



A COMPARATIVE STUDY OF DEXMEDETOMIDINE AND FENTANYL AS AN ADJUVANT TO EPIDURAL BUPIVACAINE IN LOWER LIMB SURGERIES

Anaesthesiology

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ABSTRACT

Background: Epidural anesthesia is the most commonly used technique for inducing surgical anesthesia and postoperative analgesia in patients undergoing lower limb surgeries. Fentanyl as an adjuvant to epidural local anesthetic has been used for a long time. Dexmedetomidine is a potent and highly selective α -2-adrenoceptor agonist with analgesic potency.

Aim: The aim of the present study was to compare the effect of dexmedetomidine and fentanyl as an adjuvant to epidural bupivacaine in lower limb surgeries.

Materials And Methods: Sixty patients belonging to the American Society of Anesthesiologists' Grade I or II who were undergoing lower limb surgery were randomly divided into two groups. Group BD: received epidural study solution of 38 ml of 0.25% bupivacaine hydrochloride + 1 ml of 100 μ g dexmedetomidine + 1 ml of normal saline. Group BF: received epidural study solution of 38 ml of 0.25% bupivacaine hydrochloride + 2 ml of 100 μ g fentanyl. Onset and maximum level of sensory blockade, time to attain maximum sensory level, time to complete motor blockade, time for two-segment regression, duration of analgesia and motor block, heart rate, and blood pressure were observed. Pain and sedation were assessed by numerical rating scale and Ramsay Sedation Scale, respectively. Data were recorded and statistically analyzed.

Results: The onset of sensory blockade and time to attain maximum sensory level in Group BD were earlier than that of Group BF ($P < 0.001$). Duration of analgesia and motor blockade in Group BD were significantly more than that of Group BF ($P < 0.001$). Postoperative visual analog scale was reduced statistically significantly in Group BD ($P < 0.001$).

Conclusion: Dexmedetomidine as an adjuvant to epidural bupivacaine is a better alternative to fentanyl with higher analgesic property.

KEYWORDS

Dexmedetomidine, fentanyl, epidural, anesthesia

INTRODUCTION

Epidural anesthesia is the most commonly used technique for inducing surgical anesthesia and postoperative analgesia in lower abdominal and limb surgeries. Postoperative pain management is one of the most important areas of anesthesia. Early postoperative mobilization and rehabilitation with minimally associated pain and discomfort is the most desirable quality that has been needed in modern orthopedic surgery. For achieving this effect, large volumes of local anesthetics were used which also increase the possibilities of local anesthetic toxicity and hemodynamic instability.

Fentanyl acts as an agonist at μ -opioid receptors to enhance the analgesia, it is 100 times more potent than morphine. Dexmedetomidine is a potent and highly selective α -2-adrenoceptor agonist. It has a relatively high ratio of α -2/ α -1 activity (1620:1). The improved specificity of dexmedetomidine for the α -2 receptor causes it to be with much more effective sedative, anxiolytic, analgesic, antihypertensive, and sympatholytic properties with much less unwanted cardiovascular effects from α -1 receptor activation. It improves the quality of perioperative anesthesia and analgesia.

The aim of the present study was to compare the effect of dexmedetomidine and fentanyl as an adjuvant to epidural bupivacaine in lower limb surgeries.

MATERIAL AND METHODS

The present prospective randomized study was done in sixty patients aged between 18 and 60 years of both sex. Patients belonging to the American Society of Anesthesiologists (ASA) Grades I and II posted for lower limb surgeries were included in the study. Patients not willing to be a part of the study, having local skin infection along lumbar spine, spinal deformity, chronic backache, headache, drug addiction, neurological deficit, bleeding/clotting disorder, cardiovascular disease, systemic metabolic disorders such as severe hepatic or renal disease, and a history of treatment with antihypertensive were excluded from the study. All the sixty enrolled patients were randomly divided into two groups: Group BD and Group BF.

- Group BD (n = 30): Received epidural study solution of 38 ml of 0.25% bupivacaine hydrochloride + 1 ml of 100 μ g dexmedetomidine + 1 ml of normal saline
- Group BF (n = 30): Received epidural study solution of 38 ml of 0.25% bupivacaine hydrochloride + 2 ml of 100 μ g fentanyl keeping the total volume of 40 ml in both the groups.

Every patient was evaluated with a thorough preanesthetic checkup including routine preoperative investigations one day prior to the surgery. Patients were asked to have 6–8 h fasting before surgery. On entering operation theater, baseline (preoperative) vital parameters such as noninvasive blood pressure, pulse oximetry, and electrocardiography were recorded and intravenous (IV) line was secured. All the patients were catheterized with Foley's catheter before induction. Bupivacaine hydrochloride sensitivity test was done in all the patients. All patients were reassured about the anesthetic procedure. All vital signs were recorded.

Under all aseptic conditions, local infiltration was done with 2 ml of 1% lignocaine using 26-gauge needle in sitting position. An 18-gauge Tuohy's needle was introduced into the epidural space at the L3–L4 lumbar inter space using the loss-of-resistance technique. With the bevel of the Tuohy needle in cephalic direction, an epidural catheter was inserted 5 cm into the epidural space and secured. The position of catheter was checked by aspiration for blood or cerebrospinal fluid. A test dose of 60 mg lignocaine containing 1:200,000 epinephrine was administered to detect intrathecal or IV injection and patients turned to supine position. After 3 min, the study drug solution was administered at the rate of 1 ml/3 s through the epidural catheter.

The onset of sensory blockade with maximal cephalic spread was assessed by bilateral pinprick method along the midclavicular line using a short-beveled 26-gauge hypodermic needle using a 3-point scale: 0 = normal sensation, 1 = loss of sensation of pin prick (analgesia), and 2 = loss of sensation of touch (anesthesia).

The motor block was assessed by Bromage 3-point score for the lower

extremity (0–3); 0: no motor impairment (able to move the hip, knee, and ankle joints); 1: unable to raise either extended leg (able to move joints of knee and ankle); 2: unable to raise extended leg and flex knee (able to move joint of ankle); and 3: unable to move the knee and foot.

The following block characteristics were observed and recorded:

1. Onset of sensory block: It is defined as the time interval between administrations of local anesthetic epidurally to the loss of pinprick sensation at the site of surgical incision
2. Maximum level of sensory blockade: It is the maximum sensory dermatome level after 30 min of administering the local anesthetic in the epidural space
3. Time to attain maximum sensory level: It is defined as the time in minutes at which maximum sensory level was attained after administering the drug epidurally
4. Time to complete motor blockade: It is defined as the time interval between administering of drug epidurally to complete loss of motor activity (modified Bromage scale score of 0–3)
5. Time for two-segment regression: It is defined as the interval between the onset of analgesia epidurally to regression of two segments from the maximum sensory level attained
6. Duration of analgesia: The duration of analgesia was taken from the time of epidural drug administration to the time of first supplementation with rescue analgesic
7. Duration of motor block: Duration of motor block was recorded from the onset time to time when the patient was able to lift the extended leg
8. Postoperative pain: It was assessed using a 10-point numerical rating scale (NRS) (0 = no pain and 10 = worst pain imaginable)
9. Grading of sedation: It was evaluated using Ramsey sedation scale (1 = awake, conscious, no sedation; 2 = calm and compose; 3 = awake on verbal command; 4 = brisk response to gentle tactile stimulation; 5 = awake on vigorous shaking; and 6 = unarousable). Sedation scores were recorded just before the initiation and at every 20 min during surgery. Maximum sedation score was noted.

Intraoperatively, supplemental oxygen was given. For the present study, hypotension was defined as a fall in systolic blood pressure of more than 20% of baseline value or <100 mmHg and was treated with volume expansion and, if required, by incremental doses of mephentermine 3–6 mg. Bradycardia (heart rate < 50/min) was treated with 0.3 mg of IV atropine.

Statistical Analysis

Statistical analysis was done using SPSS version 11.0 (IBM Corporation) software. t-test, Chi-square test, repeated ANOVA, and Mann–Whitney test were applied according to the requirement. The level of significance was fixed at 95%. $P < 0.05$ was considered statistically significant.

RESULTS

The demographic data of the patients in the two groups were comparable with respect to age, sex, weight, height, ASA status, and duration of surgery ($P > 0.05$) [Table 1]. The onset of sensory blockade, time to attain maximum sensory block, and complete motor block in Group BD were significantly earlier than those of Group BF ($P < 0.001$) [Table 2]. Two-segment regressions were prolonged in Group BD when compared to Group BF which was statistically significant ($P < 0.001$) [Table 2]. Duration of analgesia and motor blockade were significantly longer in Group BD than those of Group BF ($P < 0.001$) [Table 2]. There was a significant decrease in postoperative NRS in Group BD at 12, 18, and 24 h postoperatively ($P < 0.001$) [Table 3]. The maximum Ramsey sedation scores in Group BD were significantly higher than those of Group BF [Table 4] ($P < 0.001$). The incidence of side effects such as bradycardia in Group BD was significantly more than that of Group BF ($P < 0.05$), although hypotension occurred in both the groups was statistically not significant ($P > 0.05$) [Table 5].

Table 1: Demographic Parameters And Duration Of Surgery

Demographic Date	Group BD	Group BF	P value
Age (years)	45.27±10.52	47.2±8.29	0.43
Sex (Male: Female)	24:6	21:9	0.08
Weight (kg)	67.30±6.95	65.73±5.53	0.34
Height (cm)	156.13±7.04	15.6±6	0.14
ASA (I:II)	23:7	21:9	0.09
Duration of surgery (min.)	120.67±15.13	125.23±16.01	0.26

P>0.05 statistically not significant.

Table 2: Comparison Of Parameters In Two Groups

Parameters	Group BD	Group BF	P value
Onset of sensory block (min.)	7.5±1.25	8.9±1.52	0.0003*
Time to attain maximum sensory level (min.)	15.2±2.01	18.4±2.37	0.0001*
Maximum level of sensory blockade	T5	T6	0.07
Time to attain complete motor block (min.)	19.65±3.57	21.9±3.59	0.01*
Time for two-segment regression (min.)	170±15.54	140.50±11.1	0.000*
Duration of analgesia (min.)	380.32±35.93	315.16±25.39	0.000*
Duration of motor block (min.)	248±34.85	220±25.93	0.001*

* $P < 0.05$, statistically significant

Table 3: Comparison Of Duration Of Postoperative Visual Analog Scale In Two Groups

Postoperative time	Group BD	Group BF
6 th h	0.2±0.4	0.3±0.46
12 th h	2.27±0.52	2.77±0.63
18 th h	3.5±0.82	4.2±0.81
24 th h	4±0.74	4.73±0.69

Repeated measure ANOVA was applied. $P = 0.001$, which is statistically significant.

Table 4: Comparison Of Sedation Score

Sedation score	Group BD (%)	Group BF (%)
1	3(10)	18(60)
2	10(33)	7(23)
3	14(47)	5(17)
4	3(10)	0

Mann–Whitney test was applied. $P = 0.001$, which is statistically significant.

Table 5: Comparison Of Side Effects

Sedation score	Group BD	Group BF	P value
Bradycardia	11	3	0.03*
Hypotension	9	7	0.8

*Chi-square test was applied. $P < 0.05$ was considered statistically significant.

DISCUSSION

Epidural analgesia offers superior pain relief and early mobilization, especially when local anesthetic dose is combined with an adjuvant as compared to LA use alone. It permits analgesic dosing through the catheter for postoperative pain management. It also avoids invasive dural penetration and spinal hypotension. The synergism between epidural local anesthetics and opioids is well established, but evidence regarding the combination of LA with dexmedetomidine through epidural route is scarce in literature.

The use of neuraxial opioids is associated with the number of side effects, hence various other drugs including α -2 agonists are extensively evaluated as an alternative to opioids as adjuvants to neuraxial blocks with emphasis on side effects such as respiratory depression, nausea, urinary retention, and pruritis. The pharmacologic properties of α -2 agonists are extensively studied and are employed clinically to achieve analgesia, anxiolysis, hypnosis, sympatholysis, and sedation in regional anesthesia.

Earlier onset of sensory and motor block, less time for complete sensory and motor block, prolonged analgesia, and motor block can be explained by the fact that epidural dexmedetomidine has greater selectivity for α -2 receptors with greater lipid solubility. Hence, it easily penetrates the meninges. They also cause augmentation of local anesthetic effects as they cause hyperpolarization of nerve tissues by altering transmembrane potential and ion conductance at locus coeruleus in the brainstem. The increase in analgesic action of local anesthetics by the use of α -2 agonists in the epidural space may be related to the reduction of the systemic absorption of the local anesthetic effect caused by local vasoconstrictor subtypes mediated by the C2 in smooth muscle and venous epidural plexus.

The analgesic effect of dexmedetomidine is possibly produced by the

stimulation of spinal cord at the dorsal root neuron level, where α -2 agonists inhibit the release of substance P in the nociceptive pathway and also inhibit the release of norepinephrine, at the nerve endings. The spinal mechanism is considered to be mainly responsible for the analgesic effects though there is some evidence of both the supraspinal and peripheral sites of action of dexmedetomidine.

Fentanyl acts primarily as an agonist at μ -opioid receptors to enhance the analgesia. The dorsal roots (primary afferent tissues) contain opioid-binding sites and fentanyl either acts directly on the spinal nerve or by penetrating the duramater to act at the spinal roots.

In the present study, dexmedetomidine group showed an earlier onset of sensory blockade and lesser time to achieve maximum sensory level as compared to fentanyl group. Time for two-segment regression, the duration of analgesia, and motor blockade were significantly prolonged in patients in whom dexmedetomidine was used as an adjuvant with bupivacaine. Our data support previous studies that used dexmedetomidine and fentanyl as additives to epidural anesthesia.

Bajwa et al. evaluated the addition of dexmedetomidine or fentanyl to epidural ropivacaine in patients undergoing lower limb orthopedic surgeries and found that the onset and establishment of sensory anesthesia were significantly earlier, and duration of postoperative analgesia was prolonged in the dexmedetomidine group. Bajwa et al. also found the early onset of analgesia and motor blockade in epidural dexmedetomidine when used with ropivacaine. Gupta et al. found similar results with epidural dexmedetomidine when used with levobupivacaine.

In the present study, dexmedetomidine group showed significant decrease in postoperative NRS at 12, 18, and 24 h as compared to fentanyl group. Our data support a previous study conducted by Soliman and Eltaweel where they evaluated the addition of dexmedetomidine and fentanyl as an adjuvant to epidural bupivacaine in patients undergoing total knee replacement surgeries. They found that dexmedetomidine provides a better postoperative analgesia and reduces the postoperative narcotics requirements.

The decrease in the heart rate caused by α -2 agonists can be explained on the basis of their central action where they decrease the sympathetic outflow and norepinephrine release. A study conducted by Soliman and Eltaweel found that the epidural dexmedetomidine is associated with a higher incidence of bradycardia and hypotension compared to epidural fentanyl which supports our study. Eskandar et al. found that the heart rate decreased significantly, but the decrease in mean arterial pressure is not significant in dexmedetomidine group. Bajwa et al. found no significant changes in the heart rate and blood pressure by adding dexmedetomidine as an adjuvant to ropivacaine compared to the control group and the same result was shown by other studies.

The sedative effect of dexmedetomidine is probably mediated by the activation of presynaptic α -2 adrenoreceptors in the locus coeruleus, leading to inhibition of release of norepinephrine, along with it, inhibition of adenylate cyclase may lead to hypnotic response. Our study also showed that dexmedetomidine group had higher sedation scores which was supported by Salgado et al. who found that patients were more sedated with lower bispectral values in dexmedetomidine group.

The limitations of this study are the relatively small number of patients that were included and the exact dose equivalence of dexmedetomidine and fentanyl that was used in epidural anesthesia.

CONCLUSION

We conclude that dexmedetomidine as an adjuvant to epidural bupivacaine is a better alternative to fentanyl as it shows faster onset of sensory block, lesser time to attain maximum sensory level, prolonged duration of analgesia, and longer motor blockade with higher sedative property.

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