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A comparative study of 0.5% levobupivacaine alone with 0.5% levobupivacaine and dexmedetomidine epidurally for major orthopedic surgeries

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ABSTRACT

Background and Aims: Alpha (α)-2 agonists as epidural adjunct to Local Anaesthetics (LA) are being increasingly used for the purpose of faster onset of sensory blockade and prolonged duration of analgesia. The present study aims at comparing the hemodynamic, sedative, and analgesia potentiating effects of epidurally administered dexmedetomidine combined with levobupivacaine versus levobupivacaine alone. **Material and Methods:** A total of 100 patients of either sex, aged between 20-60 years, ASA physical status I and II admitted for lower limb orthopaedic surgeries were enrolled into the present study. Patients were randomly divided into two groups: Levobupivacaine (Group L) and levobupivacaine + Dexmedetomidine (Group LD), comprising of 50 patients each. Injection levobupivacaine, 15 ml of 0.5% (isobaric), was administered epidurally in both the groups with addition of 1 µg/kg of dexmedetomidine in LD group. Besides cardio-respiratory parameters and sedation scores, various block characteristics were also observed which included time to onset of analgesia, maximum sensory analgesic level, time to complete motor blockade and the time to two segmental dermatomal regressions. At the end of study, data was compiled systematically and analysed using ANOVA. Value of $P<0.05$ was considered significant and $P<0.001$ as highly significant. **Results:** The demographic profile of patients was comparable in both the groups. Onset of sensory analgesia (in minutes) in group L and LD was 21.42±3.38 versus 9.26±1.82. Establishment of complete motor blockade 18.02±2.73 versus 27.90±3.81 was significantly earlier. Postoperative analgesia was prolonged significantly 344.08 ±24.40 minutes and sedation scores were highly significant on statistical comparison ($P<0.001$) in the LD group. **Conclusions:** Dexmedetomidine is a good epidural adjuvant to levobupivacaine as it provides stable hemodynamics, early onset of sensory anaesthesia, prolonged post-operative analgesia and good sedation levels.

Key words: Dexmedetomidine, epidural anaesthesia, levobupivacaine, lower limb surgery

INTRODUCTION

Epidural anaesthesia offers superior pain relief and early mobilization especially when local anaesthetic is combined with an adjuvant. The addition of adjuvants like opioids or α-2 agonists provide a dose-sparing effect of local anaesthetics. It accelerates the onset of sensory blockade of epidural anaesthesia and decreases the effective dose of local anaesthetic. Sedation, stable hemodynamics and an ability to provide prolonged postoperative analgesia are the main desirable qualities of an epidural adjuvant[1]. Levobupivacaine is an amide type of long acting local anaesthetic agent which is an S(-) enantiomer of bupivacaine. It has a lower risk of cardiotoxiciy and neurotoxicity. The decreased toxicity of levobupivacaine is attributed to its faster protein binding rate[2].

Dexmedetomidine is a new addition to the class of alpha-2 agonist which has got numerous beneficial effects when used through epidural route[3]. It acts on both pre and post synaptic sympathetic nerve terminals and central nervous

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system thereby decreasing the sympathetic outflow and nor-epinephrine release causing sedative, anti-anxiety, analgesic and sympatholytic effects[4–5]. Dexmedetomidine has the advantage of a lack of opioid-related side effects like respiratory depression, pruritus, nausea, and vomiting[6]. Considering the merits of levobupivacaine and dexmedetomidine, the present study was carried out to compare the safety and efficacy of Dexmedetomidine (1µg/kg) as an adjuvant to Levobupivacaine 0.5% with Levobupivacaine 0.5% alone in patients undergoing lower limb surgeries in terms of intraoperative haemodynamics; onset, level and duration of sensory block; onset and duration of motor block; level of sedation; postoperative analgesia and possible side effects.

MATERIAL AND METHODS

After obtaining the research ethics committee approval and the informed written consent, 100 patients of both genders, aged 20-60 years, ASA I and II admitted for lower limb orthopaedic surgery, were enrolled into the present study. Those patients who had any anatomical abnormalities of the spine, local sepsis, coagulation disorders or associated neurological or cardiovascular disorders were excluded from the study. Patients were divided randomly into two groups with 50 patients in each group. Group L received 15 ml of 0.5% isobaric levobupivacaine while as group LD received a combination of 15 ml of 0.5% isobaric levobupivacaine and 1 µg/kg of dexmedetomidine. Patients were thoroughly counselled during the pre-operative evaluation and were properly explained about the nature of study before taking the written consent. All patients were premedicated with injection midazolam 2mg and promethazine (phenargan) 25mg intramuscularly half an hour before surgery.

In the operation theatre, a good venous access was secured with 18guage cannula and all the patients were preloaded with 20ml/kg Ringer lactate solution. The baseline Heart Rate (HR), Non-Invasive Blood Pressure (NIBP), and Pulse Oximetry (SpO_2) was noted. A visual analogue scale was used for assessment of pain.

Lumbar epidural anaesthesia was induced using 18G Touhy needle with patients in the sitting position in L3-L4 interspace. The location of epidural space was confirmed by loss of resistance technique. A test dose of 3 ml of 2% lignocaine with adrenaline (1 in 200000) was administered into epidural space and thereafter epidural catheter was secured 3-5 cm into the epidural space and patients were placed supine.

In Group L: Levobupivacaine 0.5%, 15ml (75mg)+1 ml NS was injected into the epidural space at the rate of 1ml/3sec.

In Group LD: Levobupivacaine 0.5%, 15ml (75mg) +Dexmedetomidine 1 µg/kg, was injected into the epidural space at the rate of 1 ml /3 sec.

The following parameters were observed after the epidural administration of the drug: Time to onset of analgesia, time to achieve the maximum sensory level, time to complete motor blockade, and time to use of rescue analgesic (VAS score of 4).

Sedation was also assessed at 5 minute intervals for 30 minutes, intra-operatively and at intervals of 1 hour during post-operative period, using Ramsay sedation scale. Motor blockade was assessed by using the modified Bromage scale. Any untoward side effects during the study period were carefully observed for and recorded and managed. At the end of study data was compiled systematically and was subjected to statistical analysis using analysis of variance (ANOVA). Value of $P<0.05$ was considered significant and $P<0.001$ as highly significant.

RESULTS

A total of 100 patients for lower limb surgery were enrolled for the study and were randomly divided into two groups. The demographic characteristics in both the groups exhibited marked similarities and did not show any statistical significant difference (P>0.05). Table 1 shows the demographic profile of various patients.

The onset of analgesia (in minutes) at T10 dermatomal level was significantly earlier in the LD group (9.26±1.82) as compared to the group L (21.42±3.38) (P<0.001). Motor block was assessed using modified Bromage scale and complete motor block was achieved significantly earlier in LD group (18.02±2.73) patients as compared to group L (27.90±3.81) (P<0.001). The duration of sensory block was significantly prolonged in LD group (344.08±24.40) in comparison to group L (198.68±14.59). Also the duration of motor block was prolonged in LD group (196.84±16.28) in comparison to group L (118.00±15.18). All these parameters showed highly significant difference in these two groups (P<0.001) [Table 2].

Dexmedetomidine has gained a lot of popularity as a sedative agent and similar findings were observed in our study as 64% patients exhibited grade III sedation in LD

group as compared to none in the control group. These sedation scores were highly significant on statistical comparison (P<0.001) [Table 3].

Patients in the group LD had improved pain scores which were highly significant statistically in comparison to control group (p<0.001) for the initial 3 hours postoperatively [Table 4]. In the fourth hour the pain scores were still significantly better in dexmedetomidine group (p<0.05).

Table 1: Demographic profile of the patients receiving levobupivacaine 0.5%, 15 ml (75mg) (Group L) and levobupivacaine 0.5%, 15 ml (75mg) + dexmedetomidine (1 µg/kg) (Group LD). The values are mentioned in mean±standard deviation

Demographic characteristics	Group L	Group LD	P value
Age(year)	36.02±12.35	33.50±11.62	0.296
Height(cm)	162.08±4.79	163.79±5.14	0.087
Weight(kg)	68.92±6.37	66.38±6.48	0.051
Male/Female(M/F)	43/7	43/7	1.00
ASA(I/II)	46/4	46/4	1.00
Mean duration of surgery(min)	121.40±26.14	123.20±21.13	0.706

Table 2: Comparison of the sensory and motor block characteristics in patients receiving levobupivacaine 0.5%, 15 ml (75mg)(Group L) and levobupivacaine 0.5%, 15 ml (75mg) + dexmedetomidine (1 µg/kg) (Group LD). The values are mentioned in mean±standard deviation

Block characteristics	Group L	Group LD	P value
Onset time of sensory block (min)	21.42±3.38	9.26±1.82	<0.001
Maximum duration of sensory block (min)	198.68±14.59	344.08±24.40	<0.001
Onset of motor block (min)	27.90±3.81	18.02±2.73	<0.001
Duration of motor block (min)	118.00±15.18	196.84±16.28	<0.001

Table 3: Comparison of the sedation scores in patients receiving levobupivacaine 0.5%, 15 ml (75mg)(Group L) and levobupivacaine 0.5%, 15 ml (75mg) + dexmedetomidine (1 µg/kg) (Group LD). The values are mentioned in mean±standard deviation

Sedation score at 30 min	L	LD	P value
1	48(96%)	-	<0.001
2	2(4%)	18(36%)	<0.001
3	-	32(64%)	<0.001
4	-	-	-
5	-	-	-

Table 4: Comparison of visual analogue scores (VAS) in patients receiving levobupivacaine 0.5%, 15 ml (75mg) (Group L) and levobupivacaine 0.5%, 15 ml (75mg) + dexmedetomidine (1 µg/kg) (Group LD). The values are mentioned in mean±standard deviation

VAS at	L	LD	P value
1hr	2.02±1.16	1.04±0.19	<0.001
2hr	3.93±1.16	1.24±0.47	<0.001
3hr	4.84±0.68	2.26±0.59	<0.001
4hr	5.33±0.57	3.42±1.36	0.021

DISCUSSION

Early postoperative mobilization and rehabilitation with minimally associated pain and discomfort is the most desirable feature in modern orthopaedic surgery[7].

The synergism between epidural local anaesthetics(LA) and opioids is well established but evidence regarding combination of LA with dexmedetomidine through epidural route is scarce in literature[7]. This study has tried to directly compare the effects of epidurally administered Dexmedetomidine and Levobupivacaine combination (LD) with Levobupivacaine (L) alone.

We found that the time to reach peak sensory level was shorter in group LD (9.26±1.82) as compared to group L (21.42±3.38) with a P value of <0.001. In a study conducted by Gupta et al, comparing efficacy of levobupivacaine with dexmedetomidine versus levobupivacaine with fentanyl, it was observed that the mean time of onset of sensory block in levobupivacaine with dexmedetomidine group was 7.25±2.3[1]. The results of our study are consistent with the above mentioned study. A modified Bromage scale 2 was seen in all the patients before the initiation of surgical procedure. Throughout the surgery, patients were calm and composed in both the groups but sedation scores were better in the LD group. Addition of dexmedetomidine to levobupivacaine provided excellent intraoperative sedation without causing any respiratory depression. It was seen that 64% of patients had grade III sedation scores during the perioperative period in the LD group as compared to none of patients in the control group. Gupta[1] and Manal[8] in their respective studies observed that the sedation scores were better with no respiratory depression in levobupivacaine with dexmedetomidine group in comparison to levobupivacaine with fentanyl group. The sedative properties of dexmedetomidine are far superior to opioids as no patient required any other sedative during the perioperative period. Absence of respiratory depression

in the patients who were administered dexmedetomidine was one of the most remarkable observations[9,10]. Its epidural effect is dose dependant and superior than the intravenous route due to its high affinity for α-2 receptors in the spinal cord[11]. None of the patients in either of the group required any additional epidural top-up dose during the surgical period (Figure 3). The analgesia was assessed using Visual Analogue Scale (VAS) and patients in both the groups showed 0 scores during the entire surgical period. In our study, remarkable synergistic properties of LA and dexmedetomidine have been seen. Not only we were able to decrease the dose of local anaesthetic but also the duration of post-operative analgesia was significantly prolonged in patients in whom dexmedetomidine was administered as adjuvant.

Gupta et al., observed that the mean duration of motor block in levobupivacaine with dexmedetomidine group was 167.4±21 and the mean duration of analgesia in levobupivacaine with dexmedetomidine group was 187.7[1].

The mean duration of motor block (196.84±16.28) and analgesia (344.08±24.40) was prolonged in our study in comparison to study conducted by Gupta et al., the reason being that the dose of dexmedetomidine in our study was more (1 µg/kg) as compared to the other study (25 µg).

Manal et al., in their study showed that mean duration of sensory block was 390.00±87.60 in levobupivacaine with dexmedetomidine group[8]. The longer duration of sensory block can be explained as the dose used in their study for dexmedetomidine was 1.5 µg/kg body weights while it was 1 µg/kg body weight in our study.

Hemodynamic stability was one of the most remarkable features observed with addition of dexmedetomidine. In our study negative chronotropic effect was exhibited by dexmedetomidine approximately 10 minutes after the epidural injection of the drugs [Figure 1]. Similarly, Mean Arterial Pressure (MAP) decreased from the baseline in both the groups with a maximum decline of MAP at 20 minutes after the epidural injection but it never went below acceptable physiological limits [Figure 2].

Gupta et al., observed that decrease in heart rate and mean arterial blood pressure was exhibited by dexmedetomidine approximately 30-35 minutes after epidural injection of drug[1]. Postoperatively, HR and MAP remained stable in both the groups. The stable hemodynamics can possibly be explained on the basis of lower volume of local anesthetics used and a suitable selection of the dose of adjuvant.

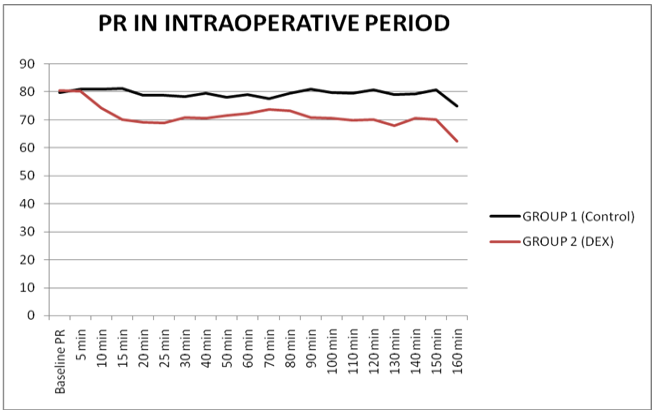

Figure 1: Mean Pulse Rate (PR) in group 1(receiving levobupivacaine 0.5%, 15ml) and group 2 (receiving levobupivacaine 0.5%, 15ml 75mg + dexmedetomidine 1µg/kg). The pulse rate is the mean pulse rate in beats per minute

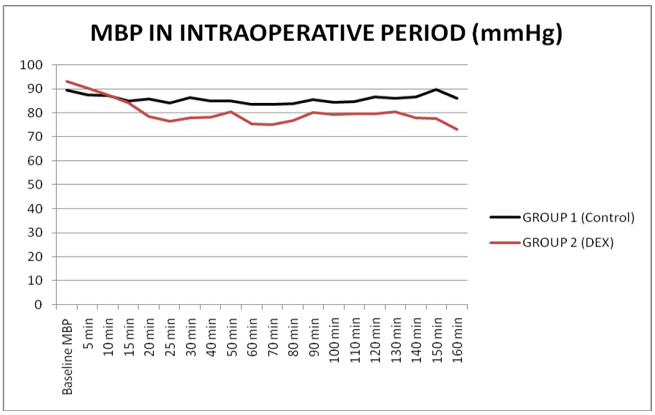

Figure 2: Mean Blood Pressure in the intraoperative period (MBP) in group 1 (receiving levobupivacaine 0.5%,15ml) and group 2 (receiving levobupivacaine 0.5%,15ml 75mg + dexmedetomidine 1µg/kg). The blood pressure is the mean blood pressure in mm Hg

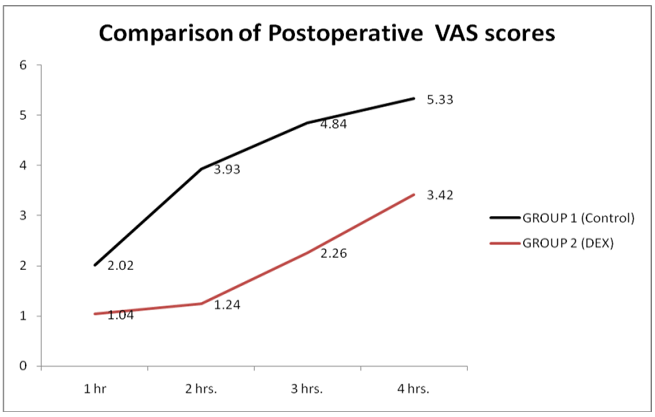

Figure 3: Postoperative Visual Analogue Scores (VAS) in group 1 (receiving levobupivacaine 0.5%, 15ml) and group 2 (receiving levobupivacaine 0.5%, 15ml 75mg + dexmedetomidine 1µg/kg)

CONCLUSIONS

We concluded that the addition of dexmedetomidine to levobupivacaine for epidural anaesthesia leads to a faster onset of action and rapid establishment of sensory and motor blockade, prolonged duration of postoperative analgesia and reduced requirement of rescue analgesia in the postoperative period with better sedation levels. The dose-sparing action of local anaesthetics and stable cardiovascular parameters makes it a very effective adjunct in regional anaesthesia.

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