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A COMPARATIVE ANALYSIS OF THE IMPACT OF FENTANYL AND DEXMEDETOMIDINE ON POST-OPERATIVE PAIN RELIEF AND HAEMODYNAMIC PARAMETERS WHEN ADMINISTERED WITH BUPIVACAINE 0.5% IN EPIDURAL ANESTHESIA FOR PELVIC AND LOWER LIMB ORTHOPAEDIC PROCEDURES

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ABSTRACT

Background: This study was designed to investigate whether the addition of fentanyl or dexmedetomidine to bupivacaine for epidural block would prolong postoperative pain relief and reduce the need for additional analgesics block in pelvic and lower limb orthopaedic surgeries. **Objective:** Comparison of effect of 1.0 mcg/kg of Dexmedetomidine and Fentanyl 2 mcg/kg on post-operative analgesia and haemodynamic when added to bupivacaine 0.5% in epidural block for pelvic and lower limb orthopaedic surgeries. **Material And Method:** In our randomized controlled trial, a total of 75 adult patients classified as ASA class I and II, who were undergoing lower limb orthopedic and pelvic surgeries, received an epidural block. The study focused on the effects of adding dexmedetomidine and fentanyl on intraoperative hemodynamics and postoperative analgesia. One group of patients was administered 20 mL of 0.5% bupivacaine, while the other two groups received dexmedetomidine at a dosage of 1.0 mcg/kg and fentanyl at 2 mcg/kg, respectively. All patients were closely monitored for the onset of effect, intraoperative hemodynamic parameters, postoperative analgesia, and any complications that arose. **Result:** The mean time for onset of sensory block was significantly rapid in dexmedetomidine and fentanyl group as compared to bupivacaine group. The offset time of sensory and motor block was prolonged in dexmedetomidine group in comparison to control and fentanyl group. Addition of Dexmedetomidine substantially prolongs postoperative pain free period than Fentanyl and Bupivacaine. **Conclusion:** The incorporation of Dexmedetomidine, an alpha-2 agonist, into the local anaesthetic solution for lumbar epidural block at a dosage of 1.0 mcg/kg significantly extends the duration of the postoperative pain-free interval without affecting the characteristics of the block provided by Bupivacaine. Furthermore, it serves as a more effective adjuvant compared to fentanyl, an opioid; however, it also extends the duration of motor blockade, which could impede the early mobilization of patients.

Keywords: Epidural Anaesthesia, Bupivacaine, Dexmedetomidine, Fentanyl.

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INTRODUCTION

Regional anaesthesia is recognized for its exceptional safety profile and its ability to extend post-operative pain relief. Among the various techniques in modern regional anaesthesia, epidural blockade stands out as one of the most effective methods, offering improved intraoperative haemodynamic stability, enhanced post-operative pain management, and expedited recovery, particularly in pelvic and orthopaedic surgeries. Bupivacaine, a long-acting amide local anaesthetic, has been in clinical use since 1957 and is available as a racemic mixture containing equal amounts of the S (-) and R (+) isomers. Numerous adjuvants have been employed alongside bupivacaine to enhance post-operative analgesia. The earliest of these was epinephrine. Although epidural neostigmine has been utilized, it is associated with a high incidence of nausea and vomiting. Epidural opioids, including morphine, pethidine, dexmedetomidine—an alpha-2 adrenoceptor agonist that is more potent and selective than clonidine—along with buprenorphine and fentanyl, have demonstrated excellent post-operative analgesic effects, albeit with potential side effects such as respiratory depression, pruritus, sedation, nausea, and vomiting. Selective alpha-2 adrenergic agonists have been incorporated as adjuvants in epidural blockade, with clonidine hydrochloride being the first drug in this category to show clinical utility during the peri-operative period.

MATERIAL AND METHOD

A randomized comparative study was conducted to evaluate the impact of adding fentanyl and dexmedetomidine to bupivacaine 0.5% in epidural blocks for postoperative analgesia in 75 patients undergoing lower limb orthopedic and pelvic surgeries. Approval was obtained from the Hospital Ethics Committee prior to the study. The participants included individuals aged 15 to 65 years, classified as ASA Grade I or II, with weights ranging from 40 to 70 kg. Exclusion criteria encompassed patients with hematological disorders, abnormal bleeding or clotting times, psychiatric conditions, diabetes, local sepsis, spinal deformities, those who did not consent, and individuals allergic to local anesthetics. Following a thorough examination and informed consent, the patients were randomly divided into three groups of 25 each. In the operating room, intravenous access was established, and monitoring devices were set up to record baseline heart rate, electrocardiogram (ECG), pulse oximetry (SpO2), non-invasive blood pressure (NIBP), and respiratory rate. The drug syringes were prepared using strict aseptic techniques. After antiseptic preparation of the back and draping the area with sterile coverings, the designated site for epidural puncture was infiltrated with 1 mL of 2% Xylocaine solution. An 18-gauge Tuohy needle (Romsons) was used to perform the epidural puncture in the midline while the patient was in a sitting position, with the epidural space identified through the loss of resistance to air technique. The procedure was consistently performed by the same anesthesiologist. Upon locating the epidural space, a test dose of 2 mL of lignocaine hydrochloride solution containing adrenaline at a concentration of 1:200,000 was administered to prevent accidental intravascular injection or an excessive intrathecal dose. After a waiting period of 2 to 3 minutes following the test dose, patients in Group C received a single injection of 20 mL of preservative-free 0.5% bupivacaine mixed with 2 mL of water for injection. Meanwhile, Group D was administered 20 mL of preservative-free 0.5% bupivacaine combined with 1.0 mcg/kg of dexmedetomidine.

After injection of drug (As per the group assigned), patient was made to lie down supine with 10-degree head low tilt and each patient was observed for:

A. Time of onset for sensory block.
B. Time of onset of motor block.
C. Highest level of sensory block achieved (by pinprick method).

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D. Duration of sensory block.
E. Duration of motor block.
F. Intraoperative muscle relaxation (On Bromage scale).
G. Degree of sedation on Ramsay sedation scale.
H. Duration of pain free period.
I. Any adverse drug effect.
J. Any complication like bradycardia, hypotension, respiratory depression, nausea, vomiting, itching, urinary retention and shivering.

An independent observer who was totally unaware of the nature of the study, recorded blood pressure and heart rate just before and after surgical incision and then every five minutes interval till the end of surgery using multiparameters. Postoperatively, patient was monitored for offset time of epidural block (Motor and sensory regression).

Table 1: Demographic Data

Group	Group C	Group D	Group F
Age in years	48.68±10.18	42.72±11.17	44.76±11.8
Sex male	14	12	12
Female	11	13	13
Weight in kg	52.6±7.26	54.4±6.83	54.04±6.94
Height in cm	165.5±6.42	165.8±7.5	165.5±6.46

RESULTS

Demographic data of patient included in the study was comparable with respect to height, weight and mean age of patient in each group. Patients included in the study had a mean age of 45.38 years (20–60 years). Male/female ratio was 38/37. The patients included in the study were adults and had vital signs within normal limits with no comorbid condition and thus belonged to grade I/II asper ASA classification.

Table 2: Duration and Adverse Effect

Group	Group C	Group D	Group F
Mean time onset of sensory block (seconds)	679.2±86.11	627.6±58.04	628.8±65.08
Mean time onset of motor block seconds	1003.2±130.21	890.4±126.9	955.2±140.62
Duration of sensory block (Minutes)	255.2±25.55	286.8±12.85	243.8±12.85
Duration of motor block (Minutes)	205±25.5	252.8±38.02	213.6±13.58
Post-operative analgesia hrs.	4.83±0.58	10.52±1.71	5.15±0.57
Hypotension	3(12%)	5(20%)	3(12%)
Bradycardia	-	3(12%)	-
Shivering	2(8%)	-	1(4%)
Nausea	3(12%)	-	1(4%)

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Vomiting	2(8%)	-	-

The average time for the onset of sensory block was notably quicker in groups D (627.6 seconds) and F (628.8 seconds) when compared to group C (679.2 seconds); however, the difference between groups D and F was not statistically significant. Similarly, the average time for the onset of motor block was significantly shorter in groups D (890.4 seconds) and F (955.2 seconds) relative to group C (1003.2 seconds), yet the difference between groups D and F did not reach statistical significance. Regarding the mean offset time for sensory block, which was measured by the recovery of sensitivity to pinprick at the S1 dermatome, the control group exhibited a time of 255.2±25.55 minutes, while group D recorded 286.8±35.79 minutes and group F 243.8±12.85 minutes.

Group D had the longest mean offset time for sensory block. Statistically significant differences were observed between groups C and D, as well as between groups C and F, while the difference between groups D and F was not statistically significant. For the mean offset time of motor block, assessed using the Bromage scale to determine the ability to flex the ankle, the control group showed a time of 205.2±25.5 minutes, compared to 252.8±38.02 minutes in group D and 213.6±13.58 minutes in group F. Group D also had the longest mean offset time for motor block. Statistically significant differences were noted between groups C and D, and between groups D and F, while the difference between groups C and F was not statistically significant.

The longest duration of the pain-free period was observed in patients from group D, averaging 10.52±1.71 hours, followed by group F with 5.15±0.57 hours. The control group had the shortest pain-free period, recorded at 4.83±0.58 hours. The duration of analgesia was greatest in the dexmedetomidine group, with a mean value that was statistically highly significant when compared to both the fentanyl and control groups.

The post-operative pain-free period between groups C and F did not show a statistically significant difference. Incidence of shivering, nausea is more in control group than fentanyl group; none of it in dexmedetomidine group. Vomiting was seen in 8% of patients in control group, but not in dexmedetomidine and fentanyl groups.

Table 3: Highest Sensory Level Achieved

Dermatome Height	**Group C (n=25)**	**Group D (n=25)**	**Group F (n=25)**
T6	9(36%)	17(68%)	19(76%)
T8	13(52%)	7(28%)	5(20%)
T10	3(12%)	1(4%)	1(4%)

Highest Level of block achieved in these patients was up to T6 dermatome in 36% in control group, 68% in group D and 76% in group F. Sensory block up to T6 level was more in dexmedetomidine and fentanyl group than control group, but no difference between dexmedetomidine and fentanyl group.

For assessment of sedation, 6 points non-parametric scale designed by Ramsay was employed in this study. No patients from study or control group receive tranquilizer or narcotic analgesics. Sedation score of 4 was seen in 28% patients of group D: score was 3 in 18 patients of group C, 15 patients of group D and 19 patients in group F. Score was 2 in 7 patients of group C, 1 in group D and 6 in group F. No patient from any group had score 1, 5 and 6.

Table 5: Degree of Muscle Relaxation

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Muscle Power Grading	Group C (n=25)	Group D (n=25)	Group F (n=25)
1	0	0	0
2	12(48%)	8(32%)	9(36%)
3	13(52%)	17(68%)	16(64%)

In majority of the patients, degree of muscle relaxation in study and control group was acceptable and provide smooth intraoperative period. Muscle power grade 3 was seen in 68% patients in group D, 64% in patients in group F and 52% in group C. The degree of muscle relaxation can be attributed to bupivacaine and not to drugs used as an adjuvant.

Table 6: Changes in Heart Rate

Groups	Preoperative HR/bpm	Minimum HR/bpm	Changes	Bradycardia
Group C (n=25)	89.28±12.12	64.36±8.76	27.91%	0
Group D (n=25)	87.36±12.08	61.52±8.54	29.57%	3 (12%)
Group F (n=25)	85.56±11.38	64± 8.01	21.56%	0

In each group, pre-operative mean heart rate and respiratory rate was tabulated and subjected to calculations. Pre-operative mean heart rate in control group was 89.28 bpm and in group D and group F it was 87.36 and 85.56 bpm respectively. Maximum lowering of mean heart rate by 29.57% was seen in group D patients. In group C and group F, fall in mean heart rate was 27.91% and 21.56% respectively. There was incidence of bradycardia in group D in 12% patients, but not in group C and group F. Bradycardia was treated with injection Atropine 0.6 mg IV.

Table 7: Changes in Mean Arterial Pressures

Groups	Pre-Block MAP (mmHg)	MAP Minimum (mmHg)	Changes (%)	Hypotension
Group C (n=25)	95.84±7.72	77.32±6.99	19.32	3(12%)
Group D (n=25)	95.96±7.62	76.84±7.66	19.92	5(20%)
Group F (n=25)	93.32±8.5	75.28±6.64	18.04	3(12%)

Changes from preoperative mean of MAP to post block period was similar in all groups and was 19.32%, 19.92% and 19.33% in group C, D and F respectively. Incidence of hypotension (MAP <70 mmHg or decrease of more than 20%) was more in group D (20%) than group C (12%) and group D (12%) and hypotension well responded to mephentermine 3- 6 mg IV and bolus IV crystalloids.

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DISCUSSION

Bupivacaine is widely recognized for providing effective anesthesia in epidural blocks. Nevertheless, anesthesiologists have consistently sought to enhance the quality of the block by incorporating adjuvant medications into local anesthetics. These adjuvants improve the efficacy and characteristics of analgesia provided by local anesthetics alone, while also extending the duration of the pain-free period post-surgery and reducing the need for systemic analgesics, all with minimal or no side effects and negligible impact on hemodynamics. The practice of administering opioids via central neuraxial routes commenced following the identification of opioid receptors in the substantia gelatinosa of the spinal cord in animal studies conducted by Paul Bert Sydner in 1973 and Wang in 1979. The safety of morphine and its analogs in human subjects was subsequently established by Yaksh and Ruddy in 1985. Numerous studies have indicated that the incorporation of morphine and its analog, such as fentanyl citrate, into local anesthetic solutions significantly prolongs both sensory and motor block durations, as well as extends the postoperative pain-free interval, primarily through their action on opioid receptors, thereby decreasing the need for postoperative analgesics. The central neuraxial administration of opioids is associated with a clinically acceptable incidence of manageable side effects, including pruritus, tingling, delayed respiratory depression, and urinary retention.

Research by Chen Hwan CherngChih Shun Wong, Shung Tai HO (2001), Habab F Khafagy *et al.* (2010), Barbra A Coda *et al.* (1994), among others, has documented the effects of adding fentanyl citrate to local anesthetic solutions. Their findings indicate that fentanyl accelerates the onset of sensory block, prolongs both sensory and motor block durations, enhances the postoperative pain-free period, and presents dose-dependent side effects. The involvement of alpha-2 adrenoceptors in pain modulation was elucidated by Yaksh in 1985, leading to the exploration of clonidine as an analgesic adjuvant in spinal administration in both small animals and human volunteers.

Dexmedetomidine, an alpha-2 adrenoceptor agonist, has recently been introduced for clinical application in our country. Numerous clinical investigations have established the role of fentanyl as an adjunct to bupivacaine, demonstrating that the inclusion of fentanyl significantly extends the duration of the postoperative pain-free period. In the following discussion, we will compare our findings with those studies in which dexmedetomidine was administered alongside bupivacaine or other local anesthetics via the epidural route. Arakawa M. and Hoka S. (1998) investigated the optimal dosage of fentanyl for epidural administration, determining that 3 mcg/kg was the ideal dose. In our current study, we utilized a dosage of 2 mcg/kg. Bajwa SJ (2011) employed a dose of 1 mcg/kg of dexmedetomidine via the epidural route, which we also adopted in our study. The demographic characteristics, including age, sex, and weight, were comparable between the control and study groups. The mean onset time for sensory block was recorded as 679.2 seconds in group C, 627.6 seconds in group D, and 628.8 seconds in group F. The mean onset time for motor block was 890.4 seconds in group D, 955.2 seconds in group F, and 1003.2 seconds in group C. Notably, the mean onset time for both sensory and motor blocks was significantly quicker in group D compared to group C. However, there was no significant difference in the onset times of sensory and motor blocks between groups D and F, nor was there a significant difference in the onset of motor block between groups C and F. Bajwa *et al.* (2011) reported an earlier onset of both sensory and motor blocks when dexmedetomidine was used in lumbar epidural blocks with the addition of fentanyl to ropivacaine. Similarly, Rajni Gupta (2011) and Al-Ghanem SM (2009) utilized dexmedetomidine and fentanyl as

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adjuncts in subarachnoid blocks with bupivacaine, finding no significant differences in the onset of sensory and motor blocks between the two agents.

The duration of sensory and motor block offset was significantly extended in the dexmedetomidine group when compared to both the control and fentanyl groups, with the difference being highly significant. However, no significant difference was observed between the dexmedetomidine and fentanyl groups. Similar findings were reported by Bajwa *et al.*, who concluded that dexmedetomidine, when used as an adjunct in epidural blocks, outperforms fentanyl regarding the offset of sensory and motor block. In their 2011 study, Bajwa *et al.* noted that the first rescue dose was considerably delayed in patients receiving dexmedetomidine as an adjunct to ropivacaine in epidural blocks compared to those receiving fentanyl. Additionally, Rajni Gupta *et al.* found that the time to rescue analgesia was extended in the dexmedetomidine group relative to the fentanyl group, although dexmedetomidine was administered intrathecally as an adjunct to bupivacaine. Our study corroborated these findings, revealing the longest postoperative pain-free duration of 10.52 hours in the dexmedetomidine group, which was significantly longer than the 5.15 hours observed in the fentanyl group and 4.83 hours in the control group. A sedation score of 4 was recorded in 28% of patients in the dexmedetomidine group, indicating that this alpha-2 agonist effectively produced sedation alongside sensory and motor block. In contrast, no patients in the control or fentanyl groups exhibited a sedation score of 4. The Ramsay sedation score was utilized in this study. Bajwa *et al.* also compared sedation scores in a similar study and found that the level of sedation was greater in the dexmedetomidine group compared to the fentanyl group on a subjective sedation scale, suggesting that sedation is more pronounced with the alpha-2 agonist than with opioids. The anxiolytic effects, sedation, and sympatholysis associated with dexmedetomidine are attributed to its action on pre- and post-synaptic sympathetic nerve terminals and the central nervous system, effects that were not observed in patients treated with fentanyl.

Muscle relaxation was found to be sufficient, with muscle power graded at 3 observed in 68% of patients in group D, 64% in group F, and 52% in group C. This level of relaxation can be attributed to bupivacaine rather than the adjunct medications used. Similar findings were reported by Bajwa *et al.* in 2011. In the current study, heart rate, mean arterial pressure, respiratory rate, and SpO2 levels were monitored for up to three hours following the block. No significant differences were noted among the three groups. The heart rate decreased by 27.91% in group C, 29.57% in group D, and 25.19% in group F. In three instances within group D, the heart rate dropped by less than 50 bpm, which was effectively managed with an intravenous injection of Atropine 0.6 mg. The average maximum reduction in mean arterial pressure post-block was comparable across all three groups, ranging from 19.32% to 19.91%. Hypotension was observed in five cases from the dexmedetomidine group, as well as in three cases from the control group and in fentanyl, which was treated with intravenous mephentermine and crystalloid solutions. These findings align with those reported by Bajwa *et al.* in 2011. The alterations in heart rate and mean arterial pressure are attributed to sympathetic blockade induced by the alpha-2 agonist, which is manageable in a clinical setting. While opioids are typically linked to respiratory depression, the present study did not record any instances of this condition. This can be explained by the fact that fentanyl is less likely to cause respiratory depression compared to morphine, and respiratory depression is not a characteristic of alpha-2 agonists. Bajwa *et al.* in 2011 noted that a reasonable degree of hemodynamic stability is achieved when dexmedetomidine and fentanyl are added to epidural ropivacaine. Shivering occurred in two cases from group C and one case from group F. Nausea was reported in three cases from group C and one case from group F, while vomiting was noted in two cases from group C. The administration of opioids is known to

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cause side effects such as itching, nausea, vomiting, respiratory depression, and urinary retention.

In a study conducted by Michael Smith and Marrof, Dexmedetomidine was effectively utilized to mitigate shivering related to anaesthesia. The occurrence of side effects was minimal in group D, primarily associated with hemodynamic changes such as bradycardia and hypotension, which were easily managed. The duration of both motor and sensory block was extended in the dexmedetomidine group when compared to the Control and Fentanyl groups. Furthermore, the dexmedetomidine group demonstrated a clinically and statistically significant improvement in the postoperative pain-free period relative to both the control and fentanyl groups.

CONCLUSION

The incorporation of Dexmedetomidine, an alpha-2 agonist, into the local anaesthetic solution for lumbar epidural block at a dosage of 1.0 mcg/kg significantly extends the duration of the postoperative pain-free interval without affecting the characteristics of the block provided by Bupivacaine. Furthermore, it serves as a more effective adjuvant compared to fentanyl, an opioid. However, it is important to note that Dexmedetomidine also prolongs motor blockade, which could impede the early mobilization of patients.

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