Surgery

Comparison of Dexmedetomidine or Buprenorphine as an Adjuvant to Levo-Bupivacaine in Spinal Anaesthesia for Lower Limb Surgeries

Dr. Prakash Chandra[1], Dr. Geeta Singariya[2*], Dr. Manoj Kamal[3], Priyanka Sethi[4], Dr. Dilip Singh Chauhan[5], Chanda Khatri[6]

[1]Consultant Om Hospital, Pali, India
[2]Professor Dr. S N Medical College, Jodhpur, India
[3]Associate Professor all India Institute of Medical Sciences, Jodhpur, India
[4]Assistant Professor all India Institute of Medical Sciences, Jodhpur, India
[5]Senior Professor Dr. S N Medical College, Jodhpur, India
[6]Assistant Professor Dr. S N Medical College, Jodhpur, India

<u>**Original Research Article**</u>

*Corresponding author
Dr. Geeta Singariya

Abstract: Buprenorphine or dexmedetomidine used as adjuvant with 0.5% levo bupivacaine intrathecal to prolong the duration of analgesia. Eighty patients were randomly allocated to two groups, Group B received 60μg of buprenorphine with 15mg of 0.5% levo-bupivacaine and Group D received 5μg of dexmedetomidine with 15mg of 0.5% levo-bupivacaine. The onset and duration of sensory and motor blockade, the sensory and motor regression times, Ramsay sedation score in post-operative period were recorded. Hemodynamic changes and time to use first rescue analgesia were also recorded. There was no significant difference in the onset time of sensory block and motor block in group B and group D. Duration of analgesia was in Groups D and group B was 495.42±24.95 min. v/s 292.22±24.94 min. respectively, with p value<0.0001. The Duration of motor block was 416.67±28.22 min in group D, as compared to 205.45 ± 13.14 min in group B. Ramsay sedation score at the end of surgery was 3.82 ±0.67 in group D as compared to 2.07 ± 0.26 in group B. The time to give first rescue analgesia was significantly prolonged in Group D compared with Group B. Dexmedetomidine produces a prolongation in the duration of the motor and sensory block and postoperative analgesia when compared to buprenorphine with preserved hemodynamic stability.
Keywords: Spinal anaesthesia, levo-bupivacaine, buprenorphine, dexmedetomidine, lower limb surgery.

INTRODUCTION

Subarachnoid blockade is the most popular regional anaesthetic technique for lower limb surgery. Intrathecal use of 0.5% levobupivacaine is appropriate for surgeries of short duration and may lead to early analgesic intervention in the postoperative period. Various adjuvants that prolong the duration of analgesia with lesser side effects such as opioids, epinephrine, neostigmine, ketamine, magnesium, midazolam and alpha agonists have been tried with local anaesthetics [1].

Opioids are commonly added to local anaesthetics to prolong the effect of spinal and epidural anesthesia. Morphine was the first opioid used intrathecally in 1979, followed by other opioids [2-4], like buprenorphine, fentanyl, sufentanyl as intrathecal adjutants. Buprenorphine, a μ receptor partial agonist, centrally acting lipid soluble analogue of alkaloid thebaine. It has low intrinsic activity and can be safely used in subarachanoid block. It exhibits analgesic property both at spinal and supraspinal levels. It prolongs the duration of sensory block and thus decreases the need for postoperative analgesia.

The huge literature of intrathecal clonidine, alpha agonist is available and there are very few studies about intrathecal use of dexmedetomidine [5]. Dexmedetomidine is a potent α2 agonist and is approximately eight-times more selective towards the α2 adrenergic receptor than clonidine. Dexmedetomidine is now commonly used as an adjuvant to regional anaesthesia and analgesia, and evolving studies can prove the evidence for its safe use in central neuraxial blocks [6].

In view of few literature [7-9] about efficacy of dexmedetomidine and buprenorphine as an adjuvant to intrathecal levo-bupivacaine, we had planned a double blind randomized prospective study to compare the spinal block characteristics and side effects in patients scheduled for lower limb surgery.

METHODOLOGY

This randomized double blinded prospective study was conducted at a tertiary care centre in western Rajasthan, India. One hundred thirty patients posted for lower limb surgeries were enrolled in the study. Twenty patients refused to participate in the study and thirty patients were found to be on beta blockers, anticoagulation drugs and uncontrolled diabetes mellitus. The remaining 80 patients of American society of Anaesthesiologist (ASA) grade I or II, age between 20-50 years and posted for elective lower limb surgeries were randomly assigned to one of the two groups. The randomization was done with computer generated random number sequence. The allocated intervention were written on slips of paper, placed in serially numbered, opaque envelopes and sealed. As consecutive eligible subjects got enrolled, the envelopes were serially opened and the allocated intervention was implemented. Group B received subarachnoid block with injection levo-bupivacaine (0.5%) 15 mg with 60μg of buprenorphine. In Group D, the patients received subarachnoid block with injection levo-bupivacaine (0.5%) 15 mg with 5μg dexmedetomidine. One anaesthetist prepared the intrathecal drugs just prior to positioning the patient for spinal anaesthesia. Patient and anaesthetist who attended patient intraoperatively and collected data in the postoperative period were blinded to the study drug.

Patients with contraindication to regional anaesthesia, ASA grade III & IV, history of significant coexisting diseases like ischemic heart disease, hypertension, diabetes, impaired renal functions, LVF, valvular heart disease rheumatoid arthritis, severe liver disease, patients on beta blockers and adrenergic receptor agonist or antagonists therapy ,body weight >120 kg, pregnant patients, chronic alcoholics and malnourished patients were excluded from the study. The routine pre anaesthetic evaluation of all patients were carried out a day prior to surgery and were explained about the visual analogue scale [10] (VAS) and its use for measuring the postoperative pain and advised fasting for 6 h. Sedatives and hypnotics were avoided in premedication drugs as well as during intraoperative period. In operating room, all routine monitoring was attached and intravenous fluid (IV) ringer lactate (R.L.) 10-15 ml/kg was started. Baseline haemodynamic parameters heart rate (HR), oxygen saturation (SpO_2), systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean blood pressure (MBP) were noted.

After all aseptic precautions, lumbar puncture was performed at L3–L4 using a 25 G spinal needle with the patient in sitting position and the study drug solution was injected as per the groups allocated. The patients were placed supine after injection and the sensory level was assessed by pinprick sensation using a blunt 25-gauge needle along the mid-clavicular line bilaterally at three-minute intervals for 30 minutes and then every 15 minutes after. The time to reach T10 dermatome and the maximum sensory level (onset of sensory block) achieved were recorded. Scoring was used to assess sensory effect as 0= no block, 1=touch sensation (analgesia) and 2= no sensation (anaesthesia). The motor block was assessed according to the modified Bromage scale [11] (0–3).The onset of motor block (time to reach Bromage score 3) and duration of motor block (time to regression of Bromage score 0) were recorded. In the intraoperative period, vital parameters (HR, SBP, DBP, MBP and SpO_2) were recorded after the block at 1 min, 3 min, 5 min, 7 min, 10 min then every 5 min in first hour and every 15 minutes up to 3 hours. On achieving T10 sensory blockade level, surgery was allowed. Hypotension (20% fall in MBP from baseline) was treated with ephedrine 6mg IV bolus and bradycardia (HR<50 beats/min) was treated with atropine 0.6mg IV. The onset and duration of sensory block, onset and duration of motor block and duration of analgesia were recorded.

All durations were calculated in relation to the time of subarachnoid block. In cases with failure of sub arachnoid block and conversion to general anaesthesia, such patients were the excluded from study. In post anaesthesia care unit (PACU), pain scores and sedation score were recorded using visual analogue scale (VAS) and ramsay sedation score (RSS) by nursing staff that were unaware of the group assignment. Initially every 30 minutes for 8 hours, then every 2 hours till 24 hours were recorded. Duration of pain relief (effective analgesia) was defined as the time from spinal injection to the first request for rescue analgesics or VAS was >4. Postoperative analgesic rescue was provided by paracetamol 1g IV. The time to request rescue analgesia (the duration of analgesia) was noted. The patients were shifted from PACU after Bromage score achieved to zero. Any side-effects like as nausea, vomiting, bradycardia, hypotension, respiratory depression (RR <8/min) and pruritus were noted and treated accordingly.

STATISTICAL ANALYSIS

We took a sample size of 80 patients with 40 in each group assuming power of study 80% and level of significance 5%. The two tailed pilot study done to detect mean difference of 142.28 min in time to give first rescue analgesia in both the groups. Descriptive statistics was used for describing frequencies, mean and standard deviation. Chi square test was applied for comparing qualitative data and Unpaired Student's test using Bonferroni multiple comparisons' test were

applied for comparing quantitative data. Time to first analgesic administration was analysed by Kaplan–Meier survival analysis and logrank test. All the data was analysed using SPSS IBM software version 22 (IBM SPSS Advanced statistics, Chicago, IL, USA). P value < 0.05 was considered statistically significant.

RESULTS

There was no statistical significant difference in patient's demographics and duration of surgery (Table 1). The time of onset of sensory and motor block in both groups was statistically insignificant (Table 2). The T10 sensory level was achieved in all patients of both groups. The duration of motor block was 416.67±28.22 min in group D and 205.45±13.14 min in group B (p=<0.0001). The duration of analgesia was 495.42±24.95 min in the group D and 292.22±24.94 min in group B (p=< 0.0001), which is statistically significant (Table 2). In group D 36 patients had Ramsay sedation score ≥3 and 4 patients had <3

Ramsay sedation score while in group B 3 patients had Ramsay sedation score ≥3 and 37 patients had Ramsay sedation score <3. Mean sedation score in group D was 3.82±0.67 and in group B was 2.07±0.26 which is statistically significant (p =<0.0001) (Table 3). The mean values of HR, SBP, DBP and MAP were comparable between the two groups throughout the intraoperative and postoperative periods (Fig: 1 and 2). All patients had SpO_2 greater than 95% at all the times and did not require additional oxygen in PACU. Two patients in groups B and five patients in group D received one dose of ephedrine. Four patients in group D and two patients in group B required atropine but statistically insignificant. VAS values were <3 observed in both the groups during the whole duration of the surgery and none of the patients required additional analgesics. Intra-operative and post-operative nausea or vomiting occurred in 4 patients in group D and 7 patients in group B.

Table-1: Patients demographics and duration of surgery

Variable	Group D (Mean ±SD)	Group B (Mean ±SD)	p value
Age (years)	38.6+13.64	37.37+13.43	0.686
Sex (M/F)	35/5	34/6	-
ASA (I/II) Number of patients	15/25	19/21	-
Height (in cm)	161.86±3.72	161.96±4.16	0.899
Weight (kg)	61.08±4.16	59.90±4.04	0.153
Duration of surgery (minutes)	47.90±8.08	49.30 ±6.22	0.414

Table-2: Characteristics of spinal block

Variable	Group D (Mean±SD)	Group B (Mean±SD)	P value
Time of onset of motor block(Bromage score 3)(min)	4.7±1.24	4.35±1.46	0.25
Time of onset of sensory block (reach sensory score 2) (min)	4.1±1.27	3.65±0.94	0.077
Duration of motor block (regression to Bromage score 0) (min)	416.67±28.22	205.45±13.14	<0.0001
Duration of analgesia (time of first rescue analgesic)(min)	495.42±24.95	292.22±24.94	< 0.0001

Table-3: Ramsay sedation score (At the end of surgery)

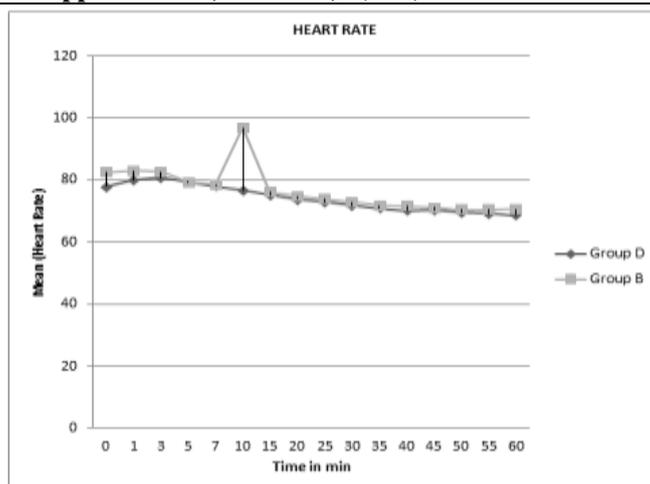| RSS	Group D (number of patients)	Group B (number of patients)	P value
<3	4	37	<0.0001
≥3	36	3	
Mean±SD	3.82±0.67	2.07±0.26	

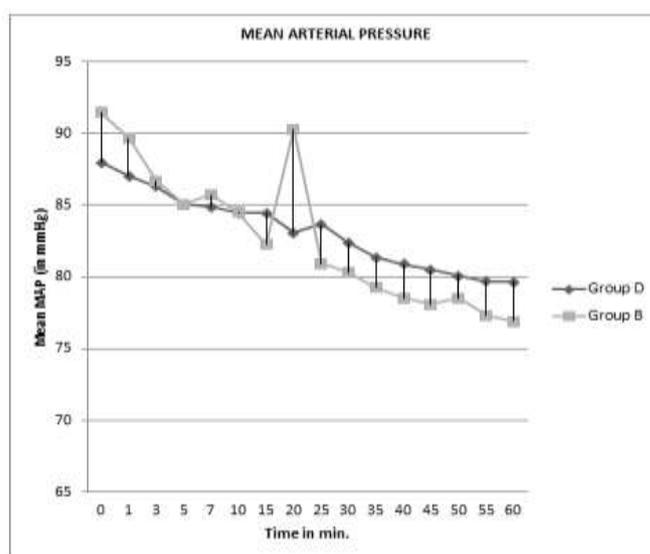**Fig-1**: **Trend of heart rate in both groups**

Fig-2: **Trend of mean blood pressure in both groups**

DISCUSSIONS

In this study we found that, dexmedetomidine 5 μg supplemented to intrathecal levo-bupivacaine significantly prolonged the duration of postoperative analgesia compared with the addition of buprenorphine 60μg. Both dexmedetomidine and buprenorphine prolonged duration of sensory and motor blockade and reduced the need of rescue analgesia for the first 24 postoperative hours. Literature is scarce about use of intrathecal dexmedetomidine and buprenorphine as an adjuvant to spinal local anaesthetics. Intrathecal α2-adrenoceptor agonists produce analgesia by binding and depressing the release of pre-synaptic C-fibre neurotransmitters and also by hyperpolarisation of post-synaptic dorsal horn neurons [12, 13]. This anti nociceptive effect may explain the prolongation of the sensory block while prolongation of motor block may be due to the binding of α2-adrenoceptor agonists to motor neurons in the dorsal horn [14].

Dexmedetomidine; a highly selective, α2-adrenergic agonist; has analgesic, sedative, anaesthetic sparing effects when used in systemic route [15]. Dexmedetomidine has been used intrathecally in varying doses ranging from 3 μg to 15 μg[16,17]. The optimal dose of intrathecal dexmedetomidine has not been established. Based on previous studies on human where no neurotoxic effects have been observed, the intrathecal dexmedetomidine was selected [9, 18, 19]. Kanazi *et al*. [9] and Al Ghanem *et al*.[18] found that dexmedetomidine and clonidine added to bupivacaine produced a similar prolongation in the duration of the motor and sensory block, with preservation of haemodynamic stability. Time of onset of sensory block was comparable in both the groups. Hala *et al*. [17] and Al-Mustafa *et al*.[19] observed dose dependent prolongation of motor and sensory blockade with reduced analgesic requirement with increasing dosages of intrathecal dexmedetomidine.

Buprenorphine is a thebaine derivative, long acting, lipid soluble, with a partial agonist activity at the μ-Opioids receptor. Buprenorphine dissociates slowly from μ-Opioids receptor, it has long duration of action

and less addiction potential [20]. There was statistically no change in perioperative BP and HR in both the groups. The sympathetic blockade is near maximal at the usual doses used for spinal anaesthesia so it is not or only minimally affected by an inclusion of a low dose of α2-agonist. Bradycardia and hypotension are most common and important side effect of intrathecal α adrenergic receptor agonists. In our study, these side effects were not significant may be because of small dose of intrathecal dexmedetomidine and buprenorphine was used in our study.

Similar results were found in previous study by Mahima gupta *et al.* [7], compared intrathecal buprenorphine and dexmedetomidine for their hemodynamic profile and was found similar in both the groups. The total 6 patients had episode of bradycardia in both the groups following subarachnoid block (4 in Group D and 2 in Group B), which was treated by injection atropine. Dexmedetomidine causes bradycardia but the effect is more prominent when administered intravenously and with a higher dose [21]. They also found that mean SBP, DBP and MBP was also low in buprenorphine group as compared to dexmedetomidine group but it was statistically insignificant.

Kanazi *et al*. [9] and Ghanem *et al*. [18] also used intrathecal dexmedetomidine without any adverse neurological consequences. Various preclinical animal neurotoxicity studies, using dexmedetomidine in a dose range from 2.5–100μg failed to show any untoward neurological effects [22-24]. Our study has shown that the addition of 5 μg dexmedetomidine with levo-bupivacaine significantly prolongs both sensory and motor block. Both dexmedetomidine and buprenorphine provided good quality intra operative and post-operative analgesia and hemodynamic stability. The analgesia was clinically better in dexmedetomidine group as compared to buprenorphine group and it was statistically significant.

CONCLUSION

Our study concluded that the supplementation of levobupivacaine with low dose of dexmedetomidine in subarachnoid block produces longer duration of sensory and motor block, with slightly more time to attain complete motor block in comparison to 60μg of intrathecal buprenorphine.

This study adds to the current knowledge on dexmedetomidine and buprenorphine but the results should be considered taking into consideration the various limitations. As all patients were either ASA physical status I or II, so results cannot be generalised to ASA physical status III and IV patients. Our patients were young and otherwise healthy patients, free of significant comorbidities that might have exaggerated the cardiovascular side effects of intrathecal buprenorphine or dexmedetomidine. Hence, further

studies that compare the effect of intrathecal dexmedetomidine and buprenorphine on the spinal levo-bupivacaine with large sample size are needed.

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