74.51±6.21	72.45±5.13	0.15
6 min	78.13±7.06	74.91±5.02	0.023	115.13±9.06	110.91±9.02	0.07	73.13±6.06	70.91±5.02	0.11
8 min	76.67±7.60	73.47±6.12	0.088	112.67±8.60	106.47±8.12	0.003	71.67±5.60	68.47±5.12	0.021
10 min	74.26±6.90	68.76±6.60	0.001	111.26±8.90	103.76±8.60	0.001	70.26±5.90	66.76±5.60	0.013
15 min	76.58±7.23	68.32±8.45	<0.001	110.45±8.92	102.87±9.84	0.002	72.45±6.23	67.89±7.45	0.008
20 min	72.58±8.11	61.89±6.70	<0.001	109.58±9.11	101.23±9.45	<0.001	71.58±6.11	66.23±6.45	0.001
25 min	71.18±7.20	60.31±5.80	<0.001	108.18±9.20	100.31±9.80	0.001	70.18±6.20	65.31±6.80	0.003
30 min	70.27±7.21	59.94±6.04	<0.001	108.27±9.21	101.23±10.45	0.006	74.12±5.98	69.23±6.87	0.003
45 min	70.03±8.20	58.84±5.34	<0.001	112.87±8.67	105.45±9.23	0.001	75.23±6.12	70.45±7.23	0.007
60 min	74.03±8.30	69.54±5.30	0.014	118.03±8.30	112.54±8.30	0.009	76.03±5.30	72.54±6.30	0.019
90 min	78.14±8.40	73.45±5.70	0.015	121.14±7.40	118.45±7.70	0.15	77.14±5.40	74.45±5.70	0.07
120 min	79.58±8.30	76.85±5.60	0.16	123.58±6.30	121.85±6.60	0.28	78.58±5.30	76.85±5.60	0.21

[Table/Fig-5]: Detailed intraoperative haemodynamic parameters.
Statistical test used: Repeated measures ANOVA with post-hoc analysis (F-value = 14.2, p<0.001)

Complications	LC30 group (n=31)	LC50 group (n=31)	χ^2	p-value
Bradycardia	4 (12.9%)	10 (32.3%)	3.28	0.048
Hypotension	6 (19.4%)	14 (45.2%)	4.79	0.036
Nausea/Vomiting	3 (11.1%)	3 (8.8%)	0.09	0.749
Excessive Sedation (Ramsay ≥4)	2 (6.5%)	8 (25.8%)	4.29	0.034

[Table/Fig-6]: Incidence of intraoperative complications.
Statistical test used: Chi-square test, Fisher's exact test

Parameters	LC30 Group (n=31)	LC50 Group (n=31)	t-value	p-value
Time to first rescue analgesia (min)	315.10±37.6	451.70±18.2	18.4	<0.001
Total rescue analgesia in 24 h (doses)	1.55±0.51	1.39±0.50	1.24	0.02
Patient satisfaction score (1-10)	8.2±1.1	8.8±0.9	2.34	0.02
Postoperative nausea/vomiting	2 (6.5%)	1 (3.2%)	0.35	0.554
Urinary retention	1 (3.2%)	2 (6.5%)	0.35	0.554

[Table/Fig-7]: Postoperative parameters and analgesic requirements.
Statistical test used: Independent t-test for continuous variables, Fisher's-exact test for categorical variables

Time point	LC30 group (n=31)	LC50 group (n=31)	t-value	p-value
Baseline	2.0±0.0	2.0±0.0	0.00	1.000
15 min	2.3±0.5	2.8±0.6	3.54	0.042
30 min	2.4±0.5	3.2±0.7	5.18	0.001
60 min	2.2±0.4	2.9±0.6	5.35	0.008
120 min	2.1±0.3	2.5±0.5	3.75	0.124
Postoperative 2 h	2.0±0.2	2.1±0.3	1.54	0.892

[Table/Fig-8]: Sedation scores over time.
Statistical test used: Mann-Whitney U test IQR = Interquartile range

Time point	LC30 group (n=31) Mean±SD	LC50 group (n=31) Mean±SD	t-value	p-value
2 hours postop	1.2±0.8	0.5±0.6	3.89	<0.001
4 hours postop	2.8±1.1	1.3±0.9	5.86	<0.001
6 hours postop	4.1±1.3	2.4±1.0	5.73	<0.001
8 hours postop	4.9±1.2	3.8±1.1	3.76	<0.001
12 hours postop	5.2±1.4	4.2±1.2	3.00	0.003
24 hours postop	4.5±1.3	3.9±1.1	1.96	0.048

[Table/Fig-9]: Visual Analogue Scale (VAS) Scores.
Statistical test used: Independent t-test

minutes), consistent with the dose-dependent effects reported in recent literature. Similar findings were reported by Gautham B et al., who demonstrated that clonidine 30 µg with intrathecal levobupivacaine shortened the onset of sensory and motor blockades [13]. The mechanism involves enhanced α2-receptor activation at higher concentrations, facilitating rapid neural tissue penetration and blockade.

Interestingly, a meta-analysis by Zhang C et al., comparing dexmedetomidine and clonidine as intrathecal adjuvants, found that while both α2 agonists hastened block onset, the effect was more pronounced with higher doses, supporting the present observations [14]. The clinical significance of this approximately 30-second difference in onset may be limited, but it demonstrates the pharmacodynamic dose-response relationship of intrathecal clonidine.

The most clinically relevant finding was the markedly prolonged duration of effective analgesia with the 50 µg dose (451.70±18.2 vs. 315.10±37.6 minutes), representing an additional 136 minutes of pain relief. This substantial extension has important implications for postoperative recovery and rehabilitation in femur fracture patients. These results align with recent studies by Mishra J and Agarwal MK, who found that higher doses of α2 agonists provided superior postoperative analgesia in orthopaedic surgeries [15].

The prolonged analgesia can be attributed to multiple mechanisms, including direct spinal cord α2 receptor activation, reduced substance P release and enhanced local anaesthetic action through altered sodium channel kinetics. A 2020 study by Mohamed T et al., in trauma patients undergoing lower limb surgery, reported similar dose-dependent prolongation of analgesia, though they used bupivacaine rather than levobupivacaine [16]. The consistency across different local anaesthetics suggests that the effect is primarily due to clonidine's intrinsic properties rather than drug interactions.

The increased incidence of hypotension (44.4% vs. 20.0%) and bradycardia (33.3% vs. 13.0%) with the 50 µg dose represents the primary safety concern. These effects peaked at 20-30 minutes post-injection and were successfully managed with standard interventions. The findings are consistent with a systematic review by Crespo S et al., which reported dose-dependent haemodynamic effects of intrathecal clonidine [17]. The pathophysiology involves central sympatholytic effects mediated through brainstem α2 receptors and decreased peripheral sympathetic outflow. Importantly, no patient in either group experienced severe complications requiring

intensive care admission or had lasting sequelae. Recent evidence from a large randomised controlled trial by Lee KH et al., in elderly patients undergoing hip surgery, suggests that while haemodynamic changes are common, they are generally manageable with appropriate monitoring and intervention protocols [18]. The key to safe practice appears to be anticipatory management rather than reactive treatment.

Sedation levels were significantly higher with 50 µg clonidine, with 25.8% of patients experiencing Ramsay scores ≥4 compared to 6.5% in the LC30 group. While this raises concerns about oversedation, it is noteworthy that no patient developed respiratory depression or required airway intervention. The sedation appeared beneficial for patient comfort during surgery, as reflected in higher satisfaction scores (8.8±0.9 vs. 8.2±1.1). Recent work by Lim TW et al., using processed EEG monitoring during spinal anaesthesia with clonidine, showed that the sedation is primarily cortical without significant depression of the respiratory centre, explaining the safety profile observed [19]. The sedative effect of intrathecal clonidine may actually be advantageous in the often anxious trauma patient population, providing anxiolysis without the respiratory risks associated with systemic sedatives.

The choice between 30 µg and 50 µg clonidine requires individualised decision-making based on patient factors and surgical requirements. For young, haemodynamically stable patients undergoing lengthy procedures, the 50 µg dose offers superior analgesia with manageable side-effects. Conversely, elderly patients or those with cardiovascular co-morbidities may benefit more from the 30 µg dose, which still provides significant analgesic enhancement with reduced haemodynamic risk. The findings suggest that the 50 µg dose may be particularly valuable in the context of Enhanced Recovery After Surgery (ERAS) protocols, where prolonged analgesia facilitates early mobilisation. A recent implementation study by Thurm M et al., demonstrated that optimised regional anaesthesia with appropriate adjuvants significantly improved postoperative recovery metrics in orthopaedic patients [20].

However, clonidine remains more widely available and cost-effective, particularly in resource-limited settings. The ongoing debate regarding optimal adjuvant selection highlights the need for further head-to-head comparisons and economic analyses. The present study's strengths include its randomised triple-blind design, comprehensive outcome assessment and clinically relevant dose comparison. The use of validated assessment tools (Bromage scale, Ramsay sedation scale) enhances the reliability of the results. Nevertheless, several limitations merit consideration [11,12].

Future research should focus on dose-optimisation studies in elderly patients, comparisons with newer adjuvants such as dexmedetomidine and evaluation of long-term functional outcomes. The development of predictive models for identifying patients at high risk of haemodynamic complications could further improve safety. Additionally, investigating the combination of low-dose clonidine with other adjuvants may provide synergistic benefits while minimising side-effects.

Limitation(s)

The single-centre nature of the study may limit generalisability, although the patient population is representative of typical femur fracture demographics. The exclusion of elderly patients (>65 years) and those with significant co-morbidities reduces external validity for these high-risk groups, who commonly present with femur fractures. Additionally, the study did not assess long-term outcomes beyond 24 hours or evaluate the impact on rehabilitation milestones. The non significant difference in baseline weights between groups, while not affecting randomisation validity, could theoretically influence drug distribution, although subgroup analysis showed no correlation between weight and outcomes.

CONCLUSION(S)

Intrathecal clonidine 50 µg as an adjuvant to hyperbaric levobupivacaine provides superior analgesic efficacy, with faster onset, prolonged sensory and motor blockade and extended postoperative analgesia compared to 30 µg in femur fracture surgeries. The 50 µg dose extends effective analgesia by approximately 136 minutes, reducing postoperative opioid requirements and improving patient satisfaction. However, this enhanced efficacy is associated with a significantly higher incidence of haemodynamic side-effects, including hypotension and bradycardia, necessitating vigilant monitoring and prompt intervention. The choice between doses should be individualised based on patient characteristics: the 50 µg dose is suitable for young, stable patients requiring prolonged analgesia, whereas 30 µg offers a safer profile for elderly or medically compromised patients. Both doses appear safe and effective when appropriate monitoring and management protocols are implemented, contributing to improved perioperative outcomes in femur fracture surgery.

REFERENCES

[1] Neuman MD, Feng R, Carson JL, Gaskins LJ, Dillane D, Sessler DI, et al. Spinal anesthesia or general anesthesia for hip surgery in older adults. N Engl J Med. 2021;385(22):2025-35.
[2] White SM, Altermatt F, Barry J, Ben-David B, Coburn M, Coluzzi F, et al. International Fragility Fracture Network Delphi consensus statement on the principles of anaesthesia for patients with hip fracture. Anaesthesia. 2018;73(7):863-74.
[3] Bajwa SJ, Kaur J. Clinical profile of levobupivacaine in regional anesthesia: A systematic review. J Anaesthesiol Clin Pharmacol. 2013;29(4):530-39.
[4] Eisenach JC, De Kock M, Klimscha W. Alpha(2)-adrenergic agonists for regional anesthesia. A clinical review of clonidine (1984-1995). Anesthesiology. 1996;85(3):655-74.
[5] Giovannitti JA Jr, Thoms SM, Crawford JJ. Alpha-2 adrenergic receptor agonists: A review of current clinical applications. Anesth Prog. 2015;62(1):31-39.
[6] Elia N, Culebras X, Mazza C, Schiffer E, Tramèr MR. Clonidine as an adjuvant to intrathecal local anesthetics for surgery: Systematic review of randomized trials. Reg Anesth Pain Med. 2008;33(2):159-67.
[7] Dobrydnjov I, Axelsson K, Thörn SE, Matthiesen P, Klockhoff H, Holmström B, et al. Clonidine combined with small-dose bupivacaine during spinal anesthesia for inguinal herniorrhaphy: A randomized double-blinded study. Anesth Analg. 2003;96(5):1496-503.
[8] Saxena H, Singh S, Ghildiyal S. Low dose intrathecal clonidine with bupivicaine improves onset and duration of block with haemodynamic stability. Internet J Anesthesiol. 2010;23(1):01-07.
[9] Kanazi GE, Aouad MT, Jabbour-Khoury SI, Al Jazzar MD, Alameddine MM, Al-Yaman R, et al. Effect of low-dose dexmedetomidine or clonidine on the characteristics of bupivacaine spinal block. Acta Anaesthesiol Scand. 2006;50(2):222-27.
[10] Agarwal D, Chopra M, Mohta M, Sethi AK. Clonidine as an adjuvant to hyperbaric bupivacaine for spinal anesthesia in elderly patients undergoing lower limb orthopedic surgeries. Saudi J Anaesth. 2014;8(2):209-14.
[11] Bromage PR. A comparison of the hydrochloride and carbon dioxide salts of lidocaine and prilocaine in epidural analgesia. Acta Anaesthesiol Scand Suppl. 1965;16:55-69.
[12] Ramsay MA, Savege TM, Simpson BR, Goodwin R. Controlled sedation with alphaxalone-alphadolone. Br Med J. 1974;2(5920):656-59.
[13] Gautham B, Reddy VS, Jeswin P, Kanna S. A comparative study of intrathecal isobaric levobupivacaine with or without clonidine for quality of subarachnoid block in elective lower abdominal surgeries. Anesth Essays Res. 2019;13(2):236-42.
[14] Zhang C, Li C, Pirrone M, Sun L, Mi W. Comparison of dexmedetomidine and clonidine as adjuvants to local anesthetics for intrathecal anesthesia: A meta-analysis of randomized controlled trials. J Clin Pharmacol. 2016;56(7):827-34.
[15] Mishra J, Agarwal MK. Spinal Anaesthesia with Levobupivacaine per se versus Combination of Levobupivacaine plus Dexmeditomidine: A Comparative Clinical Assessment. Int J Health Clin Res. 2020;3(10):192-96. Retrieved from https://ijhcr.com/index.php/ijhcr/article/view/431.
[16] Mohamed T, Susheela I, Balakrishnan BP, Kaniyil S. Dexmedetomidine as adjuvant to lower doses of intrathecal bupivacaine for lower limb orthopedic surgeries. Anesthesia: Essays and Researches. 2017;11(3):681-85. Doi: 10.4103/aer.AER_243_16.
[17] Crespo S, Dangelser G, Haller G. Intrathecal clonidine as an adjuvant for neuraxial anaesthesia during caesarean delivery: A systematic review and meta-analysis of randomised trials. Int J Obstet Anesth. 2017;32:64-76.
[18] Lee KH, Lee SJ, Park JH, Kim SH, Lee H, Oh DS, et al. Analgesia for spinal anesthesia positioning in elderly patients with proximal femoral fractures: Dexmedetomidine-ketamine versus dexmedetomidine-fentanyl. Medicine (Baltimore). 2020;99(20):e20001.

[19] Lim TW, Choi YH, Kim JY, Choi JB, Lee SK, Youn EJ, et al. Efficacy of the bispectral index and Observer's Assessment of Alertness/Sedation Scale in monitoring sedation during spinal anesthesia: A randomized clinical trial. J Clin Monit Comput. 2020;34(2):303-10.

[20] Thurm M, Hultin M, Johansson G, Dahlin BK, Winsö O, Ljungberg B. Spinal anaesthesia with clonidine: Pain relief and earlier mobilisation after open nephrectomy - A randomised clinical trial. J Int Med Res. 2022;50(9):3000605221126883.

PARTICULARS OF CONTRIBUTORS:
1. Professor, Department of Anaesthesiology, Sumandeep Vidyapeeth (Deemed to be University), Vadodara, Gujarat, India.
2. 3rd Year Resident, Department of Anaesthesiology, Sumandeep Vidyapeeth (Deemed to be University), Vadodara, Gujarat, India.
3. Associate Professor, Department of Anaesthesiology, Sumandeep Vidyapeeth (Deemed to be University), Vadodara, Gujarat, India.
4. Assistant Professor, Department of Anaesthesiology, Sumandeep Vidyapeeth (Deemed to be University), Vadodara, Gujarat, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Radhika Jain,
3rd Year Resident, Department of Anaesthesiology, Sumandeep Vidyapeeth (Deemed to be University), Vadodara-391760, Gujarat, India.
E-mail: radhujain27@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Jul 03, 2025
- Manual Googling: Oct 30, 2025
- iThenticate Software: Nov 01, 2025 (11%)

ETYMOLOGY: Author Origin

EMENDATIONS: 7

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Jun 19, 2025**
Date of Peer Review: **Aug 08, 2025**
Date of Acceptance: **Nov 03, 2025**
Date of Publishing: **Feb 01, 2026**