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Original Research Article

Comparative Study of the Effects of Dexmedetomidine and Butorphanol as Epidural Adjuvants in Lower Limb Orthopaedic Surgery under Intrathecal Levobupivacaine Anaesthesia

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Abstract

Objective: To evaluate the effect of Butorphanol versus Dexmedetomidine as epidural adjuvant to intrathecal Levobupivacaine block on the onset and duration of blockade, post-operative analgesia, haemodynamic changes and minimal sedation in patients undergoing elective lower limb orthopaedic surgeries.

Methods: Prospective, randomized, double blind, interventional study was conducted on 46 patients of 18-50 years age of either sexes having body weight between 40-70 kgs, ASA grade I-II, underwent elective lower extremity orthopaedic surgeries under spinal anaesthesia in orthopaedic operation theatre over a period of one year. Using computer generated randomization, the patients were allocated into two groups: Group LD (n = 23), Group LB (n = 23).Both the group received 15 mg of 0.5% Levobupivacaine (heavy) intrathecally plus Group LD received Dexmedetomidine 1 µg/kg in 10 ml saline and Group LB received Butorphanol 10 µg/kg in 10 ml saline epidurally. The haemodynamics block characteristics, sedation, VAS score and side effects were observed. The data was analysed using student's t-test and Chi square test. P value of ≤0.05 was considered statistically significant.

Results: Time taken for adequate sensory ($p< 0.05$), motor block ($p< 0.001$) was shorter for Dexmedetomidine group than Butorphanol group. Regression to S-2 level, duration of motor block, time for rescue analgesia was significantly more for Dexmedetomidine group ($p<0.001$). Sedation score was better in group LD than group LB.

Conclusion: Epidural Dexmedetomidine is a better alternative than epidural Butorphanol when combined as an adjuvant to intrathecal 0.5% hyperbaric Levobupivacaine in terms of prolonged block duration, post-operative analgesia with minimal adverse effects.

Keywords: Dexmedetomidine, Butorphanol, Levobupivacaine, Epidural Anaesthesia

Introduction

Pain has been best defined as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" [1]. Pain is not only very distressing to the patients but also causes sympathetic over activity in the postoperative period, often prolonging hospital stay, increasing cost and unanticipated re-admission in hospital [2]. By reducing the physiological and psychological response to tissue injury; satisfactory peri-operative analgesia improves the surgical outcome with reduced morbidity, organ dysfunction, need for hospitalisation and convalescence, which is a prerequisite for early recovery [3,4].

Regional anaesthesia is the preferred mode of anaesthesia for infraumbilical surgeries in present times [5]. Combined spinal epidural technique has become increasingly popular because of the advantages of each technique, minimizing specific disadvantages, namely, combines the efficacy of spinal anaesthesia and flexibility of epidural anaesthesia [6]. Adjuvant in epidural anaesthesia is being used in practice since long for improvement of peri-operative analgesia following spinal anaesthesia.

Levobupivacaine is the levo-stereoisomer of the racemic bupivacaine, having similar pharmacology to Bupivacaine; with wider safety of margin and less cardio-toxic and neurotoxic in comparison with Bupivacaine.

Butorphanol, a synthetic opioid, exhibits partial agonist and antagonist activity at the μ opioid receptor and agonist activity at the k receptor. Side effects are very less, if it is used in low doses as an adjuvant in epidural analgesia.

Dexmedetomidine, a highly selective α adrenergic agonist has evolved as a panacea for various applications and procedures in the peri-operative and critical care settings [7]. It is also emerging as a valuable adjunct to regional anaesthesia and analgesia.

The aim of this study was to evaluate the effect of Butorphanol versus Dexmedetomidine as epidural adjuvant to intrathecal Levobupivacaine block on the onset and duration of blockade, post-operative analgesia, haemodynamic changes and minimal sedation in patients undergoing elective lower limb orthopaedic surgeries.

Materials and Methods

This prospective, randomized, double blinded, interventional study was conducted after obtaining Institutional ethical committee approval and written informed consent from study population. This study was conducted on 46 patients of 18-50 years of age of both sexes having body weight between 40-70 kg, ASA physical classification I-II, had underwent elective lower extremity orthopaedic surgeries under spinal anaesthesia over a period of one year. Patients with uncontrolled hypertension, allergic to study drugs, opium addiction, on sedative drugs, contraindications to central neuraxial blockade, failed spinal block and received general anaesthesia were excluded.

Based on a previous study, using a web based sample size calculator, assuming $\alpha = 0.05$ and $\beta = 0.2$ or power $(1\beta) = 0.8$. Assuming a 5% drop out, we have enrolled 23 patients in each group. Using computer generated randomization, the patients were allocated into two groups: Group LD (n = 23), Group LB (n = 23).

Group LD received 15 mg of 0.5% Levobupivacaine (heavy) intrathecally plus Dexmedetomidine 1 μg/kg in 10 ml saline epidurally. Group LB received 15 mg of 0.5% Levobupivacaine (heavy) intrathecally plus Butorphanol 10 μg/kg in 10 ml saline epidurally.

Isobaric Inj. Levobupivacaine 0.5% was made hyperbaric solution by adding 0.5 ml of 50% dextrose.

Following the inclusion and exclusion criteria patients were selected for this study and pre-anaesthetic check-up was done. Willing patients were explained about study procedure and visual analogue pain scale (VAS) for pain in their own vernacular language.

Preoperatively all the patients were kept on fasting for8 hours and tab. Alprazolam 0.25 mg and tab. Pantoprazole 40 mg were given previous day night of surgery. After arrival of patients into the operating room multichannel monitors were attached and baseline heart rate, ECG, non-invasive blood pressure and oxygen saturation were noted and intravenously preloaded with 10 ml/kg body weight inj. Ringer lactate.

In sitting position under strict aseptic method, epidural site skin was infiltrated with 2% inj. Lignocaine with adrenaline.18G Tuohy needle was used in midline approach and the epidural space between L2-L3 was located by loss of resistance to air technique and a 20Gmultiorifice epidural catheter was inserted 4 cm into the epidural space and fixed after confirming the absence of CSF or blood. To exclude intrathecal or intravascular placement of the epidural catheter 3 ml of test dose of inj. Lignocaine with adrenaline 1:200,000 was injected through the catheter.

Then subarachnoid block was given at L3-4 interspace with 25G Quincke needle. After checking free flow of clear CSF, Inj. 0.5% hyperbaric Levobupivacaine 15mg was delivered into the sub-arachnoid space over 15 seconds with the bevel of the needle facing cephalad. After intrathecal injection, patients were placed in supine position; the study drug was prepared by an anaesthesiologist not involved in the study in a 10 ml syringe in equal volume. Epidurally LD group received Dexmedetomidine (1µg/kg dosage/10 ml saline) and Group LB received Butorphanol (10 µg/kg/10 ml saline). Throughout the surgery the table was kept in neutral position irrespective of sensory block level. Oxygen 2 L/min was given through a face mask. The anaesthesiologist performed the block was blinded to the study drug and perioperative data.

All durations were calculated from the time of intrathecal injection as time '0' (zero). Hemodynamic parameters, oxygen saturation (SpO_2) were recorded at 5 minutes interval till 30 minutes, thereafter every 10 minutes till 60 minutes and every 20 minutes till 2 hours of surgery and in the post-operative period till the administration of rescue analgesia.

First complaint of tingling and numbness in the lower limb after intrathecal injection was taken as the sensory onset time (seconds). Sensory testing was assessed by loss of pinprick sensation by pricking with 23 G blunt hypodermic needle (0= normal sensation , 1= blunt pain , 2 = complete analgesia) along the midclavicular line bilaterally every minute until the highest level was achieved for four consecutive tests, then every 5 minutes until the two point segment regression of the block. Time to analgesic block at T10 dermatome, the peak sensory block level, time to reach peak sensory block level, a two segment dermatomal regression and sensory regression to the S2 dermatome were recorded accordingly.

After achieving the T-10 sensory block level, surgery was allowed.

The motor block was assessed by modified Bromage scale. Sedation scores was assessed using Ramsay Sedation scale starting from the epidural administration of the drug, sedation score was monitored at 5

minutes interval till 20 minutes then at 10 minutes interval till 30 minutes then at 15 minutes interval till 60 minutes and thereafter at 30 minutes interval till 2 hours.

Postoperative pain assessment was done using VAS between 0-10 (0 = no pain,10 =worst pain).Duration of analgesia was recorded from the completion of anaesthesia to the time of the first complaint of pain or at VAS>4.Rescue analgesia was provided by intramuscular inj. Diclofenac 75 mg. Starting from the epidural administration of the drug VAS score was monitored every 15 minutes till 2 hours and thereafter at 30 min interval for next 1 hour.

The regression time for sensory and motor block was recorded and patients were discharged from PACU after sensory regression to S1 dermatome and motor block regression to Bromage 0.

Hypotension [systolic blood pressure (SBP) <100 mm Hg or <20% of baseline SBP] was corrected with fluids or intravenous inj. Mephentermine. Bradycardia (heart rate <50 bpm) was treated with intravenous inj. Atropine 0.3–0.6 mg. The incidence of adverse effects such as nausea, vomiting, shivering, pruritus, respiratory depression, sedation, hypotension, bradycardia and urinary retention were recorded.

Time interval for the recovery of the sensory level of the block to T10 was ascertained by the data collector3 hour postoperatively.

Statistical Analysis

Data collected and statistical analysis was performed with the SPSS, version 20.0 for Windows Statistical Software Package (SPSS Inc., Chicago, IL, USA). Categorical data and the incidence of adverse events were presented as numbers and proportion and the difference in proportion was inferred by Chi-square test.

Demographic data, duration of surgery, VAS score, total duration of analgesia, requirement of rescue analgesia and all other numeric data were expressed as mean ± standard deviation and were compared in two groups and difference in means were inferred by unpaired t-test. P value ≤ 0.05 was considered as statistically significant and p ≤0.01 was considered highly significant.

Results

Table 1: Demographic profile of patients, ASA physical classification, and duration of surgery

Parameters	Groups		P value
	LB	LD	
Age (years)	44.43±10.55	42.52±9.32	≥0.05
Body weight in kg	57.48± 5.91	57.09± 5.96	
Gender ratio (M:F)	12:11	12:11	
ASA I:ASA II	14:9	15:8	
Duration of surgery (mins)	111.56±24.12	108.47±13.93	

In our study the demographic profile, ASA physical status, duration of surgery, haemodynamic parameters were comparable among the two groups (p≥0.05).

Time taken to reach T-10 level was 2.57± 0.51 minutes and 2.22 ± 1.0 minutes for LB and LD groups respectively and not statistically significant (p≥0.05). Time taken to reach peak sensory level was significantly shorter for Dexmedetomidine (3.26 ± 0.91 minutes) than Butorphanol (4.58 ± 0.65 minutes) (p <0.0001).In LB group 13 (56.5%) and 10 (43.47%) patients peak sensory level reached T4 and T6

respectively. In LD group19 (82.6%) and 4 (17.39%) patients peak sensory level reached T4 and T6 level respectively. Highest sensory dermatomal block was achieved in Dexmedetomidine group but not statistically significant (p >0.05). Time taken to reach peak Bromage-3 motor block was significantly very shorter for Dexmedetomidine (1.91 ± 1.16 minutes) than Butorphanol group (3.91±1.2 minutes) (p< 0.001). S-2 level regression time of sensory block was significantly more for Dexmedetomidine group (219.13 ± 22.75 minutes) than Butorphanol group (144.61 ± 27.9 minutes) (p<0.001).

Dexmedetomidine group (302.39 ± 60.71 minutes) had taken more time to return Bromage 0than Butorphanol group (184.43 ± 42.37 minutes), was statistically highly significant (p< 0.0001). Delayed demand for rescue analgesia for Dexmedetomidine group (LB vs LD =220.22 ± 33.32 vs 405.22 ± 73.95) (p<0.001). Both the groups showed similar haemodynamic stability. There was no statistically significant difference in heart rate, systolic blood pressure, diastolic blood pressure and mean blood pressure among the two groups.

Episodes of bradycardia and hypotension were significantly more in Dexmedetomidine group, (p<0.05) whereas incidence of nausea and vomiting was more in Butorphanol group but was not statistically significant (p>0.05).Incidence of respiratory depression, urinary retention, pruritus, headache were absent in either groups.

Postoperative VAS score was significantly less for Dexmedetomidine group than Butorphanol group, signifies that Dexmedetomidine produces better analgesia than Butorphanol. Sedation score for Dexmedetomidine was significantly more than Butorphanol.

Table 2: Comparison of block characteristics among two groups

Parameters	LB (Mean ± SD)	LD (Mean ± SD)	P- Value
Time taken to reach T-10 level (Min)	2.57± 0.51	2.22 ± 1.0	0.1433
Time taken to reach peak sensory level (Min)	4.58 ± 0.65	3.26 ± 0.91	< 0.0001
Peak sensory level reached in two groups (T4 : T6)	13 : 10	19 : 4	0.107
Time taken to reach peak Bromage-3 motor block (Min)	3.91 ± 1.2	1.91 ± 1.16	< 0.0001
Time taken for S-2 level regression in the two groups (Min)	144.61 ± 27.9	219.13 ± 22.75	< 0.0001
Time taken for regression of motor block to Bromage-0 in two groups ((Min)	184.43 ± 42.37	302.39 ± 60.71	< 0.0001
Time to first analgesic rescue in two groups (Min)	220.22 ± 33.32	405.22 ± 73.95	< 0.0001

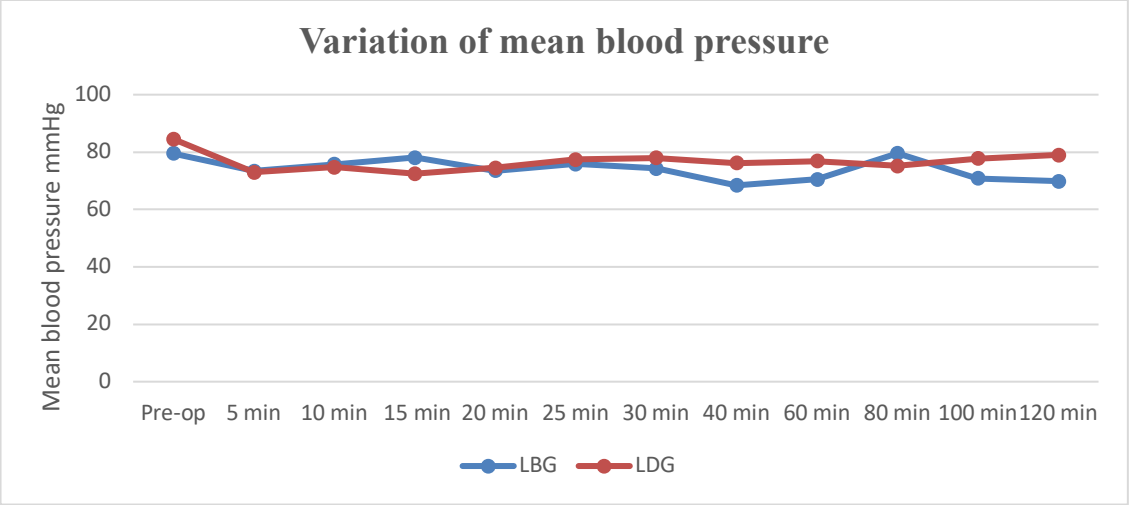

Figure 1: Variation in mean blood pressure among the two groups

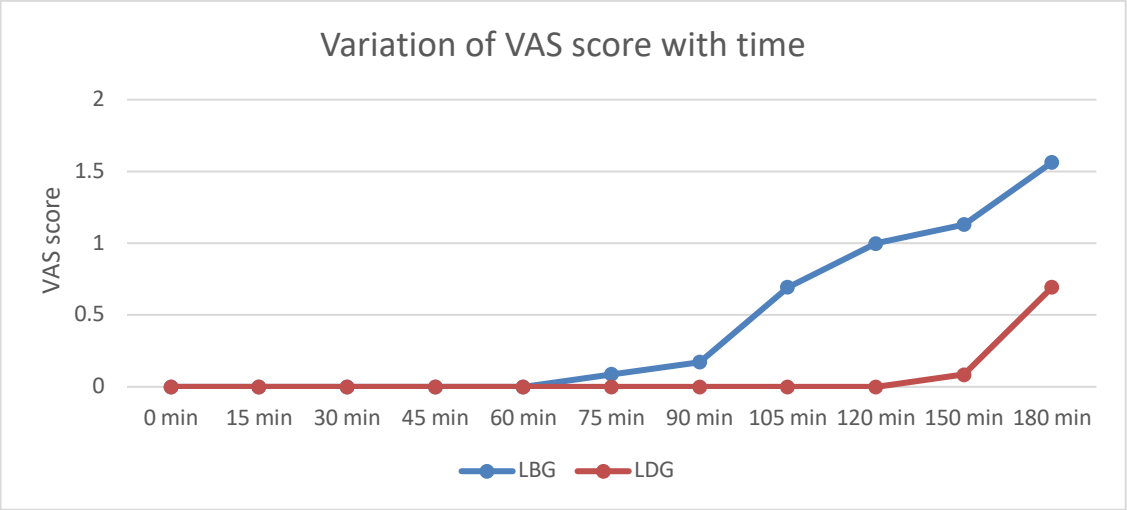

Figure 2: Trends in postoperative visual analogue scale

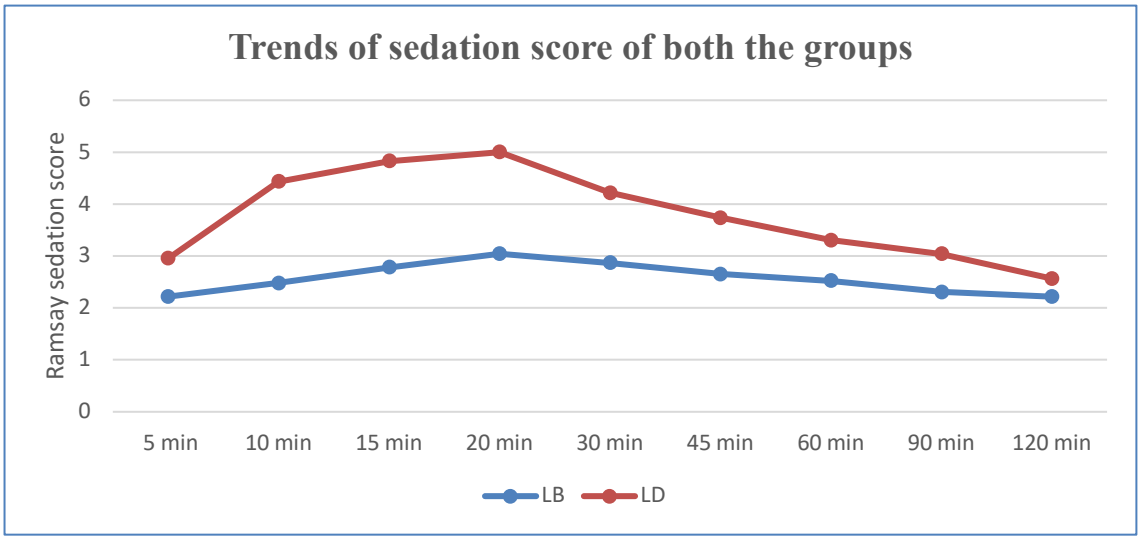

Figure 3: Trends of sedation score of both the groups

Discussion

Lower limb orthopaedic surgery is the most common major lower limb operation. Spinal and epidural anaesthesia may offer advantages over general anaesthesia including reduced stress response to surgery and analgesia, which generally extends into the postoperative period [8]. Epidural analgesia offers superior pain relief and early mobilization especially when local anaesthetic dose is combined with an adjuvant [9].

The use of Dexmedetomidine [10-16] and Butorphanol [17-20] as epidural adjuvants has been studied by various authors and observed its synergism with local anaesthetics without any additional morbidity. However there is scarcity of comparative studies between Dexmedetomidine and Butorphanol as epidural adjuvants to Levobupivacaine.

In our study both the groups' demographic profile, ASA physical status, duration of surgery, hemodynamic parameters were statistically comparable. Study drug dosage of epidural Dexmedetomidine1μg/kg and for epidural Butorphanol 10μg/kg was chosen based on previous studies.

In our present study Dexmedetomidine group took shorter time for sensory block to reach T10 level than Butorphanol group. However the difference in duration of sensory block to reach T10 level was not statistically significant. This corroborates with the study done by Fatima *et al* [21]. This study shows statistically significant difference for time taken for block to reach highest dermatomal sensory level among the two groups, with Dexmedetomidine group having the shorter time than Butorphanol group. Fatima *et al* [21] had found no statistical difference among the two groups. Verma *et al* [22] compared intrathecal. Dexmedetomidine and Fentanyl as adjuvants to Bupivacaine, found no statistically significant difference regarding time taken for block to reach highest dermatomal level.

In this study even though the proportion of patients on Dexmedetomidine reaching higher dermatomal level of sensory block (T4) was more than in Butorphanol group, but the difference was not statistically significant [16,21,22]. The reason for peak sensory level being insignificant is due to the fact that associated sympathetic block is usually near maximal with the doses used for spinal anaesthesia, epidural adjuvants addition had no influence on near maximal action of sympathetic block of Levobupivacaine. Time taken for S-2 level regression of sensory block was more for Dexmedetomidine than Butorphanol, which was statistically significant. This finding was concordant with the study by Fatima *et al*. [21] Gupta *et al* [22], Mahendru *et al* [23], Oriol-lopez *et al* [24]. In our study time taken to achieve Bromage score 0was significantly longer for Dexmedetomidine than Butorphanol [23,25]. Motor block induced by spinal injection of Levobupivacaine might be prolonged by intrathecal and systemic absorption of Dexmedetomidine, which was partially dependent on activation of α2 adrenoceptor. Time to rescue analgesic was significantly more for Dexmedetomidine than Butorphanol group which corroborates with other studies [16,21-23]. The mechanism of action by which intrathecal α2-adrenoceptor agonists prolong the motor and sensory block of local anaesthetics is not well known. The local anaesthetics act by blocking sodium channels, whereas the α2-adrenoceptor agonist acts by binding to pre-synaptic C-fibres and post-synaptic dorsal horn neurons. The analgesic action of intrathecal α2-adrenoceptor agonists is by depressing the release of C-fiber transmitters and by hyperpolarisation of post-synaptic

dorsal horn neurons [26]. It may be an additive or synergistic effect secondary to the different mechanisms of action of the local anaesthetics and the α2-adrenoceptor agonist as studied by Salgado *et al*. [27]. This antinociceptive effect may explain the prolongation of the sensory block when added to spinal anaesthetics. The prolongation of the motor block of spinal anaesthetics may be due to the binding of α2-adrenoceptor agonists to motor neurons in the dorsal horn.

In this study although there were sporadic statistically significant changes in haemodynamic parameters in some occasions, non consistent in pattern, without haemodynamic instability. Bradycardia was significantly more with Dexmedetomidine group [21]. It may be attributed to the dose-dependent effect, mediated primarily by the decrease in sympathetic tone, partly by baroreceptor reflex and enhanced vagal activity [28].

Greater proportion of hypotension was found in Dexmedetomidine than Butorphanol ($p<0.05$) [21,22].Probably due to the dominant action of α2-adrenoceptor agonists, centrally mediated sympatholysis and by the inhibition of neurotransmission in sympathetic nerves by Dexmedetomidine [28].

Higher incidence of nausea and vomiting was found in Butorphanol group, but not statistically significant [21-23]. The incidence of nausea and vomiting following intrathecal and epidural opioids like Butorphanol is approximately 30%. Most probably due to cephalad migration of drug in cerebrospinal fluid and subsequent interaction with opioid receptors located in the area postrema [29].

In our study there was no incidence of respiratory depression. Epidural opioids can cause urinary retention by inhibition of sacral parasympathetic nervous system outflow which causes detrusor muscle relaxation and an increase in maximal bladder capacity leading to urinary retention [29]. In our study there was no incidence of urinary retention in any of the groups which can be due to their low dosage.

There was only one case of shivering in each group out of a total of 46 patients, which can be attributed to the anti-shivering properties of both Dexmedetomidine and Butorphanol.

In our study none of the patients had pruritus. This can be due to the low dosage of the drug used.

Post-operative VAS score showed that Dexmedetomidine group had statistically the most favourable profile than the Butorphanol group [16,21].

Sedation score [30] was more for Dexmedetomidine group and it was statistically significant [14,21,24]. The sedative effects of α2 adrenoceptor agonists are mediated by the activation of presynaptic α2 adrenoceptors in the locus ceruleus, which inhibit the release of norepinephrine.

Conclusion

Epidural Dexmedetomidine at 1μg/kg dosage seems to be a better alternative than epidural Butorphanol at 10 μg/kg dosage when combined as an adjuvant to intrathecal 0.5% hyperbaric Levobupivacaine in lower limb orthopaedic surgical procedures. It has an excellent quality of postoperative analgesia with minimal adverse effects.

Limitations of the study

The baricity of hyperbaric Levobupivacaine not determined. Height of the patients could not be measured due to non-ambulatory patients.

Presence of ceiling effect and any significant effect at a higher dose range was not determined. Large sample size could have increased the strength of this study.

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