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Effects of Epidural Dexmedetomidine and Low-Volume Bupivacaine on Postoperative analgesia after Orthopedic Lower-Limb Surgery

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Abstract

Introduction: Postoperative pain after orthopedic lower limb surgery is a major interest. Epidural analgesia is considered the preferable method of postoperative analgesia for orthopedic lower limb surgery in many countries. Dexmedetomidine is an α-2 agonist, which has many beneficial effects when administered epidurally.

Material and Methods: A total of 50 patients who were 20–60 years of age, had ASA physical status I–II, and who were undergoing elective orthopedic lower limb surgery were randomly divided into two equal groups: group D received continuous epidural infusion at the rate of 2.5 ml/hr containing a mixture of bupivacaine 0.125% and dexmedetomidine 0.2 μg/kg and group B received only 0.125% bupivacaine at 5 ml/h rate for postoperative analgesia. Postoperative pain was scored by visual analogue scale; ramsay sedation score and cardio-respiratory parameters were recorded every hourly till 6 hours and after that every 6 hourly for 48 hours postoperatively. Data were recorded and statistically analyzed.

Results: The demographic data were comparable in both groups. Visual analogue scale of pain showed a significant reduction between the two groups at both rest and movement, and the requirement of rescue analgesia (diclofenac 75 mg IM) during the study period was significantly reduced (P value=0.0006) in group D (1.21

± 0.89) than in group B (2.64 ± 1.74) Sedation scores were significantly higher in group D compared with group B. Heart rate was significantly reduced in group D from 18 h postoperative until the end of the study, and the mean arterial blood pressure was significantly reduced in group B than in group D from 5 hours postoperative until the end of the study.

Conclusion: Dexmedetomidine is an ideal adjuvant to epidural bupivacaine for postoperative analgesia in patients undergoing orthopedic lower limb surgery.

Keywords: bupivacaine, dexmedetomidine, continuous epidural infusion, orthopedic surgery

Introduction

Planning for proper postoperative pain management is an essential component of good anaesthetic practice since the consequences of untreated pain can be devastating. Adequate analgesia aids to restore normal functions including ventilation, coughing and mobility, thereby facilitating early rehabilitation and shortened hospital stay.[1]

The epidural route is more popular for postoperative pain management as the technique can be used alone or in combination with general anaesthesia. Epidural technique has been found to provide better pain relief than systemic opioids and also decreased incidence of post-operative complications. Adjuvants are co-administered with local anaesthetics in epidural route to improve the speed of onset, duration of analgesia and to reduce the dose thereby eliminating quite a few side effects associated with larger doses. Nowadays trend of addition of several adjuvants like ketamine, tramadol, fentanyl, clonidine, dexmedetomidine etc. in epidural analgesia to modify local anaesthetic drug effect and reduce side effects.[2]

The epidural administration of drugs via continuous infusion or intermittent bolus is a well established technique. Continuous infusion not only produces a constant block to maintain analgesia and minimize cardiovascular disturbances, it also reduces the medical and nursing workload. Continuous epidural infusion provide superior analgesia with fewer side effects and no tachyphylaxis.[3]

Bupivacaine is a long-acting, effective local anaesthetic that is commonly administered by the epidural route for the relief of postoperative pain. The concentration of bupivacaine exceeding 0.125% may be associated with excessive motor blockade when used in epidural infusions in the lumbar region.[4]

Dexmedetomidine is an opioid-sparing adjuvant to epidural administration. Dexmedetomidine is a potent and highly selective α-2 adrenoceptor agonist. It has a relatively high ratio of α2/α1 activity (1620:1). The improved specificity of dexmedetomidine for the α-2 receptor causes it to be a much more effective sedative and analgesic agent, with much less unwanted cardiovascular effects from α-1 receptor activation.[5]

The aim of the study was to provide effective postoperative analgesia with hemodynamic stability through reduction in the amount of local anesthetic administered epidurally using dexmedetomidine as an adjuvant to epidural bupivacaine.

Materials And Methods

50 adult patients of ASA grade I and II, of either sex, belonging to 20-60 years of age, planned for elective lower limb orthopedics surgeries were selected for this prospective, single-blind, randomized controlled study after taking institutional ethical committee approval and informed written consent from all patients. The procedure was explained to the patient in details.

Patients were randomly divided into two groups (25 patients in each group)

GROUP D [Dexmedetomidine group] patients received continuous epidural infusion of {Inj. Bupivacaine 0.125 % + Inj. Dexmedetomidine 0.2 mcg/kg } @ 2.5 ml/hr.

GROUP B [Bupivacaine group] patients received continuous epidural infusion of Inj. Bupivacaine 0.125 % Only @ 5 ml/hr

Inclusion Criteria: (1) Patients with ASA physical status Classes I and II (2) Scheduled for elective lower limb orthopedic surgery. (3) Adult patients of age group 20–60 years.

Exclusion Criteria: (1) Patient refusal (2) Patients with cardio-respiratory disorders, renal and/or hepatic disorders (3) Contraindications for epidural anaesthesia. (4) Patients having bleeding disorders. (5) Patients with neurological and spine deficit. (6) Patients with local skin infection. (7) Patients who are morbid obese. (8) History of allergy or sensitivity to any of the study drugs in previous surgeries.

Technique

First, IV line was taken, and each patient was preloaded with 15ml/ kg of Ringer's lactate solution before procedure. Pulse oximeter, non-invasive blood pressure monitoring and ECG were attached and base line reading was taken.

Under all aseptic and antiseptic precautions, a skin wheal was raised at L2- L3 and L3- L4 interspace with of 2% Lignocaine. The epidural space was identified using 18G sterile disposable Tuohy needle with hanging drop technique at L2- L3 interspace. Then 20G portex epidural catheter was passed through the epidural needle in upward direction till about 4cms of the catheter was in the space. The needle was withdrawn, and the catheter was fixed to the back using adhesive tape.

Subsequently, a 23-G spinal needle was advanced at L3–L4 intervertebral space (one interspace below the catheter) through an introducer until cerebrospinal fluid was obtained, then 15 mg 0.5% heavy bupivacaine was injected and the spinal needle was withdrawn and the patient was laid in the supine position.

Intraoperatively level of sensory and motor blockade, blood loss, urine output and other routine monitors described above were observed. No narcotics were administered during the intraoperative period.If there was no effect of spinal anaesthesia, general anaesthesia was given and these cases were excluded from the study.

After completion of the surgery, patient was shifted to postoperative ward and monitoring was continued. In the Immediate postoperative period, **study drug** was given through epidural catheter as continuous infusion after confirming its proper position as follows: Group D (Dexmedetomidine group) received epidural injection of a mixture of 0.125% bupivacaine and 0.2 mcg/kg dexmedetomidine at rate of 2.5 ml/h, whereas Group B (Bupivacaine group) received only epidural injection of 0.125% bupivacaine at 5ml/h rate.

The postoperative data (e.g. pain, sedation) and cardiorespiratory parameters (heart rate, mean arterial blood pressure, respiratory rate and oxygen saturation) were monitored and recorded every hourly for first 6 hour and after that every 6 hourly for 48 h postoperatively. Quality of sedation after giving the study drug was based on Ramsay sedation score. Postoperative pain was assessed using a 10-point VAS (0 - no pain and 10 - worst pain). As and when the patient complains of further pain during the period of observation, intensity of pain was assessed using VAS to

know the effect of the study drug given. If it was more than 4, rescue analgesia was given in form of Inj. Diclofenac 75 mg IM. (Provided RFT is normal)

Patients were watched for any complications like Nausea, vomiting, headache, respiratory depression, pruritus, bradycardia and hypotension. Urinary retention could not be studied, as most patients in the study had indwelling urinary catheter inserted as part of the surgical management.

Master chart was prepared for all patients. Statistical analysis was prepared using GraphPad software and mean value was calculated for each parameter and P value < 0.05 was considered significant.

Statistical Analysis

Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean + SD (Min-Max) and results on categorical measurements are presented in Number (%).Demographic data was analysed using Student's t-test assuming equal variance for both the study groups.Efficacy of analgesia, VAS scores, Ramsay sedation scores and hemodynamic parameters were analysed using Student t test (two tailed, unpaired). P value < 0.05 was considered statistically significant.The statistical software namely Instat 3 was used for the analysis of the data and to find the significance of each parameter between the two groups.Microsoft word and Excel have been used to generate graphs, tables etc.

Results

The demographic data of the patients in the two groups were comparable with respect to age, sex and weight (Table 1). Heart rate was significantly reduced in group D from 18 h postoperative until the end of the study (Table 2). In contrast to heart rate, the mean arterial blood pressure was significantly reduced in group B than in group D from 6 h postoperative until the end of the study (Table 3). VAS of pain showed a significant reduction between the two groups at both rest and movement (Table 4,5) throughout the study period. Dexmedetomidine is a potent sedative agent, which can be observed in the present study findings, as the sedation score was significantly higher in group D compared with group B (Table 6). Table 7 shows that the total rescue analgesia requirement during the study period was significantly reduced in group D (1.21 ± 0.89) compared to group B (2.64 ± 1.74)

There was insignificant difference between the two groups with respect to SpO2 and Respiratory Rate.

Table 1: Demographic data

Parameters	Group D (n=25)	Group B (n=25)	P Value	Result
AGE (Yrs)	32.12 ± 9.94	34.44 ± 13.35	0.4892	NS
SEX RATIO (M:F)	17 : 8	17 : 8		
WEIGHT (Kg)	55.24 ± 10.29	55.12 ± 9.34	0.9657	NS

Table 2: Mean Heart rate (Beats/min)

Time Interval	Group D	Group B	P value
Baseline	87.6 ± 6.95	88.76 ± 5.75	0.5236
1 hour	86.64 ± 6.34	87.92 ± 6.11	0.4708
2 hours	85.52 ± 5.90	87.64 ± 6.58	0.2363
3 hours	84.64 ± 4.15	86.56 ± 6.59	0.2237
4 hours	84.32 ± 5.15	86.48 ± 5.97	0.1771
5 hours	84.16 ± 4.24	86.28 ± 6.09	0.1596
6 hours	83.92 ± 3.80	86.08 ± 5.71	0.1219
12 hours	83.44 ± 3.24	85.88 ± 5.43	0.0596
18 hours	82.8 ± 3.32	85.68 ± 6.47	0.0534
24 hours	80.56 ± 5.53	85.04 ± 5.61	0.0067
30 hours	79.28 ± 5.35	84.64 ± 7.63	0.0060
36 hours	77.92 ± 4.42	85.24 ± 7.62	< 0.0001
42 hours	74.32 ± 5.09	83.88 ± 7.08	< 0.0001
48 hours	72.28 ± 4.27	83.32 ± 7.33	< 0.0001

Table 3: Mean Blood Pressure (in mm Hg)

Time Interval	Group D	Group B	P value
Baseline	93.52 ± 4.66	96.2 ± 5.24	0.0620
1 hour	93.24 ± 4.76	95.48 ± 3.28	0.0586
2 hours	93.08 ± 2.84	92.96 ± 2.85	0.8821
3 hours	91.96 ± 2.99	91.4 ± 3.34	0.5352
4 hours	90.08 ± 4.62	88.8 ± 5.24	0.3642
5 hours	89.18 ± 7.25	87.72 ± 4.17	0.3936
6 hours	88.68 ± 5.48	85.68 ± 4.87	0.0463
12 hours	89.12 ± 3.92	85.88 ± 5.09	0.0151
18 hours	88.28 ± 5.74	84.4 ± 3.84	0.0072
24 hours	87.84 ± 7.09	83.24 ± 4.75	0.0097
30 hours	85.44 ± 6.34	81.44 ± 3.90	0.0365
36 hours	87.48 ± 6.18	81.56 ± 6.18	0.0208
42 hours	87.12 ± 4.99	78.6 ± 5.07	< 0.0001
48 hours	85.52 ± 5.65	77.28 ± 4.00	< 0.0001

Table 4: Mean VAS (At Rest)

Time Interval	Group D	Group B	P value
Baseline	2.56 ± 0.65	3.24 ± 0.52	0.0002
1 hour	2.52 ± 0.51	3.08 ± 0.76	0.0036
2 hours	2.48 ± 0.51	3.04 ± 0.54	0.0004
3 hours	2.44 ± 0.51	3.00 ± 0.58	0.0007
4 hours	2.40 ± 0.51	2.96 ± 0.54	0.0004
5 hours	2.36 ± 0.49	2.88 ± 0.67	0.0030
6 hours	2.32 ± 0.48	2.92 ± 0.49	< 0.0001
12 hours	2.36 ± 0.57	2.80 ± 0.58	0.0094
18 hours	2.32 ± 0.56	2.84 ± 0.47	0.0009
24 hours	2.36 ± 0.57	2.76 ± 0.44	0.0078
30 hours	2.12 ± 0.66	2.64 ± 0.57	0.0045
36 hours	1.92 ± 0.58	2.56 ± 0.57	< 0.0001
42 hours	1.56 ± 0.51	2.44 ± 0.51	< 0.0001
48 hours	1.48 ± 0.59	2.36 ± 0.49	< 0.0001

Table 5: Mean VAS (At Movement)

Time Interval	Group D	Group B	P value
Baseline	3.64 ± 0.70	4.08 ± 0.49	0.0132
1 hour	3.40 ± 0.76	4.04 ± 0.73	0.0039
2 hours	3.28 ± 0.84	4.00 ± 0.71	0.0020
3 hours	3.24 ± 0.59	3.96 ± 0.84	0.0011
4 hours	3.28 ± 0.68	3.92 ± 0.70	0.0019
5 hours	3.32 ± 0.63	3.84 ± 0.62	0.0050
6 hours	3.28 ± 0.68	3.88 ± 0.60	0.0018
12 hours	3.24 ± 0.66	3.88 ± 0.53	0.0004
18 hours	3.36 ± 0.86	3.84 ± 0.75	0.0407
24 hours	3.36 ± 0.76	3.80 ± 0.65	0.0327
30 hours	3.20 ± 0.65	3.72 ± 0.61	0.0054
36 hours	3.08 ± 0.40	3.60 ± 0.58	0.0006
42 hours	2.60 ± 0.50	3.52 ± 0.51	< 0.0001
48 hours	2.36 ± 0.49	3.44 ± 0.51	< 0.0001

Table 6: Mean Ramsay Sedation Score

Time Interval	Group D	Group B	P value
Baseline	1.36 ± 0.49	1.08 ± 0.28	0.0167
1 hour	1.56 ± 0.51	1.20 ± 0.41	0.0084
2 hours	1.64 ± 0.49	1.24 ± 0.44	0.0039
3 hours	1.68 ± 0.48	1.36 ± 0.57	0.0369
4 hours	1.72 ± 0.46	1.44 ± 0.51	0.0470
5 hours	1.80 ± 0.65	1.44 ± 0.51	0.0343
6 hours	1.84 ± 0.62	1.48 ± 0.51	0.0296
12 hours	1.88 ± 0.67	1.52 ± 0.51	0.0377
18 hours	1.96 ± 0.73	1.56 ± 0.65	0.0462
24 hours	1.92 ± 0.64	1.52 ± 0.51	0.0183
30 hours	1.96 ± 0.54	1.48 ± 0.51	0.0022
36 hours	1.92 ± 0.49	1.52 ± 0.51	0.0068
42 hours	1.96 ± 0.54	1.48 ± 0.51	0.0034
48 hours	2.08 ± 0.49	1.56 ± 0.51	0.0006

Table 7: Total Rescue Analgesia Requirement

Time Interval	Group D (Out of 25 Pts)	Group B (Out of 25 Pts)
Baseline (0 hour)	2	4
1 hour	1	5
2 hours	3	6
3 hours	1	4
4 hours	2	3
5 hours	1	3
6 hours	1	3
12 hours	1	2
18 hours	2	2
24 hours	2	2
30 hours	1	2
36 hours	0	1
42 hours	0	0
48 hours	0	0
Mean ± SD	1.21 ± 0.89	2.64 ± 1.74
P value	0.0006 = Extremely Significant	

Discussion

Major orthopedic lower limb surgery is associated with intense early postoperative pain. So that, Improving this pain management techniques and rehabilitation programs have significant impact on postoperative outcome.[7] The early ambulation and participation in the physical therapy to restore the range of movement of the joint after major orthopedic surgery are facilitated by excellent early analgesia.[6] Early ambulation and rehabilitation are essential for normal function of the fibroblasts and chondrocytes, which enhance normal healing.[8] Prolonged immobilization can lead to muscle atrophy, cartilage ulceration, and development of

connective tissue adhesions.[8] Continuous epidural infusion reduces the risk of thromboembolic complication like DVT which is associated with Prolonged immobilization after major orthopedics surgery. We concluded that the early rehabilitation, which is facilitated with continuous epidural infusion postoperatively in the present study, can help to prevent complications from immobilization and to promote early recovery of the joint function postoperatively.

Epidural analgesia with opioid and/or local anaesthetics provides superior pain relief compared with other previous techniques. However, it is associated with side effects, such as nausea, pruritus, urinary retention, and respiratory depression with opiates, and bilateral motor blockade and arterial hypotension with local anaesthetics.[6,9,10]

Hence, in the present study we have tried to reduce these complications and provide suitable postoperative analgesia for patients undergoing major orthopedic lower limb surgery by adding non-opioid α-2 agonist agent- dexmedetomidine to low-volume bupivacaine through continuous epidural infusion.

Epidural dexmedetomidine is an α-2 agonist, which has numerous beneficial effects.[11] It acts on both presynaptic and postsynaptic sympathetic nerve terminal and central nervous system, thereby decreasing the sympathetic outflow and nor epinephrine release causing sedative, anti anxiety, analgesic, sympatholytic, and hemodynamic effects.[11,12]

In Our study, we found that Mean heart rate does not reduced much in both the groups till 18 hours After that significantly reduced in group D compared to Group B till the end of the study(P value < 0.05). This decrease in heart rate caused by α-2 agonist can be explained by its central action decreasing the sympathetic outflow and nor-epinephrine release. In contrast to heart rate results, the mean arterial pressure was decreased in both groups from the baseline, with a significant decrease in the Group B than in the Group D after 5 hours to end of study (P < 0.05) ,which can be explained by using lower volume (2.5 ml/h) of local anesthetic in group D than (5 ml/h) in group B. Although this decrease in heart rate and mean arterial blood pressure was reported in the dexmedetomidine group, it rarely going less than 20% of the baseline values, which proved that the use α-2 agonist- dexmedetomidine as an adjuvant provides a hemodynamic stability during the postoperative period.

In our study, there is no statistical difference found between patients of both groups with respect to Respiratory Rate and Oxygen Saturation (P value > 0.05).

SJS Bajwa et al,[12] observed a more prominent reduction in heart rate in patients receiving epidurally 1mcg/kg dexmedetomidine compared to 1mcg/kg fentanyl as adjuvant to 15 ml of 0.75% ropivacaine undergoing lower limb orthopedics surgery. They also reported significant decreases in MAP compared with baseline in both groups of patients.

Shilpi Agrawal et al,[13] in their study found hemodynamically, highly significant fall in pulse rate and blood pressure in patients receiving epidurally 50 mcg (1 ml) dexmedetomidine compared to 75mcg (1 ml) clonidine as an adjuvant to 16 ml of 0.5% bupivacaine in infraumbilical surgeries. They also found that all patients of dexmedetomidine group had no significant change in their oxygen saturation and respiratory rate while in clonidine group there was no change in respiratory rate but there was significant change in oxygen saturation as compared to pre- epidural value.

Neerja Bharti et al,[14] in their study of analgesic efficacy of 50 mcg dexmedetomidine versus 50 mcg fentanyl as

an adjunct to 10 ml 0.125% bupivacaine via thoracic epidural in patients undergoing upper abdominal surgery noticed a significant decrease in the heart rate in both groups as compared with their baseline value, whereas heart rate in the dexmedetomidine group was significantly lower than the fentanyl group during the intraoperative as well as in the postoperative period. However, there was no significant fall in blood pressure in either group.

In Our study, we noticed group D patients postoperative mean VAS score at rest and at movements significantly less compared to group B patients. We also noticed that total rescue analgesia requirement during the study period was significantly reduced in group D (1.21 ± 0.89) than in group B (2.64 ± 1.74) indicating superiority for postoperative analgesia in group D patients. The analgesic effect of dexmedetomidine is mediated by its action at the brain, brainstem, spinal cord and peripheral tissues. Dexmedetomidine causes hyperpolarisation of nerve tissues by altering transmembrane action potential and ion conductance at the brainstem locus ceruleus. In the spinal cord, the analgesic effect is related to the activation of the descending medullospinal noradrenergic pathway or to the reduction of spinal sympathetic outflow at presynaptic ganglionic sites.[14]

Elhakim et al,[5] evaluated the effects of dexmedetomidine administration in thoracic epidural in patients undergoing thoracic surgery and reported significantly decreased consumption of intraoperative fentanyl and improved postoperative analgesia in patients receiving dexmedetomidine as compared with bupivacaine only.

Arindam Sarkar et al,[15] In their study found that rescue analgesia need was lower in dexmedetomidine group where only 6.7% patients required more than 3 rescue dosages compared to fentanyl group, where 80% of patients required more than 3 rescue analgesic dosages.

Gill et al,[16] also recorded lower 24 hours analgesic need in dexmedetomidine as compare to fentanyl group.

Bajwa et al,[12] have also shown that dexmedetomidine provided superior postoperative analgesia compared with fentanyl in patients undergoing orthopaedic procedures under regional anaesthesia. The study found less postoperative ropivacaine consumption over 24 hours in the dexmedetomidine group with comparable VAS scores.

In our study, Ramsay sedation score (RSS) was significantly higher in group D compared with group B throughout whole study(P value<0.05). Dexmedetomidine exerts its sedative effects through central actions in the locus coeruleus.

Safiya I Shaikh et al,[17] in their study clearly showing the effectiveness of epidural dexmedetomidine as adjuvant to bupivacaine in providing sedation, more patients in dexmedetomidine group had sedation score 3 and were arousable by gentle tactile stimulation as compared to clonidine group patients undergoing lower limb orthopedics surgeries.

Shilpi Agrawal et al,[13] clearly indicated in their study that epidural dexmedetomidine produced profound sedation in 46.6% patients who were arousable by gentle tactile stimulation (grade-3) compared to achievement of similar sedation level in 13.3% in clonidine group, and statistically this difference was found to be significant (P < 0.05)

Conclusion

Then after further comparisons with previous works of different authors in the similar or nearly similar direction, we were able to conclude that:

Dexmedetomidine is an ideal adjuvant to continuous epidural bupivacaine for postoperative analgesia in patients undergoing lower limb Orthopedics surgery because of its stable hemodynamics, prolonged postoperative analgesia and superior sedation levels with reduction in epidural local anesthetic volume and postoperative rescue analgesic requirements.

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