DOI: https://doi.org/10.62644/iajlb.2026.v23.i3.pp103-111 Indo-Am. J. of Life Sc & Bt | Vol. 23, Issue 3, 2026 | pp 103-111

ISSN : 2347 - 2243

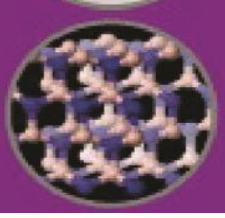


Indo - American Journal of Life Sciences and Biotechnology









www.iajlb.org
Email : editor@iajlb.com or iajlb.editor@gmail.com

Indo-American Journal of Life Sciences and Biotechnology

Indo-Am. J. of LifeSc & Bt., 2026 *ISSN 2347-2243 www.iajlb.org*

Vol. 23, Issue 3, 2026

Intrathecal Clonidine Versus Midazolam as an Adjuvant to Hyperbaric Bupivacaine for Lower Limb Surgery: A Prospective Comparative Study

Dr Atodaria Ami Gaurangsinh[1], Dr Kanabar Sonal Vijaybhai[2], Dr Janhavi Chauhan[3]*

[1,2]MD Anaesthesia, Department of Anaesthesia, Narendra Modi Medical College, Ahmedabad, Gujarat, India

[3]Third Year Resident Doctor, Department of Anaesthesia, Narendra Modi Medical College, Ahmedabad

*Corresponding Author: Dr Janhavi Chauhan
Third Year Resident Doctor, Department of Anaesthesia, Narendra Modi Medical College, Ahmedabad
Email: Janhavichauhan25@gmail.com

Abstract:

Background: Intrathecal adjuvants are used with local anaesthetics to modify the onset and duration of spinal blockade and postoperative analgesia. This study compared clonidine and preservative-free midazolam as adjuvants to hyperbaric bupivacaine in patients undergoing elective lower limb surgery.

Methods: In this prospective comparative study, 60 adults aged 18–70 years with American Society of Anesthesiologists physical status I or II were assigned by alternate sequencing to two groups of 30. The clonidine group received 15 mg of 0.5% hyperbaric bupivacaine with clonidine 30 µg; the midazolam group received the same dose of bupivacaine with preservative-free midazolam 1 mg. Sensory and motor block characteristics, time to first rescue analgesia, perioperative vital signs and complications were assessed.

Results: Mean time to T10 sensory blockade was 5.11 versus 4.93 minutes, and mean time to grade 3 motor blockade was 2.58 versus 1.74 minutes, in the clonidine and midazolam groups, respectively. Mean sensory block duration was 277.2 versus 239.7 minutes, motor block duration was 315.7 versus 268.2 minutes, and analgesia duration was 399.3 versus 375.2 minutes. The dissertation reported $p < 0.0001$ for these comparisons, although the onset p-values require verification. One patient in the clonidine group experienced nausea and vomiting; one in the midazolam group experienced shivering.

Conclusion: At the doses studied, clonidine was associated with longer sensory and motor blockade and a longer interval to first rescue analgesia, whereas midazolam was associated with shorter onset times. The findings require cautious interpretation because allocation was by alternate sequencing, the sample was small, and discrepancies in the source data need clarification.

Keywords: spinal anaesthesia; clonidine; midazolam; hyperbaric bupivacaine; lower limb surgery; postoperative analgesia

Received: 14 May 2026 **Accepted:** 17 Aug 2026 **Published:** 14 Nov 2026

© 2026 Atodaria Ami Gaurangsinh, Kanabar Sonal Vijaybhai and Janhavi Chauhan. This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International License (CC BY 4.0), which permits unrestricted use, distribution and reproduction in any medium, provided the original author and source are credited. https://creativecommons.org/licenses/by/4.0/

Indo-American Journal of Life Sciences and Biotechnology

Indo-Am. J. of LifeSc & Bt., 2026 *ISSN 2347-2243 www.iajlb.org*

Vol. 23, Issue 3, 2026

Introduction

Spinal anaesthesia is used for lower limb procedures because it can provide sensory and motor blockade without the need for general anaesthesia in appropriately selected patients. Hyperbaric bupivacaine is a commonly used intrathecal local anaesthetic, but the duration of anaesthesia and postoperative analgesia following a single injection may be limited. Intrathecal adjuvants have therefore been investigated as a means of modifying block characteristics and extending postoperative pain relief [1,2].

Clonidine, an alpha-2 adrenergic agonist, has been studied as an adjuvant to neuraxial local anaesthetics. Its actions include inhibition of nociceptive transmission at spinal sites, potentially prolonging blockade and analgesia [3]. Midazolam, a benzodiazepine, has also been investigated as an intrathecal adjuvant; its proposed analgesic action involves gamma-aminobutyric acid receptors in the spinal dorsal horn [2,4].

The choice of adjuvant involves consideration of several outcomes. A shorter onset may facilitate the start of surgery, whereas prolonged sensory blockade and analgesia may reduce early postoperative discomfort. At the same time, prolonged motor blockade may delay recovery of movement. Perioperative haemodynamic changes and adverse effects are also relevant when comparing regimens. Previous studies cited in the dissertation have compared clonidine and midazolam using different doses and surgical populations, making the effects of a particular dose combination important to examine [5,6].

The present study compared intrathecal clonidine 30 µg and preservative-free midazolam 1 mg, each added to 15 mg of 0.5% hyperbaric bupivacaine, in adults undergoing elective lower limb surgery. The primary objectives were to compare the onset and duration of sensory and motor blockade and the duration of analgesia. Secondary objectives were to assess perioperative vital signs and adverse effects.

1. Materials and Methods

Study design and setting

This prospective, interventional comparative study was conducted at Narendra Modi Medical College during 2024–2025. Sixty adult patients scheduled for elective lower limb surgery under spinal anaesthesia were included. The dissertation describes the study as randomised; however, it specifies **alternate sequencing** as the allocation method. The design is therefore described here as an alternately allocated comparative study rather than a randomised trial.

Ethical approval and consent

The study protocol was reviewed and approved by the Institutional Review Board (IRB) of Narendra Modi Medical College, Ahmedabad, Gujarat, India (Approval No: NaMoMC/IRB/2024/Dissertation/56, dated 24/07/2024). The study was conducted in accordance with the ethical principles of the Declaration of Helsinki, and written informed

Indo-American Journal of Life Sciences and Biotechnology

Indo-Am. J. of LifeSc & Bt., 2026 *ISSN 2347-2243 www.iajlb.org*

Vol. 23, Issue 3, 2026

consent was obtained from all participants prior to enrollment.

Eligibility criteria

Patients of any sex were eligible if they were aged 18–70 years, had American Society of Anesthesiologists (ASA) physical status I or II, were scheduled for elective lower limb surgery and consented to participate. Exclusion criteria included refusal, allergy to a study drug, local infection, bleeding disorder or altered coagulation, inability to cooperate, gross spinal deformity, peripheral neuropathy and pregnancy.

Study groups

Patients were assigned to one of two groups, with 30 patients in each:

- **Group C:** 3.0 mL of 0.5% hyperbaric bupivacaine, equivalent to 15 mg, plus 0.2 mL of clonidine, equivalent to 30 µg.
- **Group M:** 3.0 mL of 0.5% hyperbaric bupivacaine, equivalent to 15 mg, plus 0.2 mL of preservative-free midazolam, equivalent to 1 mg.

The total intrathecal volume was 3.2 mL in each group. The dissertation's methods and discussion identify the midazolam dose as 1 mg, although one entry in its case-record form states 10 mg; the intended and administered dose should be verified against the study records.

Preoperative assessment and anaesthetic procedure

Preoperative assessment included history, general and systemic examination, and routine investigations. Additional investigations were performed when required. Patients were instructed about sensory and motor assessments and the visual analogue scale (VAS) for pain. The VAS was described as a 10-cm scale, with 0 indicating no pain and 10 indicating the worst imaginable pain. Patients were kept nil by mouth for at least eight hours before the procedure.

In the operating theatre, an 18-gauge intravenous cannula was inserted, intravenous fluid was started, and electrocardiography, non-invasive blood pressure and pulse oximetry monitors were attached. Baseline vital signs were recorded. Under aseptic precautions, spinal anaesthesia was administered with the patient sitting, using a 23-gauge spinal needle at the L2–L3 or L3–L4 interspace. The allocated study solution was injected intrathecally, and the patient was then placed supine.

Outcome assessment

Sensory blockade was assessed by loss of pinprick sensation at one-minute intervals for the first 20 minutes or until the maximum sensory level was reached. Motor blockade was assessed using the modified Bromage scale. Surgery was permitted when sensory blockade reached the T10 dermatome and motor blockade reached grade 3, defined in the dissertation as inability to move the knees or feet.

The study recorded time to T10 sensory blockade, sensory regression, duration of sensory blockade, time to grade 3 motor blockade and motor recovery. The case-record form defined sensory block duration from intrathecal injection to regression to S1. It also recorded the

Indo-American Journal of Life Sciences and Biotechnology

Indo-Am. J. of LifeSc & Bt., 2026 *ISSN 2347-2243 www.iajlb.org*

Vol. 23, Issue 3, 2026

time to first request for rescue analgesia at a VAS score of at least 4. The dissertation's results table labels one sensory regression outcome as regression by two dermatomes, while its narrative describes the same values as regression to S1; this endpoint requires clarification before publication.

Heart rate, blood pressure, respiratory rate and oxygen saturation were monitored during the perioperative period. The methods describe observations through 24 hours. Complications recorded included hypotension, bradycardia, nausea, vomiting, respiratory depression, shivering and urinary retention.

Sample size and statistical analysis

The dissertation reports that a sample size calculation based on a previous study indicated a minimum of 15 participants per group, with 30 per group recruited for convenience. It describes analysis using SPSS version 15.0 and reports the use of Student's t-test, Mann–Whitney U test and tests for categorical data, with statistical significance set at $p \leq 0.05$. The description of which test was used for each variable is not sufficiently clear to reproduce the analysis.

The dissertation states that values were expressed as mean ± 2 standard deviations, although the results tables do not consistently identify the dispersion measure. Accordingly, the values below reproduce the reported means and accompanying values without assuming that they represent one standard deviation.

2. Results

Participant characteristics

The study reported results for 60 patients, with 30 in each group. The mean age was 45.23 years in Group C and 43.25 years in Group M. Group C included 12 men and 18 women, while Group M included 14 men and 16 women. ASA physical status I was recorded in 18 patients in Group C and 16 in Group M; the remaining patients were ASA II. The dissertation reported no statistically significant between-group differences in these characteristics.

Baseline pulse, blood pressure, respiratory rate and oxygen saturation were also reported as not significantly different between groups. However, some baseline values in the preoperative table differ from the corresponding zero-minute values in the subsequent monitoring tables; the underlying records should be checked before finalising the manuscript.

Sensory blockade

The reported mean time to sensory blockade at T10 was 5.11 minutes in Group C and 4.93 minutes in Group M, a difference of 0.18 minutes. The reported mean duration of sensory blockade was 277.2 minutes in Group C and 239.7 minutes in Group M, a difference of 37.5 minutes. The dissertation reported $p < 0.0001$ for both comparisons.

The dissertation also reported sensory regression values of 277.3 minutes in Group C and 234.8 minutes in Group M. Because the table identifies this as regression by two dermat-

This article can be downloaded from https://iajlb.org/index.php/iajlb/index

Indo-American Journal of Life Sciences and Biotechnology

Indo-Am. J. of LifeSc & Bt., 2026 *ISSN 2347-2243 www.iajlb.org*

Vol. 23, Issue 3, 2026

Table 1. Baseline characteristics

Characteristic	Group C (n = 30)	Group M (n = 30)	Reported p-value
Age, years	45.23 ± 12.93	43.25 ± 12.96	0.7981
Male/female, n	12/18	14/16	0.643
ASA I, n (%)	18 (60.0)	16 (53.3)	0.794
ASA II, n (%)	12 (40.0)	14 (46.7)	0.794

Values are reproduced as reported. The dissertation describes continuous data as mean ± 2 standard deviations; this should be verified. ASA, American Society of Anesthesiologists.

omes whereas the accompanying narrative identifies it as regression to S1, the measure is presented in Table 2 with its label unresolved.

Motor blockade

The reported mean time to grade 3 motor blockade was 2.58 minutes in Group C and 1.74 minutes in Group M. Thus, the observed mean onset was 0.84 minutes shorter in Group M. Reported motor block duration was 315.7 minutes in Group C and 268.2 minutes in Group M, a difference of 47.5 minutes. The dissertation reported $p < 0.0001$ for both comparisons.

The reported time for regression from grade 3 to grade 0 was 316.7 minutes in Group C and 282.3 minutes in Group M. The relationship between this measure, the reported onset times and the separately reported motor block duration is not clear from the dissertation's definitions and should be checked against the original data.

Duration of analgesia

The mean reported duration of analgesia, assessed using the time to first analgesic request at VAS ≥4, was 399.3 minutes in Group C and 375.2 minutes in Group M. The observed mean difference was 24.1 minutes. The dissertation reported $p < 0.0001$.

Perioperative observations and complications

The dissertation reported no statistically significant differences between the groups in heart rate, blood pressure, respiratory rate or oxygen saturation at the recorded time points. These findings describe the comparisons reported in this sample; they do not establish equivalence between the regimens.

One patient in Group C experienced nausea and vomiting, and one patient in Group M experienced shivering. No hypotension, bradycardia, pruritus, urinary retention or respiratory depression was reported in either group. With 30 participants per group, these observations cannot exclude clinically important differences in adverse events.

3. Discussion

Principal findings

In this study of 60 patients undergoing elective lower limb surgery, the two intrathecal adjuvant regimens showed different reported block profiles. Midazolam 1 mg was associated with shorter mean times to T10 sensory

Indo-American Journal of Life Sciences and Biotechnology

Indo-Am. J. of LifeSc & Bt., 2026 *ISSN 2347-2243 www.iajlb.org*

Vol. 23, Issue 3, 2026

Table 2. Sensory and motor block characteristics and duration of analgesia

Outcome	Group C (n = 30)	Group M (n = 30)	Reported p-value
Time to T10 sensory block, min	5.11 ± 0.79	4.93 ± 0.22	<0.0001
Sensory regression time, min*	277.3 ± 12.38	234.8 ± 10.27	<0.0001
Duration of sensory block, min	277.2 ± 11.87	239.7 ± 10.30	<0.0001
Time to grade 3 motor block, min	2.58 ± 0.89	1.74 ± 0.12	<0.0001
Motor regression from grade 3 to 0, min	316.7 ± 12.52	282.3 ± 7.31	<0.0001
Duration of motor block, min	315.7 ± 10.68	268.2 ± 8.89	<0.0001
Duration of analgesia, min	399.3 ± 12.70	375.2 ± 12.01	<0.0001

Values and p-values are reproduced from the dissertation. The dispersion measure and statistical calculations require verification. *The dissertation's table describes regression by two dermatomes, while its narrative describes regression to S1.

blockade and grade 3 motor blockade. Clonidine 30 µg was associated with longer mean sensory and motor block duration and a longer mean interval to first rescue analgesia. These findings relate to the doses studied and should not be generalised to all dose combinations.

The observed difference in sensory onset was small: 0.18 minutes, or approximately 11 seconds. The motor onset difference was 0.84 minutes, or approximately 50 seconds. The clinical importance of these differences depends on the surgical and anaesthetic context, particularly because surgery was permitted only after both the sensory and motor criteria were met. Moreover, the dissertation's reported p-values for onset require independent recalculation from the participant-level data.

The longer block durations reported with clonidine may be relevant when prolonged anaesthesia is desired. In the present data, the mean sensory block duration was 37.5 minutes longer and the mean motor block duration was 47.5 minutes longer with clonidine than with midazolam. Longer motor blockade is not necessarily an advantage for every patient: its potential benefit during surgery must be considered alongside the timing of postoperative recovery and mobilisation. The dissertation did not report a direct assessment of time to mobilisation.

The 24.1-minute difference in mean time to first analgesic request favoured clonidine in this comparison. This outcome reflects the study's VAS-based rescue threshold rather than a complete measure of postoperative pain experience. The available report does not provide a comparative total postoperative analgesic consumption measure or a patient-centred assessment of whether the observed difference was important to participants.

Comparison with previous studies

The dissertation cites earlier comparative work when discussing these findings. It reports that Suraj and Chendraya Perumal observed prolonged blockade with clonidine using higher doses of both adjuvants [5]. It also describes work by Joshi and colleagues using clonidine 30 µg and midazolam 2 mg with hyperbaric

Indo-American Journal of Life Sciences and Biotechnology

Indo-Am. J. of LifeSc & Bt., 2026 *ISSN 2347-2243 www.iajlb.org*

Vol. 23, Issue 3, 2026

bupivacaine [6]. Differences in dose and clinical setting limit direct comparison with the present regimen. These descriptions are drawn from the dissertation's discussion; the cited articles were not independently reviewed for this draft.

The dissertation also attributes prolonged sensory regression with clonidine to a comparative study by Sengar and colleagues [7]. It cites Kim and Lee's study of intrathecal midazolam with bupivacaine in haemorrhoidectomy when discussing postoperative analgesia [8]. The latter comparison involved a different surgical procedure and does not directly establish the relative effect of clonidine versus midazolam in lower limb surgery.

Perioperative observations

No between-group differences in recorded perioperative vital signs were reported, and only two adverse events were listed. Nevertheless, absence of reported events such as hypotension or bradycardia in this small sample should not be interpreted as proof that either regimen is safe or that their safety profiles are equivalent. The dissertation notes that follow-up was limited to the early postoperative period, so longer-term effects were not assessed.

Strengths and limitations

The study prospectively compared two standardised intrathecal regimens and assessed several clinically relevant outcomes, including onset and duration of sensory and motor block, analgesia and perioperative observations. Both groups received the same reported dose and volume of hyperbaric bupivacaine, and the total intrathecal volume was the same.

Several limitations affect interpretation. First, alternate sequencing makes treatment assignment predictable and does not provide the allocation concealment of an independently generated random sequence. Second, the study was conducted at one centre with 30 patients per group, limiting precision and the ability to assess uncommon adverse events. Third, only ASA I–II patients and one dose of each adjuvant were studied; applicability to higher-risk patients and other doses remains uncertain. The dissertation does not clearly establish whether patients or outcome assessors were blinded.

Fourth, the report contains discrepancies that must be resolved before submission. These include the conflicting midazolam dose in the case-record form, the sensory regression endpoint label, the relationship between motor regression and motor duration, and differences between baseline and zero-minute vital-sign values. The stated dispersion measure and reported p-values should also be checked against the original dataset and statistical output. Until these checks are completed, the numerical findings should be treated as reported dissertation results rather than independently verified estimates.

4. Conclusion

In this alternately allocated, single-centre study, intrathecal clonidine 30 µg added to hyperbaric bupivacaine was associated with

Indo-American Journal of Life Sciences and Biotechnology

Indo-Am. J. of LifeSc & Bt., 2026 *ISSN 2347-2243 www.iajlb.org*

Vol. 23, Issue 3, 2026

longer reported sensory and motor blockade and a longer time to first rescue analgesia than midazolam 1 mg. Midazolam was associated with shorter reported onset times. Few complications were recorded, but the study was too small to establish comparative safety. Verification of the source data, endpoint definitions and statistical analyses is needed before the findings are submitted for publication.

References:

1. Morgan GE Jr, Mikhail MS, Murray MJ. Clinical anesthesiology. 4th ed. New York: McGraw-Hill Medical; 2006.
2. Swain A, Nag DS, Sahu S, Samaddar DP. Adjuvants to local anesthetics: current understanding and future trends. World J Clin Cases. 2017;5(8):307-323.
3. Eisenach JC, De Kock M, Klimscha W. Alpha2-adrenergic agonists for regional anaesthesia: a clinical review of clonidine (1984-1995). Anesthesiology. 1996;85(3):655-674.
4. Tucker AP, Mezzatesta J, Nadeson R, Goodchild CS. Intrathecal midazolam: a cohort study investigating safety. Anesth Analg. 2004;98:1512-1517.
5. Suraj HS, Chendraya Perumal RS. A comparative study of intrathecal clonidine and midazolam as an adjuvant to bupivacaine for lower limb and lower abdominal surgeries. MedPulse Int J Anaesthesiol. 2019;12(2):98-100.
6. Joshi S, Khadke V, Subhedar R, Patil A, Motghare V. Comparative evaluation of intrathecal midazolam and low dose clonidine: efficacy, safety and duration of analgesia. Indian J Pharmacol. 2012;44(3):357.
7. Sengar PK, Priyadarshini S, Setu P. To study efficacy and safety of addition of intrathecal clonidine and midazolam to hyperbaric bupivacaine as adjuvant for postoperative analgesia. Int J Curr Res. 2016;8(9):38847-38850.
8. Kim MH, Lee YM. Intrathecal midazolam increases the analgesic effects of spinal blockade with bupivacaine in patients undergoing haemorrhoidectomy. Br J Anaesth. 2001;86(1):77-79.