Original Research Article

Spinal Anaesthesia with Levobupivacaine per se versus Combination of Levobupivacaine plus Dexmeditomidine: A Comparative Clinical Assessment

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Abstract

Background: Spinal anaesthesia is a widely used technique for effective and uniformly distributed sensory and motor block with faster onset. Due to decreased cardiovascular and central nervous system toxicity, levobupivacaine is a good alternative for spinal anesthesia. Dexmedetomidine when used intrathecally is associated with prolonged motor and sensory block, hemodynamic stability, and less requirement of rescue analgesia in 24 h. **Objective:**This study was aimed to evaluate the clinical efficacy of levobupivacaine per se versus combination of levobupivacaine plus dexmedetomidine in spinal anaesthesia. **Methods:**One hundred and twenty patients between ages 30 and 60, in ASA I-II groups were included in the study with informed consent for elective surgeries under spinal anaesthesia. Subjects were randomly assigned to 2 groups. Group I: Isobaric levobupivacaine (3 ml, 15 mg, 0.5%) + 0.3 ml normal saline; Group II: Isobaric levobupivacaine (3 ml, 15 mg, 0.5%) plus dexmedetomidine (0.3 ml, 3 µg).Clinical efficacy was evaluated by assessing the arterial pressure, respiratory rate, heart rate, sensory and motor block levels, level of sedation, pain level and safety complications were monitored.**Results:**In the combination group mean onset of anaesthesia was significantly less and duration of sensory block was longer. Similarly, onset of motor block was quicker and duration was longer in the combination group. Addition of dexmedetomidine to levobupivacaine resulted into better analgesia profile and reduction in the need of analgesic of the post-operative pain management. **Conclusion:**It is concluded that addition of dexmedetomidine to levobupivacaine prolonged the postoperative analgesia and induce stable sensory and motor block which makes it preferable anaesthetic combination for major surgeries.

Keywords: Spinal Anaesthesia, Levobupivacaine, dexmedetomidine, Sensory and Motor block, Analgesia.

Introduction

Spinal anaesthesia and other regional techniques are frequently used in for major surgical operations considering the safety of anaesthesia, low intra-operative blood loss, excellent muscle relaxation and continued analgesia in the post-operative period[1,2]. Regional anaesthesia techniques are also superior to systemic opioid agents with regard to analgesia profile and adverse effects[3]. Spinal anaesthesia is the most commonly used technique due to its unmatchable reliability, simplicity, and cost-effectiveness. A fast and effective onset of sensory and motor block, prolonged postoperative analgesia and excellent muscle relaxation are effectively achieved by spinal anaesthesia[4].

Levobupivacaine is a recent alternative for spinal anaesthesia with respect to its decreased cardiovascular and central nervous system toxicity[5]. In clinical practice, levobupivacaine is the recently introduced alternatives to bupivacaine. It produces equivalent sensory block but shorter duration of motor block than intrathecal bupivacaine[6].

This is available as isobaric solutions in India and since it has been recently introduced in India, very few studies have been done for its use in spinal anaesthesia.

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The altered hemodynamics, and therefore the arterial hypotension is the most prevalent adverse effect after subarachnoid anaesthesia. Isobaric solutions of anaesthetic agent can overcome the denser and prolonged motor blockade which hyperbaric solution would offer[7].

Various adjuvants such as alpha-2 agonists, vasoconstrictors and opioids have been used in an attempt to further reduce the effects of local anaesthetics and prolong the duration of intraoperative and postoperative analgesia[8].

Dexmedetomidine is used as an adjuvant in spinal anesthesia and is associated with prolonged motor and sensory block, hemodynamic stability, and less requirement of rescue analgesia in 24 h as a result it facilitates reduction in dose of local anesthetic[9].In the present study we aimed to study and compare the clinical efficacy such as onset and duration of sensory and motor block, hemodynamic changes, postoperative analgesia, side effects, and complications of 0.5% isobaric levobupivacaine 15 mg (3 ml) and 0.5% isobaric levobupivacaine 15 mg (3 ml) with 0.3 ml (3 μg) dexmedetomidine as spinal anaesthetics.

Materials and Methods

A legal approval was received form the Institutional Ethics Committee and written informed consent from all the participating subjects.

Inclusion and Exclusion Criteria- Total 120 American Society of Anesthesiologists physical status I or II patients of either sex of age 30–60 years,, body weight 40–70 kg and height >150 cm were enrolled in this randomized, double blind study. Patients who refused to undergo procedure, any kind of contraindication to allergy to local anaesthetics, who were pregnant or lactating, patients with some coagulating/neurological disorders or with spine injury or previous spine surgery or sepsis over spine or with morbid obesityand subjects with communication difficulties (who may cause difficulty in reliable assessment) were set to exclude from the study.

Preparation for Anaesthesia and randomization-All patients were kept on fasting for 6 h. Preanesthetic medication was administered that included oral ranitidine 150 mg, ondansetron 4 mg, diazepam 5 mg and Ringer lactate solution (750 ml). They were then allocated randomly to receive spinal anaesthesia. Sell A et al, estimated minimum effective local anaesthetic dose of isobaric levobupivacaine and ropivacaine administered via a spinal catheter for hip replacement surgery.

It was 15.2±4.0mg (mean ±SD) for Levo-bupivacaine [10]. Hence in the present study, 15mg (3ml of 0.5%) isobaric solutions of levobupivacaine was used for spinal anaesthesia. The study drug for anaesthesia and post-operative analgesia was prepared by a separate anaesthesiologist. The anaesthesiologist doing the study, the surgeon, the patient, and the staff were blinded to the drug used. The constant volume (3.3 ml) of the drug was used in both the groups to avoid bias in the study. Groups were divided and treatment were provided as follows,

Control Group (Group-I, N=60): 0.5% Isobaric levobupivacaine 15 mg (3 ml) with 0.3 ml normal saline;

Study Group (Group-II, N=60): 0.5% Isobaric levobupivacaine 15 mg (3 ml) with 0.3 ml (3 μg) dexmedetomidine.

Evaluation of clinical parameters-Clinical efficacy was investigated by evaluating the time of onset of sensory block, time of onset of maximum motor block and duration of analgesia.

Assessment of pain-Visual analog scale (VAS) with 0–10 cm line was used to determine the level of analgesia in the postoperative period for 24 h and was explained to the patient a day before surgery during the preanesthetic check-up. The first end mark "0" means "no pain" and the end marked "10" means "severe pain." Rescue analgesia was given if VAS score >3.

Assessment of sensory and motor block-Assessment of sensory block by the loss of sensation to pinprick of 22-gauge blunt hypodermic needle and motor block by modified Bromage score.

Bromage scale[11]

- 0 - Full flexion of knees and feet possible, able to lift extended legs
- 1 - Unable to lift extended legs, but able to flex knees and feet
- 2 - Unable to flex knees but flexion of feet possible
- 3 - Unable to move legs and feet at all.

Assessment of hemodynamic response-Respiratory rate, heart rate, noninvasive systolic and diastolic blood pressure and SpO_2 was done for hemodynamic response. Readings were recorded preoperatively, then intraoperatively at 0, 5 min, then at an interval of every 10 min up to 30 min, every 15 min up to 120 min, half-hourly up to 180 min, hourly until 12 h, and thereafter 3 hourly till 24 h of surgery in both the groups.

Statistical analysis-Data were collected of each patient from both the groups and fed in a Microsoft Excel Worksheet. Mean value and standard deviation were computed for age, weight, duration of surgery, and duration of analgesia. The mean values of the two groups were compared using student's t-test. $P < 0.05$ was considered statistically significant.

Results

The two groups were comparable for age (43.89±7.31 vs 44.01±7.71 years) and weight (53.56±4.45vs 52.19±4.99 years). Mean age and weight of the two groups are not statistically significant.Similarly, intraoperative, and postoperative systolic blood pressure, diastolic blood pressure, mean respiratory rate, SpO_2 were also comparable (Table1). These differences are not statistically significant.

Table 1: Baseline characteristics of patients enrolled

Baseline Characteristics	Group 1	Group 2
Treatment	Levobupivacaine	Levobupivacaine+dexmedetomidine
Dose	15 mg, 3 ml, 0.5%	15 mg, 3 ml, 0.5% + 0.3 ml (3 ug)
Age (years)	43.89±7.31	44.01±7.71
Sex		
Male (68)	34	34
Female (52)	27	27
Weight (kg)	53.56±4.45	52.19±4.99
Heart rate/Min	81.67±5	82.08±7.1
Systolic BP (mmHg)	124±10.71	122±10.11
Diastolic BP (mmHg)	78±6.90	79±7.04
SpO_2 (%)	99.23±7.71	98.34±9.78
Respiratory rate/min	16.30±1.56	16.93±2.03

Time of onset of sensory block

Time of onset of sensory block was assessed from the time of drug administration.

The mean time to the onset of sensory block to T10 dermatome in Group I (Levo) was 8.65 ± 1.15 min and in Group II (Levo+Dex)was 5.10 ± 0.65 min (P<0.05). The median maximum sensory level achieved in Levo group was T6 dermatome in 17.45 ± 2.12 min and in Levo+Dexgroup was at T4 dermatome in 9.35 ± 1.11 min (P<0.01). The mean duration of sensory block (time to regression to S1 dermatome) in Group Levo was 210.05 ± 18.78 min while in Group Levo+Dex was 356.89 ± 25.77 min (**P** < 0.01). All the differences were statistically highly significant between the two groups [Table 2].

Table 2: Difference in the sensory block between two groups

Parameters	**Group 1** **Levobupivacaine**	**Group 2** **Levobupivacaine+dexmedetomidine**	**P value**
Onset of sensory block (Min)	8.65 ± 1.15	5.10 ± 0.65	<0.05
Median maximum sensory block (Min)	17.45 ± 2.12	9.35 ± 1.11	<0.01
Mean duration of sensory block (Min)	210.05 ± 18.78	356.89 ± 25.77	<0.01

Time of onset of maximum motor block

Time of onset of maximum motor block was another assessment criterion (Table 3). The mean time taken to achieve maximum motor block was 14.10 ± 1.93 for Levo group and 8.78 ± 0.93 min in Group Levo+Dex (P<0.01). Furthermore, mean of the total duration of motor block in Group Levo and Levo+Dex was 141.64 ± 11.03 min and 185.40 ± 12.51 min, respectively. Both the differences were highly significant (P < 0.001).

Table 3: Difference in the motor block between two groups

Parameters	Group 1	Group 2	P value
	Levobupivacaine	Levobupivacaine+dexmedetomidine	
Onset of maximum motor block	14.10 ± 1.93	8.78 ± 0.93	<0.01
Total duration of motor block	141.64 ± 11.03	185.40 ± 12.51	<0.001

Difference in the management of pain between groups

The increase in VAS in Group Levo was observed at 130 min and patient demanded the first dose of rescue analgesia at the 3rd h postoperatively (178.30 ± 18.32 min). Another increase in VAS score was again observed at the 9th h and second dose of rescue analgesia was given at 10th h. Third dose of rescue analgesia was given at 20th h and forth dose at 24th h.

In Group Levo+Dex, increase in VAS was observed at 250 min and the first dose of rescue analgesia was given at 7th h postoperatively (396.93 ± 30.19 min). The second dose of recue analgesia was given at 15th h and the third dose was given at 23rd h. Postoperative VAS scores at different time intervals were significantly lower in Group Levo+Dex than Group Levo, thus indicating superior analgesia.

The time of request of the first dose of rescue analgesia was delayed in Group Levo+Dex as it was demanded at 396.93 ± 30.19 min and in Group L was at 178.30 ± 18.32 min. The difference in the two groups was highly significant (**P** < 0.001). A dose-dependent reduction in rescue analgesia requirements was noted in our study. A number of rescue analgesia doses were 4.20 ± 0.39 in Group L, whereas 2.34 ± 0.21 in Group Levo+Dex and the difference was highly significant (**P** < 0.01).

Discussion

Levobupivacaine is a preferred local anaesthetic agent. This is attributed to the early onset and prolonged duration of sensory block, shorter duration of motor block, and lower cardiac and CNS related toxicity. Sell A et al, estimated minimum effective local anaesthetic dose of isobaric levobupivacaine and ropivacaine administered via a spinal catheter for hip replacement surgery. It was 15.2±4mg (mean ±SD) for Levobupivacaine[10]. Hence in the present study, 15mg (3ml of 0.5%) isobaric solutions of levobupivacaine was used for spinal anaesthesia.Combination of dexmedetomidine to levobupivacaine produces effective analgesia and prolonged the duration of motor and sensory block along with better postoperative analgesia and fewer side effects as reported previously[12]. Preoperative and postoperative physiological parameters such heart rate, systolic as well as diastolic blood pressure, saturated oxygen level, respiratory rate was not statistically different between both the groups. Lack of respiratory depression, no change in blood pressure with dexmedetomidine has also been demonstrated earlier[12]. This can be explained by the fact that dose of levobupivacaine used in the study by Basuni and Ezz was 4 mg, whereas the dose was 15 mg in the present study[13]. However, there was no statistically significant difference in the mean heart rate of both the groups during the perioperative and postoperative period (P > 0.05) in both the studies.The addition of dexmedetomidine to levobupivacaineintrathecally does not cause significant hypotension as was observed in studies done by Esmaoğlu et al[12].

The present study determined that spinal block induced by 0.5% levobupivacaine + 3 ug dexmedetomidine provided adequate spinal anaesthesia for surgery and pain management.

The mean time to onset of motor block with combination is shorter than that achieved with levobupivacaine per se. Median maximum level of sensory block was significantly less in combination and mean duration of sensory blockgot extended for combination.These effects on sensory block by this combination are supported by previous studies[14,15]. This can allow anaesthetic to perform and consider this combination for longer surgeries. These observations are coherent with earlier reports suggesting that levobupivacaine plus dexmedetomidinein combination may be a better alternative for the spinal block and post-operative pain management.Like sensory block, combination of levo+Dex also affect the motor block. However, the addition of dexmedetomidine to levobupivacaine demonstrated a prolongation of the motor block as reported[12].

In our study, duration of analgesia after administration of these anaesthetic per se or in combination was documented using the objective pain score (VAS). The results indicate that levobupivacaine and Dex combination prolonged postoperative analgesia and significantly reduced the need for subsequent postoperative analgesia by more than 50% compared with per se lovobupivacaine. It causes a reduction of the number of analgesic doses required in

the 24 h postoperatively. Better degree of analgesia in Group LD seen in our study was due to the synergism of dexmedetomidine and levobupivacaine and effectiveness of dexmedetomidine in abolishing visceral pain. Similar results are noted in the patients previously [16]. In terms of side effects, we observed no differences in the safety profile of the patients from both groups. No differences were noted in the motor block, postoperative sedation, or urinary retention. Nausea and vomiting were not a major problem in any of the groups.

Conclusion

Based on our observation we can conclude that levobupivacaine plus dexmedetomidine combination is effective in providing surgical anaesthesia and hemodynamic stability, and this combination is better than levobupivacaine alone in following aspects:

- Early onset of sensory and motor block
- Prolonged duration of sensory and motor block
- Longer duration of postoperative analgesia
- Lesser number of doses of rescue analgesia required.

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