Print ISSN: 2321-6379
Online ISSN: 2321-595X

Original Article

Comparison of Intrathecal Nalbuphine and Dexmedetomidine as Adjuvants to Levobupivacaine in Infraumbilical Surgeries

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ABSTRACT

Background: Various intrathecal adjuvants have been clinically tried for the prolongation of intraoperative and post-operative analgesia. This study aims at evaluating the effects of intrathecal nalbuphine and dexmedetomidine as adjuvants to isobaric levobupivacaine in subarachnoid block.

Materials and Methods: Sixty patients scheduled for elective infraumbilical surgeries were allocated into two groups of 30 each to receive 15 mg of 0.5% isobaric levobupivacaine with either 0.8 mg nalbuphine (Group LN) or 5 μg dexmedetomidine (Group LD) intrathecally. Characteristics of spinal anesthesia in terms of sensory analgesia and motor blockade were noted. Hemodynamic parameters and adverse effects if any were recorded. Data obtained were compiled and statistically analyzed with appropriate tests.

Results: Onset of sensory and motor blocks was faster in Group LD (2.31 ± 0.66 and 6.24 ± 0.45 min) compared to Group LN (4.33 ± 0.66 and 7.00 ± 0.45 min). Total duration of effective analgesia (402.50 ± 9.79 vs. 294.63 ± 8.95) and total duration of motor block (289.67 ± 5.94 vs. 251.87 ± 8.48 min) were significantly prolonged in Group LD than in Group LN. There was no significant difference in hemodynamic changes and adverse effects between the groups.

Conclusion: The addition of 5 μg dexmedetomidine to intrathecal 0.5% isobaric levobupivacaine as adjuvant is associated with prolonged sensory and motor blockade with better perioperative analgesia compared to 0.8 mg nalbuphine.

Key words: Dexmedetomidine, Infraumbilical surgeries, Levobupivacaine, Nalbuphine

INTRODUCTION

Subarachnoid block is the most common anesthesia technique used to conduct lower limb surgeries and lower abdominal surgeries among all methods. It has a big role in anesthesia because of its advantages in the form of reducing the metabolic stress, less blood loss, lower incidence of venous thromboembolism, reduction in pulmonary complications, early return of bowel function, and shorter admission-discharge interval. However, the limited duration of action is one of its disadvantages. Levobupivacaine has emerged as popular local anesthetic for central neuraxial blocks in this century. It is a pure s-enantiomer of bupivacaine and is a safer alternative for regional anesthesia than its counterpart with lower toxicity.[1]

Access this article online

www.ijss-sn.com

Month of Submission : 01-2021
Month of Peer Review : 01-2021
Month of Acceptance : 02-2021
Month of Publishing : 03-2021

Local anesthetic drugs used alone for spinal anesthesia do not prolong post-operative analgesia. Various adjuvants, for example, opioids, midazolam, alpha-2 agonist, and ketamine, have been used along with the local anesthetics for prolongation of post-operative analgesia in neuraxial blockade, reduction of local anesthetic dose, and thereby side effects.[2]

Opioids are an important modality of post-operative pain management. They blunt the neuroendocrine stress response

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to pain. Nalbuphine is a synthetic, mixed agonist-antagonist opioid analgesic with agonistic action at kappa receptor and antagonism at mu receptor. Nalbuphine, whenever used as adjuvant to bupivacaine, it was found to improve the quality of perioperative analgesia with comparatively lesser side effects and nil neurotoxicity.[3,4]

Among non-opioids, dexmedetomidine is a highly selective α2-agonist, which is used as neuraxial adjuvant as it provides stable hemodynamic conditions, good quality of intraoperative and prolonged post-operative analgesia with minimal side effects.[5] Dexmedetomidine has been approved by Food and Drug Administration (FDA) as a short-term sedative for mechanically ventilated intensive care unit patients. The present study was designed to evaluate the sensory and motor block characteristics, hemodynamic changes, and any adverse effects of nalbuphine and dexmedetomidine when used as adjuvants to 0.5% isobaric levobupivacaine in patients undergoing elective infraumbilical surgeries under subarachnoid block.

MATERIALS AND METHODS

After obtaining the approval from the research ethics committee and informed written consent from the patients, 60 patients between the age 18 and 60 years, American Society of Anesthesiologists Grade I and II, scheduled for infraumbilical surgeries under spinal anesthesia were enrolled in the present study. Patients with a history of allergy to local anesthetics, local infection at the site of the block, coagulopathies, pregnancy, previous neurological deficit in lower limb, spinal deformity, and those who refused the technique were excluded from the study [Figure 1].

Careful pre-anesthetic check-up was carried out in all patients with detailed clinical history, general and systemic examination. Patients were explained about the visual analog scale (VAS) and its use for measuring the post-operative pain and advised fasting for 6 h. All patients were pre-medicated with tablet alprazolam 0.25 mg a night before surgery, injection glycopyrrolate 0.2 mg intravenous (IV), and injection midazolam 0.04 mg/kg iv just before the procedure. In operating room, all routine monitors were attached and IV fluid (IV) ringer lactate (R.L.) 10–15 ml/kg was started. Baseline hemodynamic parameters, heart rate (HR), oxygen saturation (SpO_2), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean blood pressure (MBP), were noted. Spinal anesthesia was induced with the patients in lateral position. Under all aseptic conditions, L3–L4 interspace was chosen and the overlying skin was anaesthetized by means of local infiltration with xylocaine 2%. Lumbar puncture was performed in the midline using a 23 G Quincke spinal needle. After the needle was passed into the subarachnoid space and the appearance of clear cerebrospinal fluid, the intrathecal local anesthetic was injected.

Group LN patients received 3 ml of 0.5% of levobupivacaine + 0.8 mg of nalbuphine comprising a total volume of 3.5 ml

Group LD patients received 3 ml of 0.5% levobupivacaine and 5 μg dexmedetomidine comprising a total volume of 3.5 ml.

Patients and anesthesiologist (the outcomes assessor) who recorded the perioperative data were blinded to the study drugs.

Assessment of sensory block was done by loss of sensation to pinprick using a 27 G hypodermic needle. When T10 sensory blockade level was achieved, surgery was allowed. Testing was carried out every 2 min till 10 min, every 5 min up to 30 min, every 15 min up to 60 min, half hourly up to 180 min, and thereafter hourly till the 12th h and every 3 hourly till 24 h of surgery in both the groups. The onset of sensory block (when patient does not feel pinprick at T10 level), the highest level of sensory block achieved, time to maximum sensory block, regression of sensory block to L5, and total duration of sensory block (regression to S1 dermatome) were noted. Degree of motor block was assessed by modified Bromage scale. The time needed for the onset of motor block (Bromage 1), time taken for maximum motor block, and total duration of motor block (time taken for complete motor recovery to Bromage 0) were also noted. Hemodynamic parameters such as HR, SBP, DBP, mean arterial blood pressure (MAP) and respiratory rate, and Spo2 were monitored every 2 min for the first 10 min, every 5 min for the next 30 min every 15 min up to 60 min, half hourly up to 180 min and thereafter hourly till the 12th h, and every 3 hourly till 24 h of surgery in both the groups. The quality of surgical analgesia was assessed as per operating surgeon and graded as excellent, satisfactory, and unsatisfactory. Adverse effects such as hypotension, bradycardia, vomiting, shivering, pruritus, respiratory depression, and urinary retention were observed. Hypotension was defined as a fall in SBP to <90 mmHg or more, and bradycardia was defined as a HR of 60 or less. Perioperative hypotension, bradycardia, and nausea/vomiting were treated with injection ephedrine, atropine, and ondansetron, respectively.

Pain was measured using VAS rated from 0 to 10 subjectively with 0 for no pain and 10 for maximum pain. Rescue analgesia was given when the VAS was >3 in both the groups. Inj. diclofenac 75 mg was given as rescue analgesia and if needed, inj. tramadol 2 m/kg iv was given. Time to

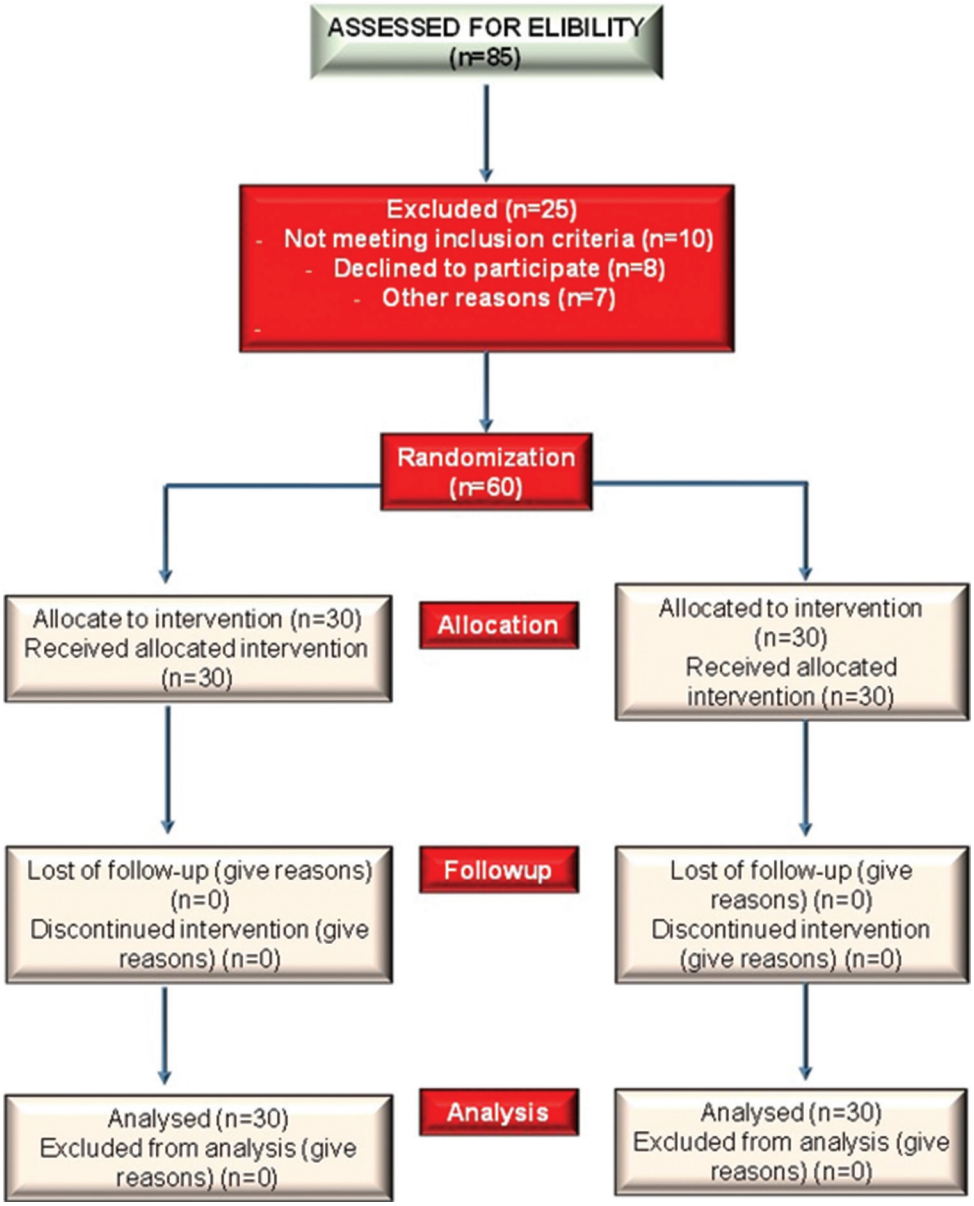

Figure 1: Consort flow diagram

first rescue analgesia (total duration of analgesia) and total number of doses of rescue analgesia were also noted.

Statistical Analysis

Data were entered into MS Excel and analyzed in SPSS V22. Descriptive statistics for qualitative data were represented with frequencies and percentages, whereas for quantitative data, descriptive statistics were represented with mean and standard deviation. Chi-square and *t*-test were applied for finding significance between the groups in qualitative and quantitative data, respectively. $P < 0.05$ was considered as statistically significant.

The mean time taken for onset of sensory block and the time to maximum sensory block were significantly lesser in Group LD ($P = 0.001$). The median maximum sensory level reached was T6 in both groups. Time to achieve maximum motor block was also lesser in Group LD as compared to Group LN ($P = 0.001$). The median maximum motor block achieved in both the groups was mBromage 2. Regression of sensory block to L5 dermatome was significantly prolonged in Group LD ($P = 0.000$). The total duration of sensory and motor block was also significantly more in Group LD as compared to Group LN ($P = 0.001$). Motor and sensory block parameters are shown in Tables 1 and 2. The total duration of effective analgesia was significantly longer in Group LD when compared to Group LN ($P = 0.001$). The total number of doses of rescue analgesia required in 24 h was also significantly less in Group LD as compared to Group LN ($P = 0.001$) [Table 1]. The

Table 1: Sensory block characteristics (Mean±SD)

Sensory block data	Group LN	Group LD	*P* value
Time of onset of sensory block to T10 (min)	4.33±0.66	2.31±0.35	0.001 (HS)
Median maximum sensory level	T6	T6	1.00 (NS)
Time to achieve maximum dermatomal level (min)	7.33±1.25	6.63±0.80	0.001 (NS)
Time to regression to L5 sensory level (min)	269.10±8.68	372.93±7.83	0.000 (HS)
Total duration of effective analgesia (min)	294.63±8.95	402.50±9.79	0.001 (HS)
Total number of doses of rescue analgesia	2.73±0.44	1.76±0.42	0.001 (HS)

HS: Highly significant, *P*<0.01; NS: Not significant, *P*<0.05

Table 2: Characteristics of motor blockade (Mean±SD)

Motor blockade data	Group LN	Group LD	*P* value
Mean maximum motor block achieved (mBromage scale)	2	2	_
Time to achieve maximum motor block (min)	7.00±0.43	6.24±0.45	0.001 (HS)
Total duration of motor block (min)	251.87±8.48	289.67±5.94	0.001 (HS)

HS: Highly significant, *P*<0.01; NS: Not significant, *P*<0.05

Table 3: Comparative incidence of adverse effects

Side effects and complications	P		LD		Total	
	No.	% age	No.	% age	No.	% age
Hypotension	3	10.00	2	6.67	5	8.33
Bradycardia	2	6.67	0	0.00	2	3.33
Nausea	2	6.67	2	6.67	4	6.67
Shivering	2	6.67	1	3.33	3	5.00
No side effect	21	70.00	25	83.33	46	76.67
Total	30	100.00	30	100.00	60	100.00

Table 4: Demographics and duration of surgery (Mean±SD)

Variable	Group LN (Mean±SD)	Group LD (Mean±SD)	*P* value
Age (in years)	37.63±13.20	36.57±13.23	0.380 (NS)
Sex (M/F)	M=21 (70%) F=9 (30%)	M=23 (76.67%) F=7 (23.33%)	0.551 (NS)
ASA I and II	I-25 (83.33%) II-5 (16.67%)	I-24 (80%) II-6 (20%)	0.739 (NS)
Weight (in kg)	67.63±6.04	67.83±6.05	0.450 (NS)
Duration of surgery (in min)	54.50±6.99	52.67±6.80	0.160 (NS)

HS: Highly significant, *P*<0.01; NS: Not significant, *P*>0.05

quality of surgical analgesia was excellent in both groups as none of the patient required supplementary analgesia intraoperatively. Regarding hemodynamic changes, there were no significant alterations in the measured parameters between the two groups ($P > 0.05$) at various time intervals, as shown in Figures 2-4. Hypotension was observed in 3 (10%) patients in Group LN and 2 (6.67%) patients in Group LD while bradycardia was seen in 2 (6.67%) patients in Group LN and 0 (00%) patients in Group LD. The incidence of nausea was similar in both groups, that is, 2 (6.67%) patients. Shivering was recorded in 2 (6.67%) patients in Group LN and 1 (3.33%) patient in Group LD [Table 3]. Other side effects such as urinary retention, pruritis, headache, backache, local anesthetic toxicity, and respiratory depression were not recorded in any of the patients in both the groups.

RESULTS

There was no statistically significant difference in patient's demographics and duration of surgery [Table 4].

DISCUSSION

Adequate pain management has become essential part in surgical patients to facilitate rehabilitation, accelerate functional recovery, and enabling patients to return to their normal activity more quickly. Spinal anesthesia is a safe and reliable method of anesthesia for abdominal and lower limb surgery, with the advantages of rapid onset of action, economical and easy to administer, and a relatively low side effects rate and shorter post-anesthesia care unit stay.[6,7] However, these advantages may be offset by the limited duration of action, or an increased likelihood of motor power recovery delay, thus delaying ambulation and prolonged hospital stay. To improve the quality of blockage and prolong the duration of analgesia, and reduce the required dose of local anesthetics, thereby reducing the incidence of side effects caused by the use of high-dose local anesthetics, such as late and severe bradycardia, hypotension, nausea, and vomiting, appropriate adjuvants are commonly used with intrathecal local anesthetics.[8,9]

The appropriate dose of intrathecal nalbuphine has been debated. It has been used as an additive with bupivacaine intrathecally in several clinical settings in doses ranging from 0.8 mg to 2.4 mg. Studies were done to evaluate the subarachnoid block characteristics with different doses of nalbuphine with bupivacaine for spinal anesthesia. It was concluded that addition of 0.8 mg of nalbuphine to 0.5% bupivacaine for subarachnoid block provides excellent analgesia with long duration of action.[10,11] Hence, based on these studies, we have chosen 0.8 mg nalbuphine for our study like various researchers.[12-14]

Various authors have studied different doses of dexmedetomidine intrathecally and concluded that better prolongation of analgesia and motor block with minimal hemodynamic changes and sedation are seen when 5 μg

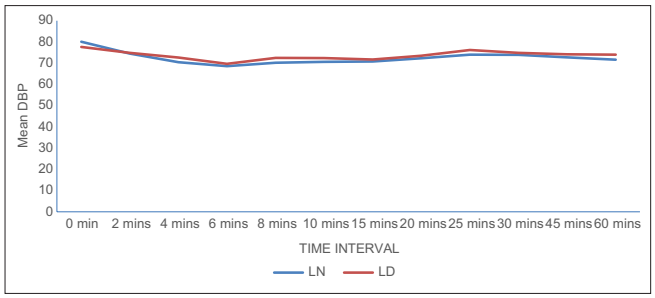

Figure 2: Systolic blood pressure in two groups at different time intervals during the intraoperative period

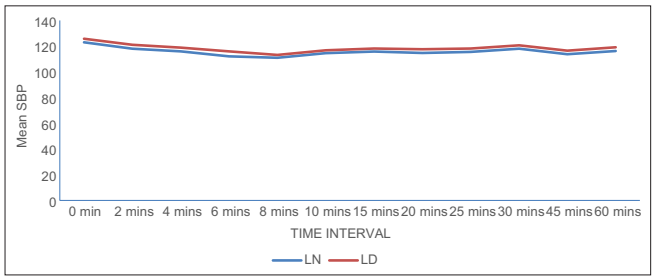

Figure 3: Diastolic blood pressure in two groups at different time intervals during the intraoperative period

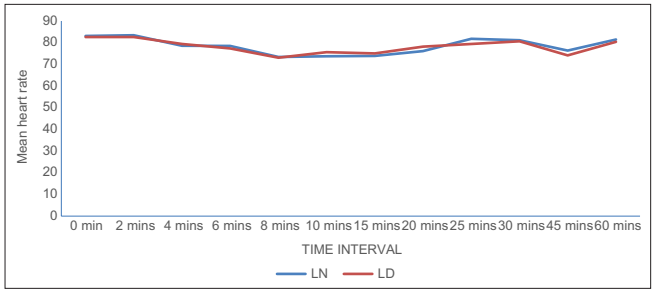

Figure 4: Heart rate in two groups at different time intervals during the intraoperative period

dexmedetomidine was used.[15-17] Based on these studies, we chose 5 μg dexmedetomidine for our study.

In our study, the onset of sensory block and motor block and time taken to achieve peak sensory level were faster in LD group compared to LN group. However, the maximum sensory level attained was comparable and statistically not significant in both groups. Srinivasan *et al.*[12] evaluated the efficacy of 3 ml of 0.5% of levobupivacaine with 0.8 mg of nalbuphine and observed that mean time to onset to T10 was 6.03 ± 1.21 min (4.33 ± 0.66 min in LN group). Shalini *et al.*[18] when evaluated the effect of 15 mg of 0.5% isobaric levobupivacaine with 1 mg nalbuphine intrathecally in patients undergoing infraumbilical surgeries observed that the mean time taken to reach maximum sensory level was 6.0 ± 2.49 min (7.33 ± 1.25 min in Group LN), time to achieve maximum motor block was 5.40 ± 2.42 min (7.00 ± 0.43 min in LN group), total duration of motor block was 235.6 ± 29.5 min (251.87 ± 8.48 in LN group), and total duration of effective analgesia was 292.1 ± 40.9 min (294.63 ± 8.95 min in LN group of the present study). Hence, the sensory and motor block characteristics of the present study are almost comparable to the above studies.

In Group LD, the onset of sensory block to T10 occurred in 2.31 ± 0.35 min. Time to maximum motor block was 6.24 ± 0.45 min and total duration of motor block was 289.67 ± 5.94 min. Duration of analgesia was 402.50 ± 9.79 min. Similar findings were observed in previous studies also. Abd Elhamid *et al.*[17] who investigated the effects of 5 μg dexmedetomidine as adjuvant to 15 mg of 0.5% levobupivacaine under spinal anesthesia observed that mean time to onset to T10 was 2.58 ± 3.25 min, total duration of motor block was 319.7 ± 92.2 min, and mean time for administering rescue analgesia was 365.4 ± 96.4 min. Kataria *et al.*[19] studied the efficacy of 3 ml (15 mg) of 0.5% levobupivacaine with 3 μg dexmedetomidine and observed that the mean time taken to maximal sensory and motor blockade (6.63 ± 0.80 min and 6.24 ± 0.45 min) was almost similar to LD group of our study.

Hemodynamic parameters revealed no statistically significant difference. Incidence of adverse effects was comparable between the groups. There was no incidence of pruritus, respiratory depression, and desaturation in both the groups. In Group LN, hypotension was observed in 3 (10%) patients and bradycardia was observed in 2 (6.67%) patients. Similar findings have been seen in a study done by Shalini *et al.*[18] using 1 mg nalbuphine as adjuvant where 10% of patients had hypotension and no patient had bradycardia. In Group LD, hypotension was seen in 2 (6.66%) patients and bradycardia was seen in 0 (0.00%) patient. Similar findings were also observed by Abd Elhamid *et al.*[17] and Elshalakany *et al.*[15] using levobupivacaine and dexmedetomidine intrathecally. Other side effects observed were nausea and shivering which were comparable in both groups.

Limitations of Study

1. Our study was done on patients of age groups of 18–60 years of age.
2. Physical Status I and II patients were included only. Hence, results may not be extrapolated to ASA Physical Status III and IV patients. Further studies are needed to know the effect of studied drugs on comorbidities such as diabetes or hypertension.
3. Measuring nalbuphine with an insulin syringe should also be meticulous as a slight mistake would alter the dosage.
4. Moreover, adding adjuvants will not only increase the sensory block duration alone but also will increase

the duration of the motor block duration which is considered as a limitation to the drug itself (not to the study) and may lead to prolonged recovery or hospital stay.

CONCLUSION

On the basis of the results of our study, we conclude that addition of 5 μg of dexmedetomidine to intrathecal 0.5% isobaric levobupivacaine as adjuvant is preferable to 0.8 mg of nalbuphine, as it provides comparatively more prolonged sensory and motor blockade with better perioperative analgesia.

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How to cite this article: Singh RP, Kataria AP, Mahajan L, Arora HS, Kaur P. Comparison of Intrathecal Nalbuphine and Dexmedetomidine as Adjuvants to Levobupivacaine in Infraumbilical Surgeries. Int J Sci Stud 2021;8(12):54-59.

Source of Support: Nil, **Conflicts of Interest:** None declared.