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Levobupivacaine with fentanyl or dexmedetomidine for lower limb surgery: A randomized comparative study

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Abstract:

Epidural adjuvants improve block quality and prolong post-operative analgesia in lower limb surgery. Therefore, it is of interest to compare the epidural levobupivacaine with fentanyl or dexmedetomidine in 84 ASA I-II patients. Sensory and motor block onset, haemodynamics, analgesia duration and complications were evaluated. Dexmedetomidine produced faster block onset and longer analgesia than fentanyl ($p < 0.0001$), with comparable haemodynamics. Thus, dexmedetomidine is a superior epidural adjuvant to levobupivacaine for lower limb surgery, providing faster block onset and prolonged analgesia.

Keywords: Dexmedetomidine, epidural anesthesia, fentanyl, levobupivacaine, post-operative pain

Background:

Epidural anaesthesia remains the preferred technique for major lower limb orthopaedic surgeries, such as total knee replacement and other procedures involving the lower extremity, owing to reduced intraoperative blood loss, fewer systemic complications and high patient and surgeon acceptance [1]. In such procedures, where post-operative pain is often severe and a major barrier to early rehabilitation, the quality and duration of epidural analgesia directly influence functional recovery and length of hospital stay [2]. Among local anaesthetics, levobupivacaine is the S (-) enantiomer of bupivacaine is increasingly preferred over racemic bupivacaine for epidural use because of comparable efficacy with significantly lower cardiotoxicity and central nervous system toxicity [3]. Adjuvants are commonly co-administered with epidural local anaesthetics to hasten block onset, improve haemodynamic stability and prolong post-operative analgesia. Fentanyl, a potent synthetic opioid, is widely used for this purpose but is associated with adverse effects including nausea, vomiting, pruritus and respiratory depression [4]. Dexmedetomidine, a highly selective α_2 -adrenergic agonist, provides analgesia, sedation and sympatholysis without these opioid-related effects, with hypotension and bradycardia as its principal, manageable adverse effects [5]. Effective post-operative analgesia after lower limb surgery is associated with earlier mobilisation; reduced post-operative complications and shorter hospital stay [6]. While fentanyl and dexmedetomidine have each been individually studied as epidural adjuvants to levobupivacaine, direct comparative data on their effects on block characteristics and post-operative analgesic duration remain limited [7]. Therefore, it is of interest to report the epidural levobupivacaine with fentanyl versus levobupivacaine with dexmedetomidine with respect to onset and quality of sensory and motor blockade, intraoperative haemodynamic stability and duration of post-operative analgesia in patients undergoing lower limb orthopaedic surgeries.

Materials and Methods:

Study design and participants:

After Institutional Ethics Committee approval and written informed consent, this prospective randomized comparative study was conducted in the Department of Anaesthesiology. Eighty-four adult patients of ASA physical status I and II, aged 19-50 years, scheduled for elective lower limb orthopaedic

surgery under epidural anaesthesia and willing to provide written informed consent, were enrolled. Patients with significant cardiovascular, renal, hepatic, pulmonary or neurological disease, diabetes mellitus, coagulopathy, body mass index (BMI) $> 30 \text{ kg/m}^2$, localized infection at the epidural site, known allergy or hypersensitivity to the study drugs, or refusal of consent, were excluded.

Sample size:

The sample size was calculated based on the expected difference in time to first rescue analgesia between the two groups, using data from prior comparable studies, at 80% power and a two-sided alpha of 0.05, yielding a minimum of 42 patients per group (total $n = 84$).

Randomisation and groups:

Patients were randomized into two groups of 42 each using a computer-generated random sequence. Group F received epidural 0.5% levobupivacaine (19 ml) with fentanyl $1 \mu\text{g/kg}$ and Group D received 0.5% levobupivacaine (19 ml) with dexmedetomidine $1 \mu\text{g/kg}$, each diluted with normal saline to a total volume of 20 ml.

Anaesthetic technique:

All patients underwent pre-anaesthetic evaluation and standard monitoring (electrocardiography, non-invasive blood pressure, pulse oximetry) was commenced on arrival in the operating room. Under aseptic precautions, an epidural catheter was placed at the appropriate lumbar interspace using the loss-of-resistance technique and following a negative test dose the study drug solution was administered as per group allocation.

Observations:

Heart rate (HR), systolic (SBP), diastolic (DBP) and mean arterial pressure (MAP) were recorded at baseline and at 5, 10, 15, 20, 25, 30, 45, 60, 75 and 90 minutes. Onset of sensory blocks (time to T10 by pinprick) and maximum sensory level (T6-T7) were recorded and motor block was assessed using the modified Bromage scale, noting time to onset (Bromage 1) and completion (Bromage 3). Sedation was assessed using the Ramsay Sedation Scale. Post-operatively, the time to first rescue analgesia (VAS ≥ 4) and the number of rescue doses over 24 hours were recorded, pain intensity was assessed using the Visual Analog Scale (VAS)

and complications including bradycardia, hypotension, pruritus, shivering, nausea and vomiting were noted.

Statistical analysis:

Data were analysed using IBM SPSS Statistics version 26.0. Continuous variables are presented as mean ± standard deviation and compared using the Student’s unpaired t-test; categorical variables are presented as numbers and percentages and compared using the Chi-square test. A p-value < 0.05 was considered statistically significant.

Results:

Eighty-four patients were randomized into Group D (levobupivacaine with dexmedetomidine, n = 42) and Group F (levobupivacaine with fentanyl, n = 42). The mean age was 29.84 ± 6.55 years in Group D and 32.48 ± 6.98 years in Group F (p = 0.0776) and most patients were female in both groups. Height and weight were comparable; a small but statistically significant difference in mean BMI was noted (23.98 vs 22.41 kg/m²; p = 0.0312), though both groups remained within the non-obese range (Tables 1–3). Systolic and diastolic blood pressure, mean arterial pressure and heart rate were comparable between the two groups at all-time points throughout the intraoperative period, with no statistically significant difference at any time point (Tables 4–7). The mean duration of surgery was comparable between Group D (89.58 ± 4.99 min) and Group F

(90.21 ± 5.28 min; p = 0.5756) (Table 8). Onset of sensory block to T10 was significantly faster in Group D (8.31 ± 1.34 min) than Group F (15.37 ± 1.89 min; p < 0.0001), as was the time to maximum sensory level (14.21 vs 21.57 min; p < 0.0001). Onset and completion of motor block were also significantly faster in Group D (15.67 and 18.37 min) than Group F (23.41 and 27.12 min; p < 0.0001 each) (Tables 9–12). Most patients in both groups had a Ramsay Sedation Score of 3 (Group D 57.14%; Group F 50.00%), with no statistically significant difference between groups (p = 0.4020) (Table 13). On the Visual Analog Scale, 54.76% of Group D patients reported no pain versus 14.29% in Group F and no Group D patient experienced severe pain compared with 19.05% in Group F (p < 0.0001). The mean time to first rescue analgesia was significantly longer in Group D (329.64 ± 16.94 min) than Group F (212.31 ± 11.24 min; p < 0.0001), representing approximately 117 minutes (≈2 hours) of additional analgesia and Group D patients required significantly fewer rescue doses (p = 0.0001) (Tables 14–16). Bradycardia occurred in 2 (4.76%) Group D patients and none in Group F (p = 0.4477); hypotension in 1 (2.38%) and 2 (4.76%) patients respectively (p = 0.6592); shivering in 1 (2.38%) Group D patient (p = 0.3865); and pruritus exclusively in 3 (7.14%) Group F patients (p = 0.1473). No oxygen desaturation, post-dural puncture headache, nausea or vomiting occurred and none of the between-group differences reached statistical significance (Table 17).

Table 1: Age distribution among groups

Age (years)	Group D (n = 42)	Group F (n = 42)	P-value
19–20	1 (2.38%)	2 (4.76%)	$\chi^2 = 1.929$; p = 0.5874 (age groups)
21–30	21 (50.00%)	15 (35.71%)	
31–40	11 (26.19%)	13 (30.95%)	t = 1.787; p = 0.0776 (mean age)
41–50	9 (21.43%)	12 (28.57%)	
Mean ± SD	29.84 ± 6.55	32.48 ± 6.98	

Table 2: Sex distribution among groups

Category	Group D (n = 42)	Group F (n = 42)	P-value
Male	9 (21.43%)	12 (28.57%)	$\chi^2 = 0.571$; p = 0.4497
Female	33 (78.57%)	30 (71.43%)	

Table 4: Intraoperative systolic blood pressure (mmHg) among groups

Time	Group D (Mean ± SD)	Group F (Mean ± SD)
Baseline	125.60 ± 6.68	126.98 ± 4.15
5 min	123.00 ± 6.51	124.65 ± 6.84
10 min	121.33 ± 6.95	123.46 ± 6.93
15 min	120.81 ± 5.94	123.68 ± 7.40
20 min	119.88 ± 7.63	118.71 ± 6.43
25 min	120.93 ± 7.36	117.92 ± 7.13
30 min	120.14 ± 7.87	118.97 ± 6.68
45 min	121.40 ± 6.97	120.50 ± 7.44
60 min	119.64 ± 8.84	118.79 ± 8.55
75 min	121.14 ± 7.50	119.47 ± 6.12
90 min	123.74 ± 7.44	122.41 ± 5.49

All between-group comparisons were statistically non-significant (p > 0.05).

Table 5: Intraoperative diastolic blood pressure (mmHg) among group

Time	Group D (Mean ± SD)	Group F (Mean ± SD)
Baseline	83.12 ± 7.53	84.41 ± 6.70
5 min	80.64 ± 6.69	82.17 ± 6.69
10 min	80.07 ± 7.85	80.91 ± 7.98

15 min	79.55 ± 7.89	76.94 ± 6.67
20 min	79.02 ± 6.67	78.94 ± 5.97
25 min	78.64 ± 5.70	79.84 ± 7.12
30 min	77.84 ± 6.60	79.67 ± 5.82
45 min	77.52 ± 5.46	76.98 ± 5.97
60 min	78.83 ± 5.40	79.15 ± 4.78
75 min	80.07 ± 6.84	81.48 ± 5.52
90 min	80.81 ± 7.13	82.48 ± 4.74

All between-group comparisons were statistically non-significant (p > 0.05).

Table 3: Anthropometric parameters among groups

Parameter	Group D (Mean ± SD)	Group F (Mean ± SD)	P-value
Height (cm)	166.54 ± 5.84	167.84 ± 6.21	p = 0.3259
Weight (kg)	65.48 ± 9.53	64.87 ± 9.15	p = 0.7655
BMI (kg/m²)	23.98 ± 3.48	22.41 ± 3.07	p = 0.0312*

*Statistically significant (p < 0.05). BMI: body mass index.

Table 6: Intraoperative mean arterial pressure (mmHg) among groups

Time	Group D (Mean ± SD)	Group F (Mean ± SD)
Baseline	97.28 ± 6.71	98.70 ± 5.48
5 min	94.76 ± 5.39	96.56 ± 4.13
10 min	93.83 ± 7.11	95.10 ± 5.20
15 min	93.30 ± 6.59	91.93 ± 5.66
20 min	92.64 ± 6.33	91.96 ± 5.21
25 min	92.74 ± 5.55	92.19 ± 6.28
30 min	92.49 ± 6.33	92.37 ± 4.46
45 min	92.15 ± 4.83	91.08 ± 4.08
60 min	92.44 ± 5.83	92.95 ± 3.98
75 min	93.76 ± 6.17	94.19 ± 4.89
90 min	95.12 ± 6.38	95.87 ± 4.92

All between-group comparisons were statistically non-significant (p > 0.05).

Table 7: Intraoperative heart rate (beats/min) among groups

Time	Group D (Mean ± SD)	Group F (Mean ± SD)
Baseline	87.62 ± 9.37	89.05 ± 9.88
5 min	87.21 ± 9.50	89.96 ± 9.59
10 min	87.71 ± 9.93	90.17 ± 9.36
15 min	86.19 ± 10.02	87.39 ± 10.02
20 min	85.00 ± 9.31	86.20 ± 9.31

Table 8: Duration of surgery among groups

Parameter	Group D (Mean ± SD)	Group F (Mean ± SD)	P-value
Duration of surgery (min)	89.58 ± 4.99	90.21 ± 5.28	t = 0.562; p = 0.5756

Table 9: Time to achieve T10 sensory block among groups

Parameter	Group D (Mean ± SD)	Group F (Mean ± SD)	P-value
Time to T10 sensory block (min)	8.31 ± 1.34	15.37 ± 1.89	t = 19.75; p < 0.0001*

Table 10: Time to attain maximum sensory level (T6–T7) among groups

Parameter	Group D (Mean ± SD)	Group F (Mean ± SD)	P-value
Time to	14.21 ± 1.34	21.57 ± 1.97	t = 20.02; p <

Table 13: Ramsay Sedation Scores among groups

Category	Group D (n = 42)	Group F (n = 42)	P-value
Score 1 (awake, anxious)	0 (0.00%)	2 (4.76%)	$\chi^2 = 2.933$; p = 0.4020
Score 2 (awake, cooperative)	12 (28.57%)	15 (35.71%)	
Score 3 (responsive to commands)	24 (57.14%)	21 (50.00%)	
Score 4 (asleep, brisk response)	6 (14.29%)	4 (9.52%)	

Table 14: Number of rescue analgesic doses required among groups.

Category	Group D (n = 42)	Group F (n = 42)	P-value
2 doses	6 (14.29%)	1 (2.38%)	$\chi^2 = 17.986$; p = 0.0001*
3 doses	26 (61.90%)	12 (28.57%)	
4 doses	10 (23.81%)	29 (69.05%)	

Table 17: Complications among groups

Complication	Group D (n = 42)	Group F (n = 42)	P-value
Bradycardia	2 (4.76%)	0 (0.00%)	p = 0.4477
Hypotension	1 (2.38%)	2 (4.76%)	p = 0.6592
Oxygen desaturation	0 (0.00%)	0 (0.00%)	—
PDPH	0 (0.00%)	0 (0.00%)	—
Shivering	1 (2.38%)	0 (0.00%)	p = 0.3865

Discussion:

The principal finding of this trial was that adding dexmedetomidine to epidural levobupivacaine produced significantly faster onset of sensory and motor block and prolonged post-operative analgesia by approximately 117 minutes compared with fentanyl, without compromising intraoperative haemodynamic stability. The faster onset of sensory block to T10 in the dexmedetomidine group (8.31 vs 15.37 min) closely mirrors the values reported by Kalbande *et al.* [8]. (8.10 vs. 15.03 min in a bupivacaine-based comparison), lending external validity to our findings. This acceleration reflects the pharmacology of dexmedetomidine, a highly selective α 2-adrenergic agonist that produces analgesia at the dorsal horn, causes local vasoconstriction that slows systemic

25 min	84.02 ± 8.70	85.22 ± 8.70
30 min	85.17 ± 8.69	86.37 ± 8.69
45 min	84.76 ± 10.16	85.96 ± 10.16
60 min	84.62 ± 10.17	85.82 ± 10.17
75 min	84.57 ± 10.33	85.77 ± 10.33
90 min	87.17 ± 9.68	88.37 ± 9.68

All between-group comparisons were statistically non-significant (p > 0.05).

maximum sensory level (min)	0.0001*
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Table 11: Onset of motor block among groups

Parameter	Group D (Mean ± SD)	Group F (Mean ± SD)	P-value
Onset of motor block (min)	15.67 ± 1.29	23.41 ± 1.67	t = 23.77; p < 0.0001*

Table 12: Time to complete motor block among groups

Parameter	Group D (Mean ± SD)	Group F (Mean ± SD)	P-value
Time to complete motor block (min)	18.37 ± 1.34	27.12 ± 1.57	t = 27.47; p < 0.0001*

*p < 0.0001: highly statistically significant

Table 15: Visual Analog Scale (VAS) pain scores among groups

Category	Group D (n = 42)	Group F (n = 42)	P-value
No pain (0)	23 (54.76%)	6 (14.29%)	$\chi^2 = 21.21$; p < 0.0001*
Mild pain (1–3)	11 (26.19%)	11 (26.19%)	
Moderate pain (4–6)	8 (19.05%)	17 (40.48%)	
Severe pain (7–10)	0 (0.00%)	8 (19.05%)	

Table 16: Time to first rescue analgesic agent among groups

Parameter	Group D (Mean ± SD)	Group F (Mean ± SD)	P-value
Time to first rescue analgesia (min)	329.64 ± 16.94	212.31 ± 11.24	t = 37.40; p < 0.0001*

*p < 0.0001: highly statistically significant; VAS: Visual Analog Scale.

Nausea	0 (0.00%)	0 (0.00%)	—
Vomiting	0 (0.00%)	0 (0.00%)	—
Pruritus	0 (0.00%)	3 (7.14%)	p = 0.1473

PDPH: post-dural puncture headache. None of the between-group differences were statistically significant.

absorption of the local anaesthetic and acts synergistically with levobupivacaine at spinal receptors [9]. The prolongation of post-operative analgesia in the dexmedetomidine group (329.64 vs 212.31 min) is consistent with Shukla *et al.* [10]. Who found dexmedetomidine superior to fentanyl and tramadol as an adjuvant to levobupivacaine. Sedation scores were likewise comparable between groups, with most patients calm but rousable, so dexmedetomidine did not produce excessive sedation—an important consideration for early post-operative mobilisation. The clinical benefit was reflected in post-operative pain: 54.76% of dexmedetomidine patients were pain-free versus 14.29% of fentanyl patients and no dexmedetomidine patient experienced severe pain compared with 19.05% in the fentanyl group, with correspondingly fewer rescue analgesic doses [11]. The complication profiles were balanced and favorable: pruritus

occurred exclusively in the fentanyl group as an opioid-related effect, while the bradycardia and shivering seen only in the dexmedetomidine group were infrequent and did not require intervention. The small but statistically significant difference in mean BMI (23.98 vs 22.41 kg/m²) is a potential confounder, although both groups remained within the non-obese range and the difference is unlikely to be clinically meaningful for block characteristics [12]. These findings are relevant to lower limb orthopaedic procedures such as total knee replacement, where quality early-recovery analgesia is a priority. The strengths of the study include its randomized design, standardised dosing enabling a direct comparison and comprehensive assessment of intra- and post-operative parameters, while its limitations, discussed below, include a single-centre setting, relatively small sample and the absence of formal blinding.

Conclusion:

In elective lower limb orthopaedic surgery, adding dexmedetomidine (1 µg/kg) to epidural levobupivacaine produced significantly faster onset of sensory and motor block, prolonged post-operative analgesia by approximately 117 minutes and lower post-operative pain scores than adding fentanyl (1 µg/kg). These benefits occurred without any clinically significant increase in complications and intraoperative haemodynamic parameters were comparable between the groups. Dexmedetomidine may therefore be considered a useful and effective alternative to fentanyl as an epidural adjuvant to levobupivacaine for lower limb orthopaedic surgeries.

Limitations:

This study was conducted at a single tertiary care centre with a relatively small sample size (n = 84), which may limit generalisability. Although randomization was performed using a computer-generated random sequence, formal allocation concealment and blinding of the assessors were not implemented, which may introduce observer bias in the

assessment of subjective parameters such as VAS scores. Future multicentric, double-blind randomized controlled trials with larger sample sizes are recommended to corroborate these findings.

Financial support and sponsorship:

Nil.

Conflicts of interest:

There are no conflicts of interest.

Data availability:

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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