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LEVOBUPIVACAINE WITH DEXMEDETOMIDINE VERSUS LEVOBUPIVACAINE WITH NALBUPHINE VIA PATIENT CONTROLLED EPIDURAL ANALGESIA IN LOWER LIMB ORTHOPAEDIC SURGERIES

Dr Veena Chatrath[1], Dr Ranjana Khetarpal[2], Dr Gagandeep kaur[3*], Dr Gurleen Kaur[4]

[1]Professor and Head, Department of Anaesthesiology and Critical Care, Government Medical College, Amritsar, Email - drveenachatrath@yahoo.com
[2]Professor, Department of Anaesthesiology and Critical Care, Government Medical College, Amritsar, Email - rkhetarpal9@hotmail.com
[3*]Assistant Professor, Department of Anaesthesiology and Critical Care, Government Medical College, Amritsar, Email - Gsandhu2454@gmail.com
[4]Junior Resident, Department of Anaesthesiology and Critical Care, Government Medical College, Amritsar, Email - gurleen00006@gmail.com

Abstract

Background: Epidural analgesia provides effective pain relief. Patient controlled epidural analgesia (PCEA) allows individualized dosing. This study compares Dexmedetomidine and Nalbuphine as adjuncts to Levobupivacaine for postoperative pain relief via PCEA.

Method: This prospective, double-blind study was conducted on 94 patients (ASA I – II, 18–65 years). All patients received 3 ml (0.5%) levobupivacaine for spinal anaesthesia. At regression of sensory block to T10, patients received 0.25% levobupivacaine either with 1 mcg/kg dexmedetomidine (Group D) or 0.1 mg/kg nalbuphine (Group N). For postoperative analgesia epidural infusion of 0.125% levobupivacaine either with 1 mcg/ml dexmedetomidine (Group D) or 0.2 mg/ml Nalbuphine (Group N) was started at 3 ml/hr and demand dose of 4ml was given.

Results: Heart rate decreased after epidural bolus in Group D and remained lower due to which 6 patients in Group D reported bradycardia. Other haemodynamic parameters were comparable. VAS was comparable initially, higher in Group N at 4–10 hours, and comparable thereafter. Group D required fewer PCEA boluses (0.98 ± 0.82) than Group N (2.66 ± 0.48) and lower drug consumption (87.91 ± 3.28ml) than Group N (94.64 ± 1.92 ml). No group required rescue analgesia. Group D demonstrated higher sedation scores relative to Group N. Itching incidents were higher in Group N (8.51%).The patient satisfaction was higher in Group D.

Conclusion: Dexmedetomidine offered better analgesia with lower VAS scores, fewer PCEA demands, reduced drug consumption.

Keywords: Combined Spinal Epidural technique, Patient Controlled Epidural Analgesia, Epidural basal infusion, Demand dose

Introduction

Regional anaesthesia is the technique of choice for most lower limb surgical procedures due to their effective intraoperative anaesthesia and postoperative analgesia. Combined spinal epidural anaesthesia offers rapid onset, dense block and prolonged analgesia. Epidural analgesia has evolved from intermittent boluses to continuous infusion to patient controlled epidural analgesia (PCEA). PCEA allows self-administeration of analgesia by programmed bolus doses, lockout intervals, and basal infusion ensuring individualized pain control. Levobupivacaine is widely used due to its lower cardiotoxicity and reduced neurotoxicity1.Adjuvants are added to enhance analgesic efficacy and reduce local anaesthetic requirements2. Dexmedetomidine, a selective α_2 agonist, provides analgesia and sedation by inhibiting nociceptive transmission. However, it may be associated with bradycardia and hypotension3. Nalbuphine, a κ-agonist and μ-antagonist, offers effective analgesia with minimal respiratory depression4. The present study compares analgesic efficacy, PCEA bolus requirement, total drug consumption, haemodynamics, sedation, patient satisfaction, and adverse effects of Dexmedetomidine versus Nalbuphine as adjunct to Levobupivacaine in PCEA for lower limb surgeries.

Material And Method

This prospective, double-blind, comparative study was conducted on 94 patients (ASA I – II, 18 – 65 years) who underwent lower limb orthopaedic surgery under combined spinal-epidural anaesthesia after approval from the Institutional Ethics Committee (IEC No.: 40882/D-26/2023 Batch) and written, informed consents from the patients. Exclusion criteria included patients with neurological disorders, contraindications to neuraxial anesthesia, hypersensitivity to study drugs, spinal deformities, cardiac, renal or hepatic disease, history of drug abuse, and cardiac arrhythmias or labile hypertension. Aims were to compare volume of epidural study drug consumed, number of PCEA boluses required, patient satisfaction scores, haemodynamics and side effects of drugs. One day prior to surgery, a comprehensive pre-anaesthetic evaluation, detailed medical history, general, systemic and airway examination was done. Patients were advised abstinence from solid food for six hours and clear liquids for two hours before surgery. Routine and special (if needed) investigations were done. In the preoperative room, consent was taken, fasting status was confirmed, baseline HR, NIBP, SpO_2, RR, and ECG were recorded. Premedication - Intravenous Midazolam (0.03mg/kg) and Glycopyrrolate (0.005mg/kg) was given. Monitoring of blood pressure (BP), pulse rate (PR), respiratory rate (RR), pulse oximetry (SpO2) & electrocardiography (ECG) was started. The combined spinal epidural technique was done under strict aseptic conditions. Either the L3–L4 or L2–L3 intervertebral space was identified by surface anatomical landmarks, and the overlying skin at the puncture site was infiltrated with 2 mL of 2% lignocaine. 18G Tuohy needle was introduced and the epidural space was recognised using the loss-of-resistance technique. Then 27G Whitacre needle was then advanced through Tuohy's needle into intrathecal space and 3 ml of 0.5% hyperbaric levobupivacaine was administered after confirming flow of CSF. After withdrawing the spinal needle, an epidural catheter was introduced 4 cm into the epidural space. Correct placement of the epidural catheter was confirmed using a 3 mL test dose of 1.5% lignocaine with adrenaline (1:200,000). Surgery commenced after achieving sensory block up to T8 with grade 3 motor block. After spinal anaesthesia participants were randomly allocated into two groups of 47 patients each using a computer-generated randomization sequence. Regression of sensory blockade to T10 was taken as time zero (0 minute), when epidural bolus and infusion of study drugs were initiated. Study drugs were

loaded into identical syringes and PCA pumps by one anaesthesiologist, while another anaesthesiologist blinded to the preparation administered study drug and monitored patients, ensuring a double-blind design. Epidural bolus dose was prepared as: In Group D: 10 ml of 0.25% Isobaric Levobupivacaine + 1mcg/kg Dexmedetomidine, In Group N: 10 ml of 0.25% Isobaric Levobupivacaine + 0.1 mg/kg Nalbuphine. After giving epidural bolus, basal infusion was initiated in each group. Epidural basal infusion was prepared as:In Group D (n=47) = 0.125% isobaric Levobupivacaine + 1 mcg/ml Dexmedetomidine, In Group N (n=47) = 0.125% isobaric Levobupivacaine + 0.2 mg/ml Nalbuphine. During surgery, if sensory block regressed to T10 after basal infusion and pain persisted, a second epidural bolus was administered and the patient was excluded from the study.Postoperative analgesia was maintained with PCEA (3 ml/h infusion, 4 ml demand dose, 20-min lockout interval) for VAS >4 in both groups.If pain (VAS >4) persisted one hour after maximum PCEA dosing, rescue analgesia with IM diclofenac 75 mg was administered. Total volume of study drug consumed, number PCEA boluses requirements were noted. Haemodynamic monitoring was done. Bradycardia (HR below 50 bpm) was managed with intravenous atropine 0.4 mg or as needed. Hypotension (>20% fall in SBP or MAP <60 mmHg) was treated with intravenous fluids and incremental ephedrine 5 mg. Sedation levels were evaluated with Ramsay's sedation score. Pain was evaluated with VAS score. Sedation and VAS scores were recorded from 0 minute (time of regression of sensory blockade to T10) till 24 hours. The total number of rescue analgesic doses administered and side effects were observed. Patient satisfaction scores were assessed by 5 points Likert Scale.

Sample Size And Statistical Analysis:

Sample size was calculated after reviewing previous studies using formula :

$$n_i = \left(\frac{Z\sigma}{\varepsilon}\right)^2$$

$$\sigma = \sqrt{\frac{(n_1 - 1)S_1^2 + (n_2 - 1)S_2^2}{(n_1 + n_2 - 2)}}$$

After calculation, each study group was allocated 47 participants, resulting in a total sample size of 94 patients. The collected data was entered into Microsoft Excel 2019 and subsequently analysed using SPSS software version 23.0 (IBM Corp., Armonk, NY, USA). Continuous variables were summarized as mean ± standard deviation (SD), whereas categorical variables were presented as frequencies and percentages. Quantitative data was compared using the independent sample Student's t-test after confirming normality of data distribution while Qualitative variables were compared using either the Chi-square test or Fisher's exact test. A p-value less than 0.05 was considered statistically significant. The study was performed with a power of 90% and a confidence level of 95% ($\alpha = 0.05$).

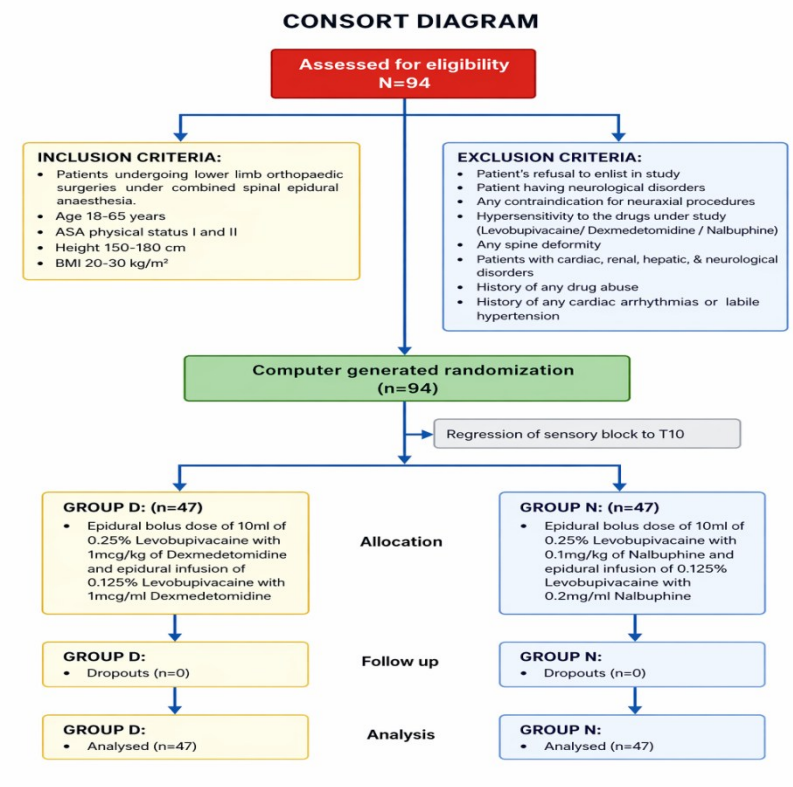


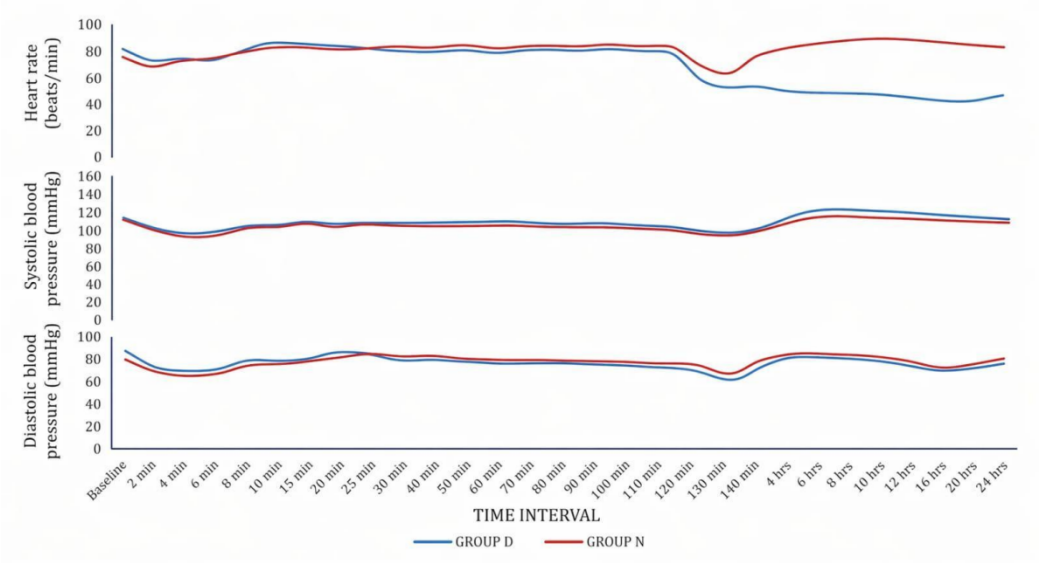
FIGURE-1: Consort Diagram

Observations And Results

In the present study of 94 patients, age, sex distribution, body mass index, ASA physical status, type of lower limb surgery, mean duration of the surgery, maximum sensory blockade level achieved, mean time for regression of sensory block to T10 were comparable between the two groups as shown in Table 1.

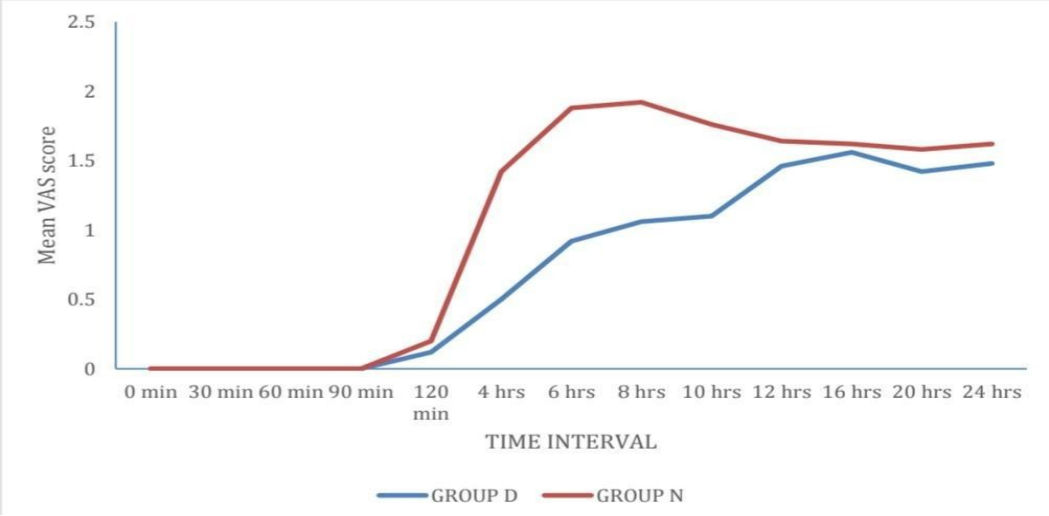
TABLE-1: Demographic variables, Type and Duration of surgery, Sensory block characteristics

Parameter	Group D	Group N	p Value
Mean age (years)	47.702 ± 11.069	46.745±10.173	0.663
Sex distribution (F/M)	26/21	24/23	0.679
Mean BMI	25.170±2.713	25.064±2.877	0.854
ASA Grade I/II	28/19	26/21	0.676
Type of surgery (Bipolar hemiarthroplasty / Dynamic hip screw/Femur nailing/ Total knee replacement)	13/2/17/15	15/4/14/14	0.768
Mean total duration of surgery (minutes)	129.148±15.959	130.212±15.878	0.747
Maximum sensory block level achieved (T6/T8)	6/41	5/42	0.748
Mean time for regression of sensory block to T10 (minutes)	119.460±11.590	120.940±11.117	0.516



GRAPH-1: Heart rate, Systolic blood pressure, Diastolic blood pressure variation in Group D and Group N

Intraoperatively, heart rate was comparable between groups. After regression to T10 and administration of epidural bolus, Group D showed reduction in heart rate (mean heart rate at 130 minutes in the Group D was 69.68±7.07 while in Group N was 72.86 ± 7.02, p = 0.01) and remained lower thereafter as shown in Graph-1. Following spinal drug administration, both groups showed decline in systolic and diastolic blood pressure that was comparable with no statistically significant difference. Even after administration of epidural bolus and start of epidural infusion, systolic and diastolic blood pressure was stable and comparable between two groups as shown in Graph-1. Regarding other haemodynamic parameters: mean respiratory rate, peripheral oxygen saturation, remained stable in both the groups during the intraoperative and postoperative period.



GRAPH-2: VISUAL ANALOGUE SCALE (VAS) in Group D and Group N

VAS was recorded from 0 minute (regression to T10). Scores were comparable for the first 120 minutes, but were significantly higher in Group N at 4–10 hours. Accordingly, the first PCEA bolus was required earlier in Group N (6–8 h) than in Group D (12–16 h). After 12 hours, VAS remained comparable between groups as shown in Graph-2.

TABLE-2: Total No. of PCEA boluses and Total volume of study drug (ml) consumed in 24 hours in Group D and Group N

	Group D		Group N			
	Mean	**SD**	**Mean**	**SD**	**t-value**	**p-value**
Total No. of PCEA boluses	0.9787	0.82064	2.6596	0.47898	-12.227	0.001
Total volume of study drug(ml) consumed in 24 hours	87.9149	3.28256	94.6383	1.91590	-12.227	0.001

The mean total number of PCEA boluses and total volume of study drug consumed in 24 hours was relatively low in Group D as shown in Table-2. Pain was adequately managed with continuous epidural infusion and PCEA boluses. Thus no rescue analgesia was required in any group. In this study, sedation scores were regularly monitored from 0 minute, which is the time of regression of sensory block to T10. Sedation scores remained comparable between the two groups till 90 minutes. However, after 150 minutes till 24 hours, sedation scores were significantly higher in Group D relative to Group N. At 24 hours, the mean sedation scores were 3.60±0.49 in Group D while 2.82±0.39 in Group N.

The incidence of nausea-vomiting was comparable in both the groups. Bradycardia was reported in 6 patients in Group D which was treated with intravenous injection of atropine. No patient in Group N reported bradycardia. Itching was reported in 4 patients in Group N, while none was observed in Group D. The incidence of hypotension was not reported in any group. Additionally, the mean patient satisfaction scores were significantly higher in Group D (4.42 ± 0.54) relative to Group N (3.98 ± 0.68).

Discussion

Orthopaedic surgeries produce severe postoperative pain, delaying mobilization and recovery if inadequately treated. Patient-controlled epidural analgesia (PCEA) provides effective, individualized analgesia with improved patient satisfaction. Levobupivacaine, owing to its favourable cardiostable profile, is commonly used local anaesthetic agent and is combined with adjuvants such as dexmedetomidine and nalbuphine to enhance analgesia.This study compares these adjuvants with levobupivacaine in PCEA for lower extremity orthopaedic surgeries. In this study, post-operative pain relief was maintained with epidural basal infusion of 0.125% levobupivacaine either with 1 mcg/ml dexmedetomidine (Group D) or 0.2 mg/ml Nalbuphine (Group N) started at 3 ml/hr and demand dose of 4ml. Observations in the present study showed that Group D reported lower heart rate compared to Group N after epidural bolus while other haemodynamic parameters : mean Systolic and Diastolic blood pressure, Respiratory Rate, Peripheral oxygen saturation remained comparable in both the groups. Group N had higher VAS scores between 4–10 hours, resulting in greater PCEA bolus requirements and total drug consumption over 24 hours. After 150 minutes of epidural infusion, patients in Group D

demonstrated significantly higher sedation scores than those in Group N. However, Group D demonstrated higher incidence of bradycardia whereas Group N demonstrated higher occurrence of itching. Patient Satisfaction scores were greater in Group D relative to Group N.

The findings indicated that after regression to T10 and epidural bolus, mean heart rate reduced significantly in the Group D and stayed lower than Group N thereafter. The results of the current study are in accordance with the findings of study by Farmawy MS et al. who observed lower heart rate after epidural bolus with dexmedetomidine compared to nalbuphine when used as adjunct to bupivacaine4. Similarly, El Fawal SM et al. found that adding dexmedetomidine to bupivacaine resulted in a lower heart rate than the combination of nalbuphine and bupivacaine during labour analgesia via epidural route5. Reduction in heart rate after dexmedetomidine is due to alpha-2 agonist activity of dexmedetomidine which decreases norepinephrine release and causes decrease in sympathetic activity. The present study's findings showed that mean Systolic and Diastolic blood pressures remained stable and comparable between Group D and Group N throughout the study period. Shukla U et al. found a transient fall in systolic blood pressure with dexmedetomidine, while diastolic blood-pressure was stable with dexmedetomidine and nalbuphine when administered with ropivacaine6. In contrast, the present study showed no significant haemodynamic changes, likely due to lower doses and continuous epidural infusion. The present study demonstrated that VAS scores were comparable for the first 120 minutes, higher in Group N at 4–10 hours, and comparable again from 12–24 hours. Farmawy MS et al. found that VAS scores were comparable at 2 hours after epidural bolus, but thereafter remained lower with dexmedetomidine compared to nalbuphine, similar to the present study4. Lakshmi EA et al. also noted that epidural dexmedetomidine produced significantly lower VAS scores than nalbuphine in lower limb surgeries7. Dexmedetomidine provides analgesia by inhibiting norepinephrine release, hyperpolarizing neurons, and reducing substance P, while nalbuphine acts mainly via kappa opioid receptor agonism to alter pain perception. The current study further demonstrated that the mean total number of PCEA boluses and total volume of study drug consumed in 24 hours was markedly reduced in Group D than Group N. Kumari P et al. also demonstrated that dexmedetomidine when used as adjuvant to ropivacaine required fewer PCEA boluses and lower total drug volume compared to fentanyl with ropivacaine.8 In the present study, none of the patient required rescue analgesia during the 24-hour postoperative period, showing that both drug combinations provided satisfactory pain relief. Consistent results were documented by Kumari P et al. who used dexmedetomedine as adjuvant to ropivacaine in epidural infusion for postoperative analgesia8. Similarly, Uma G et al. documented - epidural infusion of nalbuphine as adjuvant to bupivacaine did not need rescue analgesic in the postoperative period9. In the current study of 94 patients, the sedation scores were comparable between Group D and Group N till 90 minutes from epidural bolus but later became significantly higher in the Group D. The sedation scores varied between 2.18–3.60 in Group D and 2.18–2.82 in Group N over the course of the study. Farmawy MS et al. used epidural bolus and top up of nalbuphine or dexmedetomidine as adjuvant to bupivacaine, and found significantly higher sedation with dexmedetomidine4. Higher sedation by dexmedetomidine can be explained by its action on central α_2-adrenergic receptors located on both presynaptic and postsynaptic neurons within the locus coeruleus which leads to hyperpolarization and suppression of neuronal firing. The observed data showed that the occurrence of adverse effects like nausea, vomiting and hypotension was comparable between Group D and Group N. The incidence of bradycardia was significantly higher in Group D while incidence of itching was higher in Group N relative to Group D. Farmawy MS et al. observed significantly higher

bradycardia with dexmedetomidine compared to nalbuphine while nausea, vomiting, and hypotension were comparable between groups4. Higher incidence of itching by nalbuphine is due to histamine release, peripheral vasodilatation, and unique mixed agonist-antagonist activity. Additionally, the patient satisfaction scores were in the Group D relative to Group N which may be attributed to improved analgesia and reduced requirement for additional epidural boluses. Farmawy MS et al. assessed epidural dexmedetomidine and nalbuphine as adjuvants to bupivacaine and found significantly higher patient satisfaction with dexmedetomidine4.

Limitations

As the study was carried out in one tertiary care centre, the applicability of the findings to other settings may be limited. Patients with ASA grade III/IV, cardiovascular disorders, or those on vasoactive medications were excluded, reducing the applicability of findings to higher-risk patient populations. Including a control group receiving levobupivacaine alone would have enabled a better assessment of the independent pain relief effects of the adjuncts. The postoperative follow-up was limited to 24 hours therefore, long-term analgesic outcomes and delayed adverse events could not be assessed.

Conclusion

Both dexmedetomidine and nalbuphine provided effective postoperative analgesia as adjuvants to levobupivacaine in PCEA. However, dexmedetomidine offered superior analgesia with lower VAS scores, fewer PCEA demands, reduced drug consumption, and higher patient satisfaction.

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