# A COMPARATIVE STUDY OF PERIOPERATIVE EFFECTS OF INTRATHECAL FENTANYL AND DEXMEDETOMIDINE WITH BUPIVACAINE IN ELECTIVE LSCS

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**ABSTRACT**

**BACKGROUND**

Spinal anaesthesia is the most commonly used neuraxial anaesthetic technique for caesarean section as it is easy to perform, has accuracy rate higher than epidural anaesthesia, and procedure takes less time to perform and provides simple, effective and safe analgesia during perioperative period. Addition of various drugs to local anaesthetics reduces the dose requirement of the local anaesthetic, prolongs sensory and motor blockade and also prolongs the postoperative analgesia.

Aims and objectives: In this study, we compare the quality of motor and sensory block and the duration of analgesia produced by intrathecal bupivacaine heavy alone and in combination with fentanyl or dexmedetomidine.

**MATERIALS AND METHODS**

The randomised control trial was conducted on 90 obstetric patients divided in three groups of Group C (bupivacaine with normal saline), Group D (Bupivacaine with dexmedetomidine) and Group F (Bupivacaine with fentanyl).

**RESULTS**

It was observed that both dexmedetomidine and fentanyl with bupivacaine provided the early onset and prolonged duration of sensory and motor block with good postoperative analgesia but dexmedetomidine has more advantages than fentanyl.

**CONCLUSION**

Addition of dexmedetomidine and fentanyl has decreased the dose requirement of bupivacaine with good perioperative analgesia.

**KEYWORDS**

LSCS, Dexmedetomidine, Fentanyl, Spinal Anaesthesia.

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## BACKGROUND

Spinal anaesthesia is the most commonly used neuraxial anaesthetic technique for caesarean section as it is easy, has accuracy rate higher than epidural anaesthesia, and procedure takes less time to perform and provides simple, effective and safe analgesia during perioperative period. The surgery on uterus produces visceral pain for which block up to dermatome $T_6$ level is necessary to prevent maternal discomfort which is also accompanied with side effects like haemodynamic instability and reduced utero-placental circulation.[1]

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The development of the "low-dose spinal" technique involving the use of low doses of local anaesthetics, often in association with fentanyl, improved the quality of spinal anaesthesia in ambulatory surgical setting by increasing the sensory block without increasing motor block.[2,3] Dexmedetomidine (DXM), a highly selective $\alpha_2$ adrenergic receptor agonist, potentiates local anaesthetic effects, prolongs postoperative analgesia, and has a dose-dependent sedative effect. The mechanism of action of intrathecal $\alpha_2$-adrenoceptor agonists is not well understood; they may have an additive or synergistic effect to local anaesthetics through binding to the pre-synaptic C-fibres and postsynaptic dorsal horn neurons producing analgesia by depressing the release of C-fibre neurotransmitters and hyperpolarisation of postsynaptic dorsal horn cells.[4] Following intrathecal administration of DXM 5 μg as an adjuvant with hyperbaric bupivacaine for uncomplicated caesarean deliveries, Mahdy W R et al found good quality of spinal anaesthesia with no adverse effects on mothers and neonates.[5] Intravenous DXM has been successfully used as an adjunct for labour analgesia and caesarean delivery, with favourable maternal and foetal outcome.[6] Isolated perfused human placental studies have shown that because of the higher lipophilicity of DXM, there

is greater placental tissue retention and minimal transport into the foetal circulation.[7] However, DXM is being safely used in neonates and infants for sedation in intensive care setups.[8] DXM has been safely used as an adjuvant for subarachnoid block in urological, orthopaedic and lower abdominal surgical procedures. But, the use of intrathecal DXM with local anaesthetic agent for caesarean delivery is not extensively studied. In this study, we compared the quality of motor and sensory block, duration of analgesia and the perioperative haemodynamic changes produced by intrathecal bupivacaine heavy alone and when given in combination with fentanyl or dexmedetomidine.

## MATERIALS AND METHODS

A randomised control trial was conducted on obstetric patients aged between 18-35 years, (ASA physical status grade I and II) with uncomplicated singleton pregnancies of more than 36 weeks of gestation posted for elective lower segment caesarean section under spinal anaesthesia at Nehru Hospital, B R D Medical College, Gorakhpur. Written informed consent was taken from all patients and their attendants on a separate consent form. Ethical clearance for present study has been taken by institutional ethics committee.

The exclusion criteria were the same as for regional anaesthesia and allergies to study drugs.

Sample size was calculated as 22 in each group with 90% power of study, 95% confidence interval, 5% significance level with allowable error using G-power software. Finally, a total of 30 patients were included in each group.

**The Study Population was Randomly divided into 3 Groups According to the Drug Combinations used with 30 Parturient (N=30) in each Group**

- Group C (Control Group) (2.3 mL): 0.5% Hyperbaric Bupivacaine 9 mg (1.8 mL) + Normal saline 0.5 mL.
- Group D (2.3 mL): 0.5% Hyperbaric Bupivacaine 9 mg (1.8 mL) + Dexmedetomidine 5 µg (0.5 mL).
- Group F (2.3 mL): 0.5% Hyperbaric Bupivacaine 9 mg (1.8 mL) + Fentanyl 25 µg (0.5 mL).

Preoperative assessment was done for each patient. Under strict aseptic precautions, 2.3 mL of the study drug was injected into L3-L4 subarachnoid space in sitting position using 25 G Quincke spinal needle (BD, USA) after confirming free flow of cerebrospinal fluid and the time of injection was recorded as 0 minutes. Following this the patients were made to lie supine immediately and a wedge of 15˚ was placed below the right buttock for left uterine displacement.

Patients were monitored for occurrence of adverse events after spinal injection like nausea, vomiting, desaturation, hypotension, bradycardia, excessive sedation and others, if any.

**The following Parameters were Observed and Recorded**

- Onset of sensory blockade by pinprick method.
- Onset of motor blockade (Modified Bromage Scale).
- Time for two-segment sensory regression.
- Total duration of sensory blockade- Time taken from maximum block height attained till regression of block to S1 dermatome.
- Total duration of motor blockade- Time taken from maximum Bromage score attained to Bromage 0. It was tested at the end of surgery using modified Bromage scale.
- Total duration of analgesia.
- Postoperative pain was assessed using visual analogue scale (0 – 10) at 30 minutes, hourly for the next 6 hours, and 6 hourly till 24 hours and time to first rescue analgesic request was recorded.
- Haemodynamic changes - Heart rate, systolic, diastolic and mean arterial pressure and oxygen saturation was recorded every 5 minutes till 20 minutes, then every 10 minutes till 1 hr., then every 15 minutes for next hour.

20 units of oxytocin was be added to the intravenous drip and was allowed to flow at the rate of 2 mL/min. after delivery of the baby.

Data were tabulated and analysed using GraphPad prism version 6.0. Statistical analysis was done using ANOVA and chi square tests wherever applicable. Post-hoc test was done using Tukey's test for intergroup comparison. A 'p' value of 0.05 was taken as statistically significant difference.

## RESULTS

In present study, we found that the demographic data (Table 1) was comparable in all the three groups and no significant difference was found on statistical analysis.

The onset of sensory block i.e. time taken for the sensory block to reach $T_{10}$ dermatome was significantly faster in Group D (2.075 ± 0.572 minutes) and F (2.425 ± 0.633 minutes) when compared with the control Group C (4.44 ± 0.73). The result was statistically insignificant when Group D and F were compared against each other as shown in intergroup comparison (Table 2).

Time taken to reach the highest level of sensory block, as seen in Table 3, was also lowest in Group D (6.95 ± 0.561 minutes) followed by Group F (7.29 ± 0.415 minutes) and longest in control group (8.68 ± 0.776 minutes) and the result was significant on statistical analysis. On intergroup comparison, the difference was statistically significant when Group D and F were compared to the control Group. The comparison between Group D and F, however, did not result in any statistical significance.

The time for two-segment sensory regression, as shown in Table 4, was found to be significantly longer in Dexmedetomidine Group (130.33 ± 10.9 minutes) than Group F (106.67 ± 13.85 minutes) and Group C (79.67 ± 11.05 minutes). The time required for complete regression of sensory block (Table 5) was significantly longer in group D (305.67 ± 42.48) as compared to fentanyl (277.33 ± 44.34) and control group (139.5 ± 14.64).

The onset of motor blockade (Table 6) was significantly faster in Group D (4.375 ± 1.206 minutes) and F (5.233 ± 1.332 minutes) when compared to control group C (8.29 ± 1.594 minutes), but it was statistically not significant when comparison was done between group D and F with a 'p' value of 0.06. Recovery of motor block i.e. regression of motor blockade to Bromage 0 (Table 7) was earliest in control group C (85.16 ± 16.7 minutes). Patients who received

dexmedetomidine or fentanyl as adjuvants had longer duration of motor blockade (147.5 ± 12.15 and 123 ± 14.29 minutes respectively) when compared to control group. On comparison between group D and group F, the former took significantly longer duration for full motor recovery.

The time for rescue analgesic (Figure 1) i.e. the time when patients demanded first dose of analgesic was significantly prolonged in group D (364.83 ± 63.48 minutes) when compared to both groups F (296 ± 50.43 minutes) and C (152.66 ± 20.28 minutes) as seen in Figure 1. The time for rescue analgesic was also significantly prolonged in patients who received intrathecal fentanyl in comparison to control group.

On haemodynamics front (Figure 2), incidence of hypotension and bradycardia were almost similar in all the test and control groups. The mean pulse rate was found to be lowest in dexmedetomidine group which could be attributed not only to its $\alpha_2$ property but also to better sedation scores which lead to decreased level of anxiety. The mean pulse rate in Group F also was lower when compared to control group. Bradycardia was seen in three patients in both group D and F while in control group only 2 patients had bradycardia.

The mean systolic and diastolic blood pressures (Figure 3) in each group showed not much of variability. Three patients each in group D and F had hypotension and IV Mephentermine was used in them. Overall haemodynamic stability was good in all three groups. These haemodynamic stabilities may be attributable to lower dosage of bupivacaine as well as dexmedetomidine. As far as other complications are concerned, highest incidence of nausea and vomiting was seen in patients in control group. The incidence of itching was found only in Group F as shown in Table 8.

| | Group D | Group F | Group B | P Value |
|---|---|---|---|---|
| Age (Years) | 26.233 ± 2.528 | 27.033 ± 3.727 | 26.833 ± 3.291 | 0.60 |
| Weight (Kgs) | 65.066 ± 6.280 | 64.8 ± 6.030 | 63.733 ± 5.355 | 0.65 |
| Height (cm) | 165.266 ± 5.619 | 164.233 ± 5.399 | 164.866 ± 4.783 | 0.77 |

***Table 1. Showing Distribution of Age, Weight and Height in Each Group***

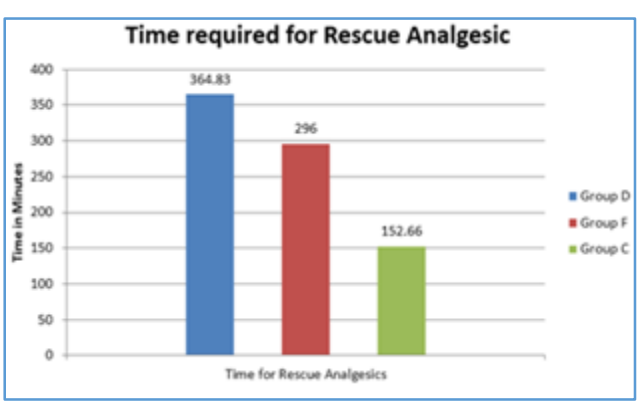


***Figure 1***

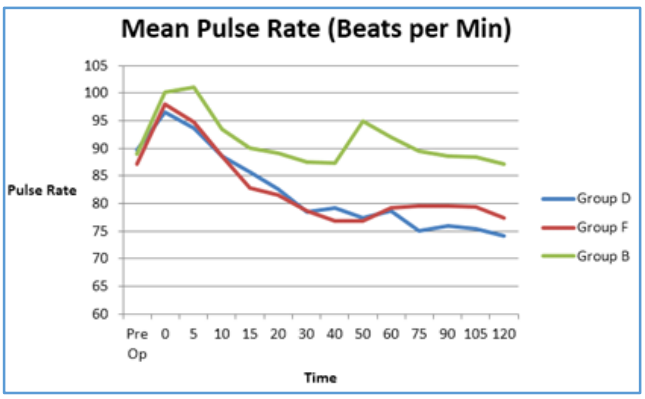


***Figure 2***

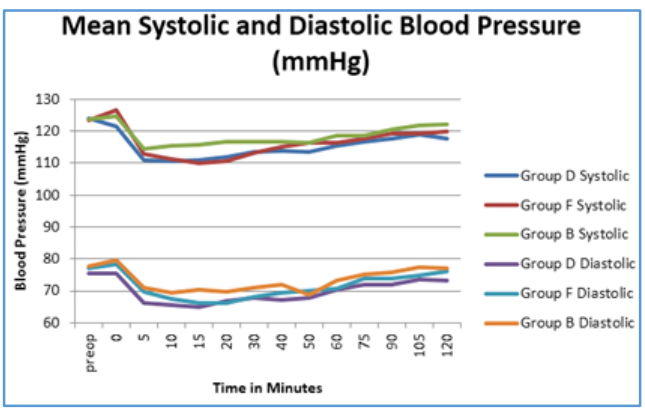


***Figure 3***

| Mean Time Required Onset of Sensory Blockade (Minutes) | Group C | Group D | Group F |
|---|---|---|---|
| | 4.441 ± 0.730 | 2.075 ± 0.572 | 2.425 ± 0.633 |
| **Intergroup Comparison** | **P Value** | | |
| Group C vs. Group D ($P_1$) | <0.0001 | | |
| Group C vs. Group F ($P_2$) | <0.0001 | | |
| Group D vs. Group F ($P_3$) | 0.1106 | | |

***Table 2. Mean time Required for onset of Sensory Blockade (Minutes)***

| Mean Time Required for Peak Level of Sensory Blockade (Minutes) | Group C | Group D | Group F |
|---|---|---|---|
| | 8.683 ± 0.776 | 6.958 ± 0.561 | 7.29 ± 0.415 |
| **Intergroup Comparison** | **P Value** | | |
| Group C vs. Group D ($P_1$) | <0.0001 | | |
| Group C vs. Group F ($P_2$) | <0.0001 | | |
| Group D vs. Group F ($P_3$) | 0.0876 | | |

***Table 3. Mean time Required for Peak Level of Sensory Blockade (Minutes)***

| Two-segment Sensory Regression (Minutes) | Group C | Group D | Group F |
|---|---|---|---|
| | 79.667 ± 11.05 | 130.33 ± 10.90 | 106.667 ± 13.85 |
| **Intergroup Comparison** | **P Value** | | |
| Group C vs. Group D ($P_1$) | <0.0001 | | |
| Group C vs. Group F ($P_2$) | <0.0001 | | |
| Group D vs. Group F ($P_3$) | <0.0001 | | |

***Table 4. Time Required for Two-segment Sensory Regression in Minutes***

| Mean Time Taken for Sensory Regression to $S_1$ (Minutes) | Group C | Group D | Group F |
|---|---|---|---|
| | 139.5 ± 14.64 | 305.67 ± 42.48 | 277.33 ± 44.34 |
| **Intergroup Comparison** | **P Value** | | |
| Group C vs. Group D ($P_1$) | <0.0001 | | |
| Group C vs. Group F ($P_2$) | <0.0001 | | |
| Group D vs. Group F ($P_3$) | <0.0095 | | |

***Table 5. Showing Mean Time taken for Sensory Regression to $S_1$***

| Onset of Motor Blockade (Minutes) | Group C | Group D | Group F |
|---|---|---|---|
| | 8.291 ± 1.594 | 4.375 ± 1.206 | 5.233 ± 1.332 |
| **Intergroup Comparison** | P Value | | |
| Group C vs. Group D ($P_2$) | <0.0001 | | |
| Group C vs. Group F ($P_3$) | <0.0001 | | |
| Group D vs. Group F ($P_1$) | 0.06 | | |

***Table 6. Time Required for Onset of Motor Blockade in Minutes***

| Mean Time for Regression Bromage 0 | Group C | Group D | Group F |
|---|---|---|---|
| | 85.167 ± 16.7 | 147.5 ± 12.159 | 123 ± 14.299 |
| **Intergroup Comparison** | P Value | | |
| Group C vs. Group D ($P_1$) | <0.0001 | | |
| Group C vs. Group F ($P_2$) | <0.0001 | | |
| Group D vs. Group F ($P_3$) | <0.0001 | | |

***Table 7. Mean Time Required for Motor Block to Regress to Bromage 0***

| Adverse Effects | Group C | | Group D | | Group F | |
|---|---|---|---|---|---|---|
| | No. | % | No. | % | No. | % |
| Hypotension | 1 | 3.33 | 3 | 10 | 3 | 10 |
| Bradycardia | 2 | 6.67 | 3 | 10 | 3 | 10 |
| Nausea and Vomiting | 6 | 20 | 3 | 10 | 2 | 6.67 |
| Pruritus | 0 | 0 | 0 | 0 | 4 | 13.34 |

***Table 8. Adverse Effects***

## DISCUSSION

Post-operative analgesia plays a pivotal role in recovery of patients. Inadequate pain control may result in significant morbidity and mortality and is also inhumane.[9,10] Surgery suppresses the immune system which is proportional to invasiveness of surgery.[11,12] Effective postoperative pain management results in patient comfort and therefore satisfaction, earlier mobilisation, fewer pulmonary and cardiac complications, a reduced risk of deep vein thrombosis, faster recovery with less likelihood of the development of neuropathic pain and reduced cost of care.

From our results, we can say that addition of dexmedetomidine when given with bupivacaine intrathecally results in faster onset of both motor and sensory blockade and also longer regression time for motor and sensory block. The higher block level improves the quality of anaesthesia. Fentanyl also increases the quality of anaesthesia by decreasing the onset time required for motor and sensory block and also increasing duration of anaesthesia and level of block but the duration of anaesthesia produced by fentanyl was significantly shorter than that produced by dexmedetomidine.

Mahdy et al (2011)[5] in their study found that there was significant difference in onset of sensory and motor blockade when Dexmedetomidine and fentanyl group was compared against the control group who received bupivacaine with saline only. When Dexmedetomidine and Fentanyl group were compared against each other the findings were not significant. Two-segment regression and regression to $S_1$ was significantly prolonged in Dexmedetomidine group although it was also prolonged in Fentanyl group. Gupta et al (2011)[13] in their study did not find any difference in time taken for onset of sensory and motor blockade, peak sensory height and time to reach peak sensory block height but the prolongation of both sensory and motor blockade was significantly more in patients receiving dexmedetomidine as an adjuvant to bupivacaine heavy. Similar findings were also reported by Rout ray et al and Kumar et al[14,15] in their studies. The results in our study were comparable to the abovementioned studies.

The time required for rescue analgesia was significantly prolonged by dexmedetomidine than fentanyl (Figure 1). Gupta et al, Honoura et al, Rout Ray et al and Kumar et al also found in their studies that the time for 1st dose of rescue analgesic was prolonged by addition of adjuvants with local anaesthetics.[13,14,15,16]

Low-dose bupivacaine along with dexmedetomidine or fentanyl provides better haemodynamic stability thereby decreasing other side effects like nausea, vomiting and shivering (Figure 2 & 3).

Mahdy et al[5] in their study found that the incidence of bradycardia and hypotension was higher in control group. In contrast, in our study, the incidence of hypotension and bradycardia was lesser and both occurring in control group could be due to the decreased dosage of bupivacaine. Other studies also demonstrated the haemodynamic stability, lesser side effects and reduced requirement of local anaesthetics when spinal anaesthesia was supplemented with adjuvants like dexmedetomidine and fentanyl.[5,13,14,15,16]

Although the study was carefully designed, there were still some unavoidable limitations and shortcomings. The study was conducted only on a small size of population, the study should have involved more participants to generalise the results and also the patient-to-patient variability of pain perception, to some extent, might have affected the results.

## CONCLUSION

On the basis of results, it can be concluded that both fentanyl and dexmedetomidine can be used as adjunct to bupivacaine in spinal anaesthesia; however, dexmedetomidine along with low-dose bupivacaine heavy provides better quality of anaesthesia during surgery, excellent post-operative analgesia for longer period when compared to fentanyl. Dexmedetomidine also provides good haemodynamic stability, decreased side effects. It also improves patient's satisfaction and reduces anxiety, thereby improving overall general patient outcome.

The data derived from our study is very promising regarding the use of dexmedetomidine as an adjuvant to spinal anaesthesia, but a large scale multicentric study is still needed to recommend it for routine clinical use.

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