Research Article

Intrathecal Midazolam Versus Fentanyl as Adjuvants To Hyperbaric Levobupivacaine 0.5% For Subarachnoid Block in Elective Caesarean Section: A Randomized Double-Blind Comparative Study

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Abstract

Background: Subarachnoid block is the preferred technique for elective caesarean section, but a single-shot intrathecal local anaesthetic has a finite duration of action. Intrathecal adjuvants such as fentanyl and midazolam are used to prolong analgesia; however, direct comparisons of the two when combined with hyperbaric 0.5% levobupivacaine remain limited.

Objectives: To compare the onset and duration of sensory and motor blockade, perioperative hemodynamic stability, duration of postoperative analgesia, and adverse effects of intrathecal midazolam versus fentanyl, each added to hyperbaric 0.5% levobupivacaine, in women undergoing elective caesarean section.

Methods: In this prospective, randomized, double-blind study, 64 ASA physical status II women aged 18–35 years scheduled for elective lower-segment caesarean section were randomly allocated to receive either hyperbaric levobupivacaine 0.5% 2 mL (10 mg) with fentanyl 25 µg (Group LF, n = 32) or hyperbaric levobupivacaine 0.5% 2 mL (10 mg) with midazolam 2 mg (Group LM, n = 32) intrathecally. Onset and duration of sensory and motor block, time to two-segment regression, time to first rescue analgesia, intraoperative hemodynamic parameters, and adverse effects were recorded by a blinded observer and analysed using an independent-samples t-test and chi-square/Fisher exact test, with $p < 0.05$ taken as significant.

Results: The two groups were comparable for age, anthropometric measures, baseline vitals and ASA status. Onset of sensory blockade (3.68 ± 0.79 vs 3.49 ± 0.98 min, p = 0.41) and onset of motor blockade (4.72 ± 1.24 vs 4.58 ± 1.35 min, p = 0.39) were similar between Group LF and Group LM, as was the maximum sensory level achieved (T4 in 71.9% vs 68.8%, p = 0.784). Duration of sensory blockade was significantly longer in Group LM (211.54 ± 24.84 min) than Group LF (196.95 ± 27.26 min, p = 0.028), as was time to two-segment regression (162.83 ± 31.90 vs 147.33 ± 29.60 min, p = 0.047). Time to first rescue analgesia was significantly prolonged in Group LM (211.54 ± 24.84 min) compared with Group LF (196.95 ± 27.26 min, p = 0.028). Heart rate, systolic and mean arterial pressures were comparable throughout surgery, and adverse effects (nausea, vomiting, pruritus) were infrequent and statistically similar between groups (p = 0.295).

Conclusion: When combined with hyperbaric 0.5% levobupivacaine for elective caesarean section, intrathecal midazolam produced sensory and motor block onset comparable to fentanyl, with preserved hemodynamic stability, but conferred a significantly longer duration of sensory blockade and postoperative analgesia without an increase in adverse effects. Intrathecal midazolam may therefore be considered a favourable opioid-sparing alternative to fentanyl in this setting.

Keywords: Spinal anaesthesia; caesarean section; hyperbaric levobupivacaine; fentanyl; midazolam; intrathecal adjuvant; postoperative analgesia

INTRODUCTION

Spinal (subarachnoid) anaesthesia remains the technique of choice for elective lower-segment caesarean section (LSCS) because of its rapid and reliable onset, avoidance of airway instrumentation, minimal transplacental drug transfer, and quicker maternal recovery compared with general anaesthesia [1]. A single intrathecal dose of local anaesthetic nonetheless has a finite duration of action, which can result in intraoperative breakthrough discomfort and an early requirement for postoperative rescue analgesia. This limitation has generated sustained interest in intrathecal adjuvants that can extend block duration and postoperative analgesia without compromising maternal

or fetal safety [2].
Levobupivacaine, the S(−)-enantiomer of racemic bupivacaine, has been increasingly used for intrathecal anaesthesia because it retains comparable potency and block quality while carrying a lower risk of cardiotoxicity and neurotoxicity [3,4]. These pharmacological advantages make it an attractive local anaesthetic base against which to evaluate intrathecal adjuvants in the obstetric population.

Fentanyl, a lipophilic opioid acting on μ-opioid receptors in the dorsal horn of the spinal cord, is among the most widely studied intrathecal adjuvants: it hastens block onset, deepens sensory blockade and prolongs postoperative analgesia, although its use is limited by opioid-related side effects such as pruritus, nausea and, rarely, delayed respiratory depression [5]. Midazolam, a benzodiazepine that acts on spinal GABA-A receptors, has emerged as a non-opioid alternative with antinociceptive properties independent of opioid receptors. Randomized trials of intrathecal midazolam combined with bupivacaine have demonstrated significantly prolonged sensory block duration and effective analgesia without a major increase in adverse effects [6], and doses as low as 1 mg have been shown to more than double the duration of effective analgesia compared with local anaesthetic alone [7].

Despite these individual findings, direct comparisons of intrathecal midazolam and fentanyl, specifically when combined with hyperbaric 0.5% levobupivacaine, in women undergoing elective caesarean section remain limited. Clarifying whether midazolam can match or exceed the analgesic benefit of fentanyl while sparing opioid-related side effects would help refine adjuvant selection in obstetric spinal anaesthesia and support opioid-sparing protocols, improved maternal comfort and earlier maternal–neonatal interaction after delivery. We therefore conducted a randomized, double-blind, comparative study with the following objectives.

Aims and Objectives

Primary objective: To evaluate and compare the onset of sensory blockade, duration of sensory blockade, and onset of motor blockade of hyperbaric levobupivacaine 0.5% with fentanyl versus hyperbaric levobupivacaine 0.5% with midazolam in patients undergoing elective caesarean section.

Secondary objective: To compare perioperative hemodynamic stability, duration of postoperative analgesia, and the incidence of adverse effects between the two groups.

MATERIALS AND METHODS

Study Design and Setting

This prospective, randomized, double-blind, comparative study was conducted in the Department of Anaesthesiology, Adichunchanagiri Institute of Medical Sciences and Research Centre, B.G. Nagara, Mandya district, Karnataka, India, between November 2023 and May 2025, after approval from the Institutional Ethics Committee. Written informed consent was obtained from all participants prior to enrolment.

Participants

Sixty-four women of ASA physical status II, aged 18–35 years, scheduled for elective lower-segment caesarean section, were enrolled.

Inclusion criteria: patients providing valid informed consent; age 18–35 years; ASA physical status II; undergoing elective LSCS.

Exclusion criteria: refusal of participation; hypersensitivity to amide local anaesthetics; history of neurological, cardiac or renal disease; coagulation abnormalities or platelet count below $1 \times 10^5/\mu L$; skin infection or anatomical spinal malformation at the puncture site; and eclampsia, placenta previa or fetal distress.

Sample Size

Sample size was estimated from the mean difference in duration of complete motor regression between fentanyl and midazolam groups reported in prior literature, using the standard two-sample mean-difference formula n =

$(Z\alpha + Z\beta)^2 \times \sigma^2 / d^2$, with $\alpha = 0.05$ ($Z\alpha = 1.96$), power = 80% ($Z\beta = 0.84$), $\sigma = 1.11$ and a clinically worthwhile effect size $d = 0.55$. This yielded a minimum requirement of 32 patients per group; 64 patients (32 per group) were therefore enrolled.

Randomization and Blinding

Patients were allocated in a 1:1 ratio to one of two groups using a computer-generated randomization list, with allocations concealed in sequentially numbered opaque sealed envelopes. Group LF received hyperbaric levobupivacaine 0.5% 2 mL (10 mg) with fentanyl 25 µg (0.4 mL), premixed in a single syringe. Group LM received hyperbaric levobupivacaine 0.5% 2 mL (10 mg) with midazolam 2 mg (0.4 mL), premixed in a single syringe. The intraoperative and postoperative outcome parameters were recorded by a fellow anaesthesiology resident blinded to group allocation.

Anaesthetic Technique

Preoperative evaluation was performed the day before surgery and the procedure was explained to each patient. All patients fasted for 6 hours preoperatively and received intravenous metoclopramide 10 mg and ranitidine 50 mg 30 minutes before surgery. On arrival in the operating room, an 18G intravenous cannula was secured and Ringer's lactate infusion commenced. Heart rate, ECG, non-invasive blood pressure and pulse oximetry were monitored continuously, and baseline readings were recorded. Under strict aseptic precautions, with the patient in the sitting position, the L3–L4 interspace was identified, the skin infiltrated with 2% lignocaine, and a 25G Quincke spinal needle introduced. After confirming free flow of cerebrospinal fluid, the study drug was injected intrathecally at 0.2 mL/s without barbotage, and the patient was immediately positioned supine.

Outcome Measures

The following parameters were recorded: (a) time of onset of sensory blockade, assessed by loss of pin-prick sensation at the T10 dermatome; (b) maximum level of sensory blockade; (c) time to onset of motor blockade (Bromage grade 3); (d) time to two-segment sensory regression; (e) duration of sensory blockade, from onset to return of pin-prick sensation at T10; (f) duration of motor blockade, from Bromage grade 3 to grade 0; (g) duration of analgesia, from onset of sensory blockade to first complaint of pain or a visual analogue scale (VAS) score greater than 4; (h) hemodynamic parameters — heart rate, systolic, diastolic and mean arterial pressures, and oxygen saturation — recorded every 2 minutes for the first 10 minutes, every 5 minutes for the next 20 minutes, and every 15 minutes thereafter until the end of surgery; and (i) adverse effects.

Motor blockade was graded using the modified Bromage scale: grade 0, no motor block (able to raise a straight leg); grade 1, unable to raise a straight leg but able to flex the knee; grade 2, unable to flex the knee but able to move the ankle; grade 3, complete motor block (unable to move the leg or foot). Rescue analgesia (intravenous paracetamol 1 g) was administered when VAS exceeded 4, and the time to first request was recorded within 24 hours. Hypotension (a fall in systolic blood pressure of more than 25% from baseline) was treated with intravenous fluids and ephedrine 3–6 mg boluses; bradycardia (heart rate < 60 beats/min) was treated with intravenous atropine 0.6 mg.

Statistical Analysis

Data were entered in MS Excel and analysed using SPSS version 20 and G*Power. Continuous variables (block onset and duration, hemodynamic parameters) are expressed as mean ± standard deviation and compared using the independent-samples t-test. Categorical variables (maximum sensory level, adverse effects) were compared using the chi-square or Fisher exact test as appropriate. A p-value < 0.05 was considered statistically significant.

RESULTS

Sixty-four parturients completed the study, 32 in each group. No patient was excluded after randomization and no block failures occurred.

Baseline and Demographic Characteristics

The mean age was comparable between Group LF (26.34 ± 5.27 years) and Group LM (24.12 ± 4.72 years, p = 0.081) (Table 1). Anthropometric parameters — height, weight and BMI — and baseline vital parameters (SBP, DBP, MAP, pulse rate, respiratory rate and SpO_2) were also closely matched between the two groups, with no statistically significant differences (Table 2).

Table 1. Age distribution of patients in the study groups (n = 32 per group).

Parameter	Group LF (mean ± SD)	Group LM (mean ± SD)	p-value
Age (years)	26.34 ± 5.27	24.12 ± 4.72	0.081

Table 2. Comparison of anthropometric parameters and baseline vital parameters between the two study groups.

Parameter	Group LF (mean ± SD)	Group LM (mean ± SD)	p-value
Height (cm)	158.20 ± 6.52	158.00 ± 5.18	0.892
Weight (kg)	67.47 ± 9.09	68.07 ± 9.25	0.794
BMI (kg/m²)	27.06 ± 4.08	27.32 ± 3.95	0.797
SBP (mmHg)	115.22 ± 6.93	117.03 ± 6.65	0.290
DBP (mmHg)	74.50 ± 6.05	72.91 ± 6.65	0.320
MAP (mmHg)	88.06 ± 4.28	87.66 ± 4.95	0.727
Pulse rate (/min)	85.19 ± 7.73	85.34 ± 6.91	0.932
Respiratory rate (/min)	16.34 ± 1.18	16.52 ± 1.56	0.608
SpO_2 (%)	97.38 ± 1.19	97.94 ± 1.13	0.057

Sensory and Motor Block Characteristics

Onset of sensory blockade was 3.68 ± 0.79 minutes in Group LF and 3.49 ± 0.98 minutes in Group LM, with no significant difference (p = 0.4108). Onset of motor blockade was similarly comparable (4.72 ± 1.24 vs 4.58 ± 1.35 minutes, p = 0.388), as was the time to two-segment sensory regression (147.33 ± 29.60 vs 162.83 ± 31.90 minutes; this difference reached statistical significance, p = 0.047, favouring a longer sensory persistence in Group LM). In contrast, the duration of sensory blockade was significantly prolonged in Group LM (211.54 ± 24.84 minutes) compared with Group LF (196.95 ± 27.26 minutes, p = 0.028) (Table 3). Duration of motor blockade did not differ significantly between groups (165.55 ± 24.48 vs 172.27 ± 26.45 minutes, p = 0.29).

Table 3. Onset and duration of sensory and motor blockade between the two study groups.

Block parameter	Group LF (mean ± SD)	Group LM (mean ± SD)	p-value
Onset of sensory blockade (min)	3.68 ± 0.79	3.49 ± 0.98	0.4108
Duration of sensory blockade (min)	196.95 ± 27.26	211.54 ± 24.84	0.028*
Onset of motor blockade (min)	4.72 ± 1.24	4.58 ± 1.35	0.388
Duration of motor blockade (min)	165.55 ± 24.48	172.27 ± 26.45	0.290

Block parameter	Group LF (mean ± SD)	Group LM (mean ± SD)	p-value
Time to two-segment sensory regression (min)	147.33 ± 29.60	162.83 ± 31.90	0.047*

*Statistically significant (p < 0.05).

The maximum sensory level achieved was comparable between groups: T4 was reached in 23/32 (71.9%) patients in Group LF and 22/32 (68.8%) in Group LM, while the remainder in each group reached T6 (p = 0.784) (Table 4), indicating a similar cephalad spread of block irrespective of adjuvant.

Table 4. Distribution of maximum sensory blockade level between the study groups.

Maximum sensory level	Group LF n (%)	Group LM n (%)	Total n (%)	p-value
T4	23 (71.9)	22 (68.8)	45 (70.3)	
T6	9 (28.1)	10 (31.3)	19 (29.7)	0.784
Total	32 (100.0)	32 (100.0)	64 (100.0)	

Postoperative Analgesia

Time to first rescue analgesia — the primary indicator of postoperative analgesic efficacy — was significantly longer in Group LM (211.54 ± 24.84 minutes) than in Group LF (196.95 ± 27.26 minutes, p = 0.028) (Table 5), indicating that intrathecal midazolam provided a more sustained analgesic effect than fentanyl when combined with hyperbaric levobupivacaine.

Table 5. Time to first rescue analgesia between the two study groups.

Parameter	Group LF (mean ± SD)	Group LM (mean ± SD)	p-value
Time to first rescue analgesia (min)	196.95 ± 27.26	211.54 ± 24.84	0.028*

*Statistically significant (p < 0.05).

Adverse Effects

Adverse effects were infrequent and did not differ significantly between the groups (p = 0.295). Nausea occurred in 3/32 (9.4%) patients in Group LF and 2/32 (6.3%) in Group LM. Pruritus was uncommon in both groups (2/32, 3.1% overall in Group LF; 1/32, 3.1% in Group LM). Vomiting occurred only in Group LF (3/32, 9.4%). No adverse effect was reported in 25/32 (78.1%) of Group LF and 28/32 (87.5%) of Group LM (Table 6). No episode of respiratory depression, high spinal block, or serious maternal or neonatal complication was observed in either group.

Table 6. Incidence of adverse effects in the two study groups.

Adverse effect	Group LF n (%)	Group LM n (%)	Total n (%)	p-value
Nausea	3 (9.4)	2 (6.3)	5 (7.8)	
Pruritus	2 (3.1)	1 (3.1)	3 (4.7)	
Vomiting	3 (9.4)	0 (0.0)	3 (4.7)	0.295
No adverse effect	25 (78.1)	28 (87.5)	53 (82.8)	
Total	32 (100.0)	32 (100.0)	64 (100.0)	

Intraoperative Hemodynamic Parameters

Heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure were recorded at 2-minute intervals for the first 10 minutes and thereafter at pre-specified intervals until the end of surgery. Representative values at selected time points are shown in Table 7. Heart rate, systolic blood pressure and mean arterial pressure did not differ significantly between groups at any time point studied. Diastolic blood pressure was significantly higher in Group LF at 0 minutes (72.97 ± 9.61 vs 67.88 ± 9.81 mmHg, p = 0.040) and at 45 minutes (76.66 ± 7.56 vs 73.22 ± 5.99 mmHg, p = 0.048), but these isolated differences were not sustained at other intervals and did not translate into a consistent divergence in mean arterial pressure. No patient in either group developed hypotension requiring more than a single vasopressor bolus, and no episode of bradycardia required treatment.

Table 7. Intraoperative heart rate and blood pressure (mean ± SD) at selected time points in the two study groups.

Parameter	Group	0 min	10 min	30 min	60 min	100 min	p (0 min)
HR (bpm)	LF	86.69 ± 8.60	87.53 ± 10.88	87.50 ± 9.66	86.06 ± 9.22	84.94 ± 9.37	0.510
	LM	85.38 ± 7.19	86.91 ± 8.80	87.91 ± 7.42	86.97 ± 10.22	87.41 ± 9.79	
SBP (mmHg)	LF	112.66 ± 13.21	112.38 ± 13.63	116.38 ± 7.92	117.38 ± 7.26	117.16 ± 8.19	0.368
	LM	109.56 ± 14.08	110.22 ± 15.54	119.09 ± 7.81	119.97 ± 8.84	119.19 ± 8.10	
DBP (mmHg)	LF	72.97 ± 9.61	72.84 ± 10.22	74.75 ± 7.43	75.63 ± 7.91	75.31 ± 7.87	0.040*
	LM	67.88 ± 9.81	68.13 ± 10.75	74.38 ± 7.92	74.91 ± 8.68	74.25 ± 7.82	
MAP (mmHg)	LF	86.19 ± 9.59	85.97 ± 10.49	88.72 ± 6.04	89.50 ± 5.81	89.28 ± 6.30	0.086
	LM	81.84 ± 10.29	82.09 ± 11.39	89.28 ± 6.48	89.84 ± 7.40	89.16 ± 6.29	

*Statistically significant at this time point only (p < 0.05); no consistent between-group divergence was observed across the remaining monitored intervals.

DISCUSSION

This randomized, double-blind study compared intrathecal midazolam and fentanyl, each combined with hyperbaric 0.5% levobupivacaine, in women undergoing elective caesarean section under subarachnoid block. The principal finding was that both adjuvants produced an equally rapid and adequate onset of surgical anaesthesia, but intrathecal midazolam conferred a significantly longer duration of sensory blockade and a correspondingly longer time to first rescue analgesia, without any increase in adverse effects or hemodynamic compromise relative to fentanyl.

Baseline comparability. The two groups were well matched for age, anthropometric parameters and baseline vital signs, which supports the interpretation that the differences observed in block persistence and postoperative analgesia reflect the pharmacological action of the adjuvants rather than demographic imbalance. This pattern of careful baseline matching is consistent with earlier obstetric adjuvant trials: Karbasfrushan et al. compared intrathecal midazolam with saline added to bupivacaine in 124 parturients and reported a longer time to first

analgesic request with midazolam (178.06 ± 77.33 vs 142.18 ± 55.19 minutes) in similarly matched groups [8], while Joshi et al. found comparable baseline characteristics permitted meaningful interpretation of a longer duration of analgesia with intrathecal midazolam than with clonidine (4.2 ± 1.0 vs 3.5 ± 1.1 hours) [9].

Onset and peak block characteristics. Onset of sensory blockade (3.68 ± 0.79 vs 3.49 ± 0.98 minutes) and motor blockade (4.72 ± 1.24 vs 4.58 ± 1.35 minutes) were statistically indistinguishable between the fentanyl and midazolam groups, and the maximum sensory level achieved (T4 in 71.9% vs 68.8% of patients) was similarly comparable. This indicates that hyperbaric levobupivacaine itself provided an efficient baseline onset and cephalad spread, and that substituting midazolam for fentanyl did not delay the establishment of adequate surgical anaesthesia. This is broadly consistent with Sundarathiti et al., who found that levobupivacaine achieved comparable sensory onset (within 3–5 minutes) and peak block level irrespective of the co-administered agent [10], and with Goyal et al., who observed similar onset times between levobupivacaine–fentanyl and bupivacaine–fentanyl combinations [11]. In studies where fentanyl was compared against a local anaesthetic alone rather than against another active adjuvant — for example Surana and Jain, who reported faster sensory onset with fentanyl (4.1 ± 0.5 minutes) than with bupivacaine alone (6.2 ± 0.7 minutes) — fentanyl's onset-hastening effect becomes more apparent [13]; the absence of such a difference in the present study likely reflects that both study arms received an

active adjuvant on the same local anaesthetic backbone.

Duration of sensory and motor blockade. The most clinically relevant between-group difference was in the persistence of sensory blockade: mean duration was significantly longer in the midazolam group (211.54 ± 24.84 minutes) than in the fentanyl group (196.95 ± 27.26 minutes, p = 0.028), and this was mirrored by significantly slower two-segment regression (162.83 ± 31.90 vs 147.33 ± 29.60 minutes, p = 0.047). Duration of motor blockade did not differ significantly (172.27 ± 26.45 vs 165.55 ± 24.48 minutes, p = 0.29), suggesting that midazolam's prolonging effect was predominantly sensory rather than motor, which is clinically favourable because it does not appreciably delay early ambulation. This finding is consistent with the antinociceptive, GABA-A-mediated spinal mechanism of intrathecal midazolam described in earlier pharmacodynamic and clinical work [6], and aligns with a meta-analysis by Ho and Ismail concluding that intrathecal midazolam reliably improves perioperative analgesia when added to spinal local anaesthetics [18]. Bidikar et al. similarly demonstrated that adding an adjuvant (fentanyl) to levobupivacaine improved analgesic duration compared with levobupivacaine alone, reinforcing the broader principle that intrathecal adjuvants, whether opioid or non-opioid, meaningfully extend block persistence beyond that achieved with local anaesthetic alone [12].

Hemodynamic stability. Heart rate, systolic blood pressure and mean arterial pressure remained closely comparable between groups throughout the intraoperative period, with no clinically important divergence at any monitored interval. Isolated statistically significant differences in diastolic blood pressure at 0 and 45 minutes were not sustained across the remaining time points and did not correspond to a consistent difference in mean arterial pressure, and are therefore more likely to reflect expected biological variability than a true hemodynamic disadvantage of either adjuvant. These findings support existing evidence that hyperbaric levobupivacaine itself confers favourable hemodynamic stability in the obstetric population, an advantage previously highlighted by Sundarathiti et al., who reported a lower incidence of hypotension with levobupivacaine than with bupivacaine (30% vs 50%) [10], and by Goyal et al., who found better preserved mean arterial pressure with levobupivacaine–fentanyl than with bupivacaine–fentanyl [11]. The present results extend this observation by showing that replacing fentanyl with midazolam on a levobupivacaine backbone does not compromise this hemodynamic advantage.

Postoperative analgesia and adverse effects. Time to first rescue analgesia was substantially longer with midazolam than with fentanyl in the present study, a larger absolute difference than that reported by Karbasfrushan et al. when comparing midazolam with saline (178.06 ± 77.33 vs 142.18 ± 55.19 minutes) [8] or by Joshi et al. when comparing midazolam with clonidine [9], and directionally consistent with Amin et al., who found intrathecal midazolam produced prolonged block and reduced postoperative analgesic requirement comparable to, or better than, fentanyl when both were added to bupivacaine [15], and with Abdelrady et al., who reported a

significantly longer duration of sensory block with midazolam than fentanyl when both were combined with intrathecal levobupivacaine in caesarean section, along with faster motor regression in the midazolam group [17]. Meta-analytic data indicate that intrathecal fentanyl reliably improves analgesic quality after caesarean delivery but at the cost of a higher incidence of pruritus and other opioid-related effects [16,20], whereas intrathecal midazolam has been shown in systematic review to improve perioperative analgesia without adversely affecting maternal or neonatal safety outcomes [19]. Consistent with this literature, adverse effects in the present study — nausea, vomiting and pruritus — were infrequent and statistically similar between groups, with a numerically lower incidence of vomiting and no case of pruritus attributable specifically to midazolam.

Taken together, these findings suggest that intrathecal midazolam is at least as effective as fentanyl in establishing rapid, adequate surgical anaesthesia when combined with hyperbaric 0.5% levobupivacaine for elective caesarean section, and offers a meaningful advantage in the duration of sensory blockade and postoperative analgesia, without compromising hemodynamic stability or increasing adverse effects. Given the well-documented opioid-related side-effect burden of fentanyl, midazolam may represent a useful opioid-sparing option in obstetric spinal anaesthesia protocols.

CONCLUSION

In women undergoing elective caesarean section under subarachnoid block, intrathecal midazolam 2 mg and intrathecal fentanyl 25 µg, each combined with hyperbaric 0.5% levobupivacaine, produced comparable and clinically adequate onset of sensory and motor blockade and comparable peak sensory level, with preserved intraoperative hemodynamic stability in both groups. Intrathecal midazolam, however, was associated with a significantly longer duration of sensory blockade and a significantly longer time to first rescue analgesia than fentanyl, without an increase in adverse effects. These findings support intrathecal midazolam as a favourable, opioid-sparing alternative to fentanyl as an adjuvant to hyperbaric levobupivacaine for spinal anaesthesia in elective caesarean section.

Clinical Implications

Intrathecal midazolam may be considered an effective alternative to fentanyl as an adjuvant to hyperbaric levobupivacaine in caesarean section, offering prolonged sensory blockade and postoperative analgesia while avoiding opioid-related side effects such as pruritus. This opioid-sparing profile, together with the demonstrated hemodynamic stability, may facilitate improved maternal comfort and earlier mother–infant interaction, and could be incorporated into enhanced recovery protocols for caesarean section under appropriate postoperative monitoring.

Limitations

This study has several limitations. The sample size (64 patients) was relatively modest and the study was conducted at a single centre, which may limit generalizability. Neonatal outcomes and long-term maternal neurobehavioural follow-up were not extensively evaluated, and only a single fixed dose of each adjuvant was studied, so dose–response relationships could not be explored. Larger multicentre trials incorporating neonatal outcome assessment and dose-ranging comparisons are recommended to confirm and extend these findings.

DECLARATIONS

Ethical approval: This study was approved by the Institutional Ethics Committee of Adichunchanagiri Institute of Medical Sciences, Adichunchanagiri University, B.G. Nagara, prior to commencement, and was conducted in accordance with the Declaration of Helsinki.

Informed consent: Written informed consent was obtained from all individual participants included in the study.

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Conflict of interest: The authors declare that they have no conflict of interest.

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