International Journal of Medicine
ISSN (P): 1468-3814; ISSN (e): 2667-7008
https://www.theinternationalmedicine.com
Volume: 5(1) 2023

Original Research

Comparative Efficacy and Safety of Low-Dose Spinal Labour Analgesia Using Levobupivacaine with Dexmedetomidine versus Levobupivacaine with Buprenorphine: A Prospective Randomised Comparative Study.

Dr. Nidhi Mali Patil[1], Dr. Leesha U[2]*
1Senior Resident, Department of Anaesthesiology, Vijayanagar Institute of Medical Sciences (VIMS), Bellary, Karnataka, India
2DNB Resident, Department of Anesthesiology, District Hospital, Dharwad, Karnataka, India

Received: 10 May 2023 / Accepted: 12 June 2023

Abstract
Background: Labour pain produces substantial physiological and psychological stress. Effective neuraxial analgesia should provide rapid pain relief while preserving maternal motor function, haemodynamic stability, labour progress, and neonatal well-being. *Objective:* To compare the analgesic efficacy, maternal safety, labour characteristics, and neonatal outcomes of low-dose intrathecal levobupivacaine with dexmedetomidine versus levobupivacaine with buprenorphine. *Methods:* This prospective randomised comparative study included 60 term parturients at Vijayanagar Institute of Medical Sciences, Ballari, Karnataka, India, from November 2022 to April 2023. Participants were randomised equally to receive intrathecal levobupivacaine with dexmedetomidine (Group LD) or levobupivacaine with buprenorphine (Group BB). Pain scores, onset and duration of analgesia, rescue analgesia, motor blockade, haemodynamic variables, adverse effects, mode of delivery, maternal satisfaction, and neonatal outcomes were recorded. *Results:* Baseline characteristics were comparable. Compared with Group BB, Group LD had a faster onset of analgesia (4.3 ± 1.1 vs 5.2 ± 1.3 min; p = 0.005), longer analgesic duration (162.7 ± 30.4 vs 138.5 ± 27.8 min; p = 0.002), fewer rescue analgesia requirements (16.7% vs 43.3%; p = 0.047), and higher maternal satisfaction (4.5 ± 0.6 vs 4.1 ± 0.8; p = 0.033). Pain scores were lower in Group LD at 5, 10, and 120 minutes. Pruritus occurred only in Group BB (20.0% vs 0%; p = 0.024). Motor blockade, haemodynamic events, mode of delivery, Apgar scores, and neonatal resuscitation were comparable. *Conclusion:* The levobupivacaine-dexmedetomidine regimen provided faster, longer, and more satisfactory labour analgesia than the levobupivacaine-buprenorphine regimen, without evidence of clinically important maternal or neonatal compromise in this sample.

Keywords: *buprenorphine; dexmedetomidine; labour analgesia; levobupivacaine; spinal analgesia; visual analogue scale*.

Introduction

Labour pain is among the most intense acute pain experiences and results from visceral afferent stimulation during cervical dilatation, followed by somatic pain from distension of the vagina, pelvic floor, and perineum. Unrelieved pain activates maternal sympathetic responses, increases circulating catecholamines, and can contribute to hyperventilation, increased oxygen consumption, anxiety, and reduced uteroplacental perfusion. Contemporary obstetric practice therefore recognises maternal request, in the absence of contraindications, as an adequate indication for labour analgesia.[1] Evidence from systematic reviews shows that neuraxial techniques provide superior pain relief compared with systemic or non-neuraxial strategies, although the selected regimen must balance analgesic quality against hypotension, motor blockade, pruritus, and fetal heart-rate changes.[2]

Epidural, combined spinal-epidural, dural puncture epidural, and continuous spinal techniques are established neuraxial options. Intrathecal administration offers rapid onset, reliable sacral analgesia, and a small total drug requirement.[3,4] Low-dose spinal or spinal components of combined techniques aim to preserve lower-limb strength and maternal participation while reducing exposure to local anaesthetics. A single-shot spinal technique can also be practical when rapid analgesia is required and epidural maintenance resources are limited, provided its finite duration and the potential need for rescue analgesia are anticipated. The clinical effect depends on local-anaesthetic potency, baricity, dose, stage of labour, and the selected adjuvant. Racemic bupivacaine has long been used for obstetric neuraxial analgesia, but its motor-blocking tendency and systemic cardiotoxicity prompted evaluation of its S(-)-enantiomer, levobupivacaine.[5-9]

Address for Correspondence Dr. Leesha U, DNB Resident, Department of Anesthesiology, District Hospital, Dharwad, Karnataka, India.

DOI: 10.61336/im/23-01-17

Levobupivacaine has a sensory-block profile similar to racemic bupivacaine and may produce less motor impairment at equal intrathecal doses.[5] Fixed-dose and dose-response studies indicate that bupivacaine generally has greater intrathecal analgesic potency or duration than levobupivacaine, making rational dose selection important when regimens are compared.[6,8,9] Dexmedetomidine, a highly selective alpha-2 adrenergic agonist, enhances spinal antinociception through pre- and postsynaptic mechanisms and has been investigated as an opioid-sparing neuraxial adjuvant. Clinical trials and meta-analyses of labour analgesia report improved pain control and prolonged analgesia, with bradycardia and sedation requiring surveillance.[10-13]

Buprenorphine is a potent, long-acting partial mu-opioid receptor agonist that can prolong neuraxial analgesia. Its opioid-related adverse effects include nausea, vomiting, sedation, and pruritus, while clinically important respiratory depression remains uncommon at low intrathecal doses with appropriate monitoring.[14] Direct evidence comparing levobupivacaine-dexmedetomidine with levobupivacaine-buprenorphine for labour analgesia remains limited. Therefore, the present study compared these low-dose spinal regimens in terms of onset and duration of analgesia, serial pain scores, rescue analgesic requirement, motor blockade, maternal haemodynamic stability and adverse effects, labour and delivery characteristics, maternal satisfaction, and immediate neonatal outcomes.

Materials and Methods

Study design and setting: This prospective, randomised, hospital-based comparative study was conducted in the Department of Anaesthesiology in collaboration with the Department of Obstetrics and Gynaecology at Vijayanagar Institute of Medical Sciences, Ballari, Karnataka, India, from November 2022 to April 2023. The study protocol was approved by the Institutional Ethics Committee, and written informed consent was obtained from every participant. The study followed the ethical principles of the Declaration of Helsinki. [AUTHOR QUERY: Insert the Institutional Ethics Committee approval number and approval date. Also provide the trial registration number and registration date, or explicitly state that the trial was not registered.]

Participants: Term parturients aged 18-35 years with a singleton pregnancy, cephalic presentation, spontaneous or induced active labour, cervical dilatation of 3-5 cm, American Society of Anesthesiologists physical status II, and a request for labour analgesia were eligible. Exclusion criteria were refusal, allergy to a study drug, coagulopathy, infection at the puncture site, neurological disease, major spinal deformity, severe pre-eclampsia or eclampsia, significant cardiac disease, antepartum haemorrhage, non-reassuring fetal status before the block, multiple pregnancy, malpresentation, or anticipated operative delivery.

Randomisation and intervention: Sixty eligible parturients were randomised in a 1:1 ratio using a computer-generated allocation sequence. Assignments were concealed in sequentially numbered, opaque, sealed envelopes. Group LD received intrathecal levobupivacaine 2.5 mg with dexmedetomidine 5 micrograms. Group BB received intrathecal levobupivacaine 2.5 mg with buprenorphine 60 micrograms. [AUTHOR QUERY: Verify the concentration, baricity, preservative-free formulation, and total injected volume of both study solutions against the approved protocol. State who generated the sequence, enrolled participants, opened the envelopes, prepared the drugs, and assessed outcomes; also describe any blinding.] Standard monitoring included non-invasive blood pressure, electrocardiography, pulse oximetry, respiratory rate, and continuous fetal heart-rate surveillance. With the participant seated and under aseptic precautions, lumbar puncture was performed at the L3-L4 or L4-L5 interspace using a 25- or 27-gauge spinal needle. After free cerebrospinal fluid flow was confirmed, the study solution was injected, and the participant was positioned supine with left uterine displacement.

Sample size: The prespecified sample size was 60 parturients, with 30 in each group. [AUTHOR QUERY: Insert the original sample-size calculation, including the primary outcome, expected group values or effect size, variability, alpha level, statistical power, attrition allowance, and source of the assumptions.]

Outcome assessment: Pain intensity was evaluated using a 0-10 visual analogue scale (VAS) at baseline and at 5, 10, 30, 60, and 120 minutes. Effective analgesia was defined as VAS <=3. Onset was the interval from intrathecal injection to effective analgesia, and duration was the interval from onset until the first request for additional analgesia. Rescue analgesia was provided according to the institutional protocol. Motor function was assessed using the modified Bromage scale. Heart rate and mean arterial pressure were recorded serially. Hypotension, bradycardia, nausea or vomiting, pruritus, shivering, sedation, respiratory depression, post-dural puncture headache, and neurological symptoms were documented. Maternal satisfaction was scored on a five-point scale. Duration of the second stage, mode of delivery, one- and five-minute Apgar scores, neonatal resuscitation, and neonatal intensive care admission were recorded. [AUTHOR QUERY: Specify the rescue-analgesia trigger, drug, dose, route, and timing; define hypotension, bradycardia, sedation, and respiratory depression; provide the anchors for the five-point satisfaction scale; and state the duration and method of postpartum follow-up.]

Statistical analysis: Continuous variables were expressed as mean ± standard deviation and compared using the independent-samples t-test. Categorical variables were presented as frequency and percentage and analysed using the chi-square test or Fisher's exact test, as appropriate. All tests were two-sided, and $p < 0.05$ was considered statistically significant. [AUTHOR QUERY: Insert the statistical software and version. Confirm that distributional assumptions were assessed and explain how repeated VAS measurements and multiplicity across time points were handled.]

Results

Participant recruitment

During the study period, 64 parturients requesting labour analgesia were assessed for eligibility. Four women were excluded: two did not fulfil the eligibility criteria and two declined participation. The remaining 60 parturients were randomised: 30 received low-dose spinal analgesia with levobupivacaine and dexmedetomidine (Group LD), and 30 received levobupivacaine and buprenorphine (Group BB). Complete maternal, labour, delivery, and neonatal outcome data were available for all participants, and all randomised participants were included in the analysis.

Baseline maternal and obstetric characteristics

The groups were comparable with respect to maternal age, body mass index, gestational age, parity, cervical dilatation, baseline pain score, heart rate, and mean arterial pressure. Mean age was 24.9 ± 3.4 years in Group LD and 25.3 ± 3.6 years in Group BB ($p = 0.660$). Primigravidae constituted 56.7% of Group LD and 60.0% of Group BB. No statistically significant between-group difference was observed in any baseline characteristic (Table 1).

Table 1. Baseline maternal and obstetric characteristics

Characteristic	Group LD (n = 30)	Group BB (n = 30)	p-value
Age, years	24.9 ± 3.4	25.3 ± 3.6	0.660
Body mass index, kg/m²	26.2 ± 2.8	26.6 ± 3.0	0.595
Gestational age, weeks	38.5 ± 1.1	38.4 ± 1.0	0.714
Primigravida	17 (56.7)	18 (60.0)	1.000
Multigravida	13 (43.3)	12 (40.0)	
Cervical dilatation at analgesia, cm	4.2 ± 0.8	4.3 ± 0.9	0.651
Baseline VAS score	8.3 ± 0.7	8.2 ± 0.8	0.608
Baseline heart rate, beats/min	88.6 ± 9.4	87.9 ± 8.8	0.767
Baseline mean arterial pressure, mmHg	94.2 ± 7.6	95.0 ± 8.1	0.694

Data are presented as mean ± standard deviation or n (%). Group LD: levobupivacaine with dexmedetomidine; Group BB: levobupivacaine with buprenorphine; VAS: visual analogue scale. P-values were obtained using the independent-samples t-test or Fisher's exact test, as appropriate.

Onset, duration, and quality of labour analgesia

Mean onset time of effective analgesia was significantly shorter in Group LD than in Group BB (4.3 ± 1.1 vs 5.2 ± 1.3 minutes; p = 0.005). Mean duration of analgesia was significantly longer in Group LD (162.7 ± 30.4 vs 138.5 ± 27.8 minutes; p = 0.002). Rescue analgesia was required by five women (16.7%) in Group LD and 13 women (43.3%) in Group BB (p = 0.047). Baseline VAS scores were comparable. Group LD had significantly lower VAS scores at 5, 10, and 120 minutes, whereas scores at 30 and 60 minutes were similar. Maternal satisfaction was higher in Group LD (4.5 ± 0.6 vs 4.1 ± 0.8; p = 0.033) (Table 2).

Table 2. Analgesic characteristics and pain scores

Outcome	Group LD (n = 30)	Group BB (n = 30)	p-value
Onset of effective analgesia, min	4.3 ± 1.1	5.2 ± 1.3	0.005
Duration of analgesia, min	162.7 ± 30.4	138.5 ± 27.8	0.002
Baseline VAS score	8.3 ± 0.7	8.2 ± 0.8	0.608
VAS score at 5 min	3.8 ± 1.0	4.4 ± 1.1	0.031
VAS score at 10 min	2.1 ± 0.8	2.6 ± 0.9	0.027
VAS score at 30 min	1.8 ± 0.7	2.1 ± 0.8	0.128
VAS score at 60 min	2.2 ± 0.8	2.5 ± 0.9	0.178
VAS score at 120 min	3.1 ± 1.0	3.8 ± 1.1	0.012
Rescue analgesia required	5 (16.7)	13 (43.3)	0.047
Maternal satisfaction score	4.5 ± 0.6	4.1 ± 0.8	0.033

Data are presented as mean ± standard deviation or n (%). VAS: visual analogue scale. Effective analgesia was defined as VAS <=3. Duration was measured from onset of effective analgesia to the first request for additional analgesia. P-values were obtained using the independent-samples t-test or Fisher's exact test, as appropriate.

Motor blockade and maternal haemodynamics

Most parturients retained normal lower-limb motor function. A modified Bromage score of 0 was recorded in 26 women (86.7%) in Group LD and 24 women (80.0%) in Group BB (p = 0.731). Mild, transient motor weakness corresponding to a score of 1 occurred in four (13.3%) and six (20.0%) women, respectively. No participant developed a score of 2 or 3. Maternal heart rate and mean arterial pressure decreased modestly after spinal analgesia in both groups, without a clinically important intergroup difference. Hypotension occurred in three women (10.0%) in Group LD and five (16.7%) in Group BB (p = 0.706). Bradycardia was observed in four (13.3%) and one (3.3%) women, respectively (p = 0.353). All events were transient and responded to standard management.

Maternal adverse effects

Pruritus was not observed in Group LD but occurred in six women (20.0%) in Group BB (p = 0.024). Nausea or vomiting occurred in two women (6.7%) in Group LD and four (13.3%) in Group BB (p = 0.671). Mild sedation was numerically more frequent in Group LD, but every affected participant remained responsive to verbal commands. No clinically significant respiratory depression, severe motor blockade, post-dural puncture headache, neurological deficit, or local anaesthetic systemic toxicity was recorded (Table 3).

Table 3. Maternal adverse effects

Adverse effect	Group LD (n = 30)	Group BB (n = 30)	p-value
Hypotension	3 (10.0)	5 (16.7)	0.706
Bradycardia	4 (13.3)	1 (3.3)	0.353
Pruritus	0 (0.0)	6 (20.0)	0.024
Nausea or vomiting	2 (6.7)	4 (13.3)	0.671
Shivering	2 (6.7)	3 (10.0)	1.000
Mild sedation	6 (20.0)	2 (6.7)	0.254
Respiratory depression	0 (0.0)	0 (0.0)	–
Post-dural puncture headache	0 (0.0)	0 (0.0)	–

Data are presented as n (%). P-values were obtained using Fisher's exact test when expected cell counts were small.

Labour, delivery, and neonatal outcomes

Mean duration of the second stage was 42.8 ± 13.6 minutes in Group LD and 44.9 ± 14.2 minutes in Group BB (p = 0.561). Spontaneous vaginal delivery occurred in 24 (80.0%) and 23 (76.7%) women, instrumental vaginal delivery in three (10.0%) and four (13.3%), and caesarean delivery in three (10.0%) women in each group. The overall distribution of delivery modes was comparable (p = 0.921). Mean one- and five-minute Apgar scores did not differ significantly. One neonate in each group required brief initial resuscitation. No neonate had a five-minute Apgar score below 7 or required neonatal intensive care admission for an analgesia-related complication (Table 4).

Table 4. Labour and neonatal outcomes

Outcome	Group LD (n = 30)	Group BB (n = 30)	p-value
Duration of second stage, min	42.8 ± 13.6	44.9 ± 14.2	0.561
Spontaneous vaginal delivery	24 (80.0)	23 (76.7)	0.921
Instrumental vaginal delivery	3 (10.0)	4 (13.3)	
Caesarean delivery	3 (10.0)	3 (10.0)	
One-minute Apgar score	8.2 ± 0.7	8.1 ± 0.8	0.608
Five-minute Apgar score	9.3 ± 0.6	9.2 ± 0.7	0.555
Neonatal resuscitation required	1 (3.3)	1 (3.3)	1.000
Neonatal intensive care admission	0 (0.0)	0 (0.0)	–

Data are presented as mean ± standard deviation or n (%). The p-value for mode of delivery represents the overall Pearson chi-square comparison across the three delivery categories. Other p-values were obtained using the independent-samples t-test or Fisher's exact test, as appropriate.

Discussion

The present study found that low-dose intrathecal levobupivacaine with dexmedetomidine produced a faster onset, longer duration, lower pain scores at selected intervals, reduced rescue analgesic use, and greater maternal satisfaction than levobupivacaine with buprenorphine. These benefits occurred without a significant difference in motor blockade, maternal hypotension, mode of delivery, or immediate neonatal condition. The findings support the principle that a low-dose local anaesthetic combined with an effective neuraxial adjuvant can provide clinically useful

labour analgesia while preserving motor function.[3,4]

The shorter onset and prolonged analgesic duration in Group LD are biologically plausible. Dexmedetomidine activates spinal alpha-2 receptors, reduces neurotransmitter release from primary afferent fibres, and enhances inhibitory interneuronal activity. Previous labour studies have reported improved analgesic quality or duration when dexmedetomidine was administered intrathecally or epidurally with local anaesthetics.[10-13] Li et al. found that intrathecal dexmedetomidine enhanced epidural labour analgesia, while Zhang et al. reported superior analgesic duration with dexmedetomidine compared with an opioid adjuvant.[11,12] The lower rescue-analgesia rate and higher satisfaction in the present cohort are consistent with these observations.

Levobupivacaine has a sensory-block profile similar to racemic bupivacaine and may produce less motor impairment at equivalent intrathecal doses.[5-9] Vercauteren et al. reported comparable analgesia with levobupivacaine and racemic bupivacaine combinations, with less motor impairment in the levobupivacaine group.[5] In the current study, both groups received the same dose of levobupivacaine; therefore, the local-anaesthetic component was controlled. Most participants retained normal motor function, and no dense motor block occurred. The observed between-group differences are consequently more consistent with the effects of the respective adjuvants, although causal interpretation remains limited by the modest sample and incompletely reported blinding.

Pruritus occurred exclusively in the levobupivacaine-buprenorphine group. Neuraxial opioids can produce pruritus through central mu-receptor mechanisms, even without histamine release. Buprenorphine has prolonged neuraxial analgesic activity, but nausea, sedation, and pruritus remain recognised dose-related effects.[14] In contrast, dexmedetomidine is not associated with opioid-mediated pruritus. Bradycardia and mild sedation were numerically more frequent in Group LD, reflecting the expected alpha-2 agonist profile, although neither difference was statistically significant and no clinically important respiratory depression occurred.[10,13]

The comparable duration of the second stage, instrumental delivery, caesarean delivery, Apgar scores, and neonatal resuscitation rates indicate that neither regimen produced an evident adverse obstetric or neonatal signal in this sample. Large systematic reviews similarly show that modern low-dose neuraxial analgesia provides superior pain relief without increasing caesarean delivery, although instrumental birth and uncommon adverse events require continued evaluation.[2] Overall, the levobupivacaine-dexmedetomidine regimen had the more favourable efficacy-tolerability profile in this cohort, but confirmation in larger, blinded trials is required.

LIMITATIONS

This single-centre study had a modest sample size and was conducted over six months, limiting precision for uncommon maternal and neonatal adverse events. Participant, clinician, drug-preparer, and outcome-assessor blinding were not described, creating a potential risk of performance and detection bias. Only one dose of each adjuvant was evaluated, and no levobupivacaine-only control group was included; therefore, dose-response relationships and the incremental effect of each adjuvant could not be determined. Serial VAS scores were reported using multiple time-specific comparisons, and the manuscript did not describe a repeated-measures model or adjustment for multiplicity. Follow-up ended in the immediate postpartum period, so delayed neurological symptoms, breastfeeding outcomes, and maternal recovery were not assessed. Plasma drug concentrations were not measured, and generalisability may be limited across institutions using different obstetric protocols, rescue regimens, and spinal drug doses.

Conclusion

Among selected term parturients, low-dose spinal labour analgesia with levobupivacaine and dexmedetomidine provided a faster onset, longer duration of effective pain relief, lower VAS scores at selected intervals, reduced rescue-analgesia requirement, and greater maternal satisfaction than levobupivacaine with buprenorphine. Both regimens preserved lower-limb motor function and maintained acceptable maternal haemodynamic stability. Labour progression, operative delivery rates, Apgar scores, neonatal resuscitation, and neonatal intensive care admission were comparable. Pruritus was more frequent with the levobupivacaine-buprenorphine regimen, whereas transient bradycardia and mild sedation occurred numerically more often with levobupivacaine-dexmedetomidine. These findings favour the levobupivacaine-dexmedetomidine regimen in this sample, but larger blinded trials are required before routine clinical adoption.

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