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## Comparative effects of dexmedetomidine and fentanyl as adjuvants to hyperbaric bupivacaine in elective caesarean sections: an observational study at tertiary care centre

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### Abstract

**Aim:** The aim of the present study to compare the effects of Dexmedetomidine and fentanyl as adjuvants to hyperbaric bupivacaine in elective caesarean sections.

**Methods:** This prospective study was done in the Department of anaesthesiology, LD hospital an associated hospital of GMC, Srinagar, India from December 2019 to November 2020. The participants included 130 parturient with gestational age  $\geq 37$  weeks and ASA I and II candidates for elective caesarean section under spinal anesthesia were included in this study. All 130 patients were randomly and equally divided into the following two groups: Group B-D received 10 mg hyperbaric bupivacaine 0.5%+10  $\mu$ g dexmedetomidine. Group B-F received 10 mg hyperbaric bupivacaine 0.5%+25  $\mu$ g fentanyl. Hemodynamic monitoring including SBP and DBP, mean arterial pressure (MAP), heart rate (HR) and peripheral oxygen saturation level (SpO<sub>2</sub>) were recorded. Patient's pain score was assessed using visual analogue scale (VAS); scored from 0–10 (where 0=no pain and 10=the worst pain imaginable) during the recovery room (T0) and at one, three, and six hours (T1, T3, and T6) in the postoperative period. If the VAS score was more than 3, a rescue dose of tramadol (100 mg) was administered intravenously.

**Results:** The mean dose of mephenetermine in the B-D and B-F groups were  $5.45 \pm 6.74$  and  $6.79 \pm 5.69$ mg, respectively. The Mann–Whitney test showed that there was no significant difference between the two groups ( $P=0.78$ ). With respect to the bradycardia, the mean dose of atropine in the B-D and B-F groups were  $0.12 \pm 0.28$  and  $0.06 \pm 0.15$  mg, respectively. According to the Mann–Whitney test, in this regard, no significant difference was seen between the two groups. ( $P=0.32$ ). The results of the Mann–Whitney *U*-test indicated that the onset of block in the B-D group ( $97.88 \pm 32.78$  seconds) was significantly faster than in the B-F group ( $112.03 \pm 36.68$  seconds) ( $P=0.041$ ). Considering the level of sensory block, T4 level was shown in 81 (62.31%) patients, from whom 47 (58.02%) and 34 (41.98%) patients were in the B-D and B-F groups, respectively. Moreover, T6 level was observed in 49 (37.69%) patients, from whom 19 (38.78%) and 30 (61.22%) patients were in the B-D and B-F groups, respectively. Chi-squared test revealed that there was no statistically significant difference between the two groups ( $P=0.13$ ).

**Conclusion:** Compared with fentanyl, it seems that adding 10 $\mu$ g dexmedetomidine to bupivacaine has a better effect on postoperative pain management in cesarean section under spinal anesthesia.

**Keywords:** spinal anesthesia, fentanyl, postoperative analgesia, dexmedetomidine

### Introduction

The need for early ambulation for caring of the neonate by mother makes postoperative pain management after caesarean delivery unique. To achieve this, various drug combinations and techniques have been tried to find out the more effective and safer analgesia. Most breast feeding women may choose to limit their systemic analgesic doses. Neuroaxial analgesic technique are gold standards for pain relief during labour and delivery [1]. The intrathecal opioids have been used to increase the duration of postoperative analgesia without affecting the sympathetic and motor functions [2]. Opioids with  $\mu$ -receptor agonists like fentanyl, buprenorphine, etc. have been tried extensively for this purpose. However, side effects due to  $\mu$ -receptor stimulation like respiratory depression, pruritus, urinary retention and abuse liability remain a concern. To alleviate this problem alpha agonist like clonidine have been used alone or in combination with opioids for lower abdominal surgery and labour analgesia [3-6]. Despite increasing the duration of postoperative analgesia, alpha 2 agonist also

causes side effects like sedation, dryness of mouth and hypotension specially in higher dose. Dexmedetomidine is another highly selective alpha 2 agonist which has been used in surgical patients intrathecally to prolong the duration of postoperative analgesia [7-9]. However there has been some reluctance on its use in obstetric patients for fear of uteroplacental transfer and untoward effects on the baby and its reckless administration could have posed difficult challenges to both mother and neonate [10]. However, dexmedetomidine is a highly lipid soluble drug with retention of the placenta (maternal to fetal index of 0.77) and it virtually do not cross the placenta [11]. And, there are numerous case reports of its successful use in obstetrics without adverse effects on fetal outcome. A recent randomized controlled trial has found intrathecal dexmedetomidine to significantly prolong the duration of labour analgesia. However, the associated prolongation of motor block may not be desirable in some obstetric patients. Hence, the search of an opioid which can prolong the duration of analgesia but without  $\mu$ -receptor related side effects like pruritus and nausea become imperative. Butorphanol to antagonize pruritus and nausea produced by morphine ( $\mu$ -agonist) while prolonging the duration of analgesia [12].

Since maternal and neonatal outcomes are a vital issue in cesarean section, choosing an appropriate drug to combine with local anesthetics has always been a great challenge for anesthesiologists. Hence, this study was done to compare the effect of adding dexmedetomidine vs fentanyl as an adjuvant to intrathecal bupivacaine in women who had undergone cesarean section. The primary outcome was to assess the postoperative analgesia. Our secondary outcomes were the onset of block, hemodynamic changes, and maternal complications as well as Apgar scores of neonates.

### Material and Methods

This prospective study was conducted by the department of anaesthesiology, LD hospital an associated hospital of GMC, Srinagar, India from December 2019 to November 2020, after taking the approval of the protocol review committee and institutional ethics committee. After taking informed consent detailed history was taken from the patient or relatives.

The participants included 130 parturient with gestational age  $\geq 37$  weeks and ASA I and II candidates for elective cesarean section under spinal anesthesia were included in this study.

The patients with emergency conditions, contraindication of spinal anesthesia, history of valvular heart disease, history of allergy or sensitivity to applied drugs and patients with placenta previa as well as failed blockade or need for induction of general anesthesia were excluded from this study.

### Procedures

When patients entered the operating room, basic standard monitoring, including non-invasive blood pressure, electrocardiography and pulse oximetry were done, and initial hemodynamic parameters were measured. Before the initiation of spinal block, all patients received 10 mL/kg Ringer solution. All 130 patients were randomly and equally divided into the following two groups:

- Group B-D received 10 mg hyperbaric bupivacaine

0.5%+10  $\mu$ g dexmedetomidine.

- Group B-F received 10 mg hyperbaric bupivacaine 0.5%+25  $\mu$ g fentanyl.

The total volume of intrathecal injection in both groups was equal (2.5 mL). Aseptic technique with 25 G Quincke spinal needle was used for spinal anesthesia in all study subjects by an anesthesiologist in the sitting position at the level of L4-L5 intervertebral space. After observing free flow of transparent cerebrospinal fluid, the intrathecal drugs were injected. Then, patients were positioned to supine (slightly tilted to the left side) and 6 L/min oxygen was delivered with a simple face mask. The sensory block was checked by the pinprick test, and motor block was assessed using the Bromage scale [13]. When the adequate level of sensory block (T4-T6) was reached and confirmed, the surgery was allowed to begin.

### Measurements

Hemodynamic monitoring including SBP and DBP, mean arterial pressure (MAP), heart rate (HR) and peripheral oxygen saturation level (SpO<sub>2</sub>) were recorded intra and post operation as follows: at the baseline values (before block); immediately after block, during the operation at 5, 10, 15, 30, and 60 min after spinal block, at the end of the procedure and every 10 min in the recovery room.

Hypotension was defined as SBP  $< 90$  mmHg or reduction in MAP more than 20% from baseline values and treated with 6mg mephentermine intravenously. Likewise, bradycardia (HR  $< 50$  beats/minute) was treated with 0.6 mg of intravenous atropine. All of these episodes of hypotension and bradycardia were noted in both groups.

The onset of sensory block (time to reach T4-T6) was assessed with a pinprick test (using a blunt 25-gauge needle along the mid-clavicular line bilaterally) every two minutes and modified Bromage scale (0=no motor block, 1=inability to flex the hip, 2=inability to flex the knee, and 3=complete motor block of limb) was used to evaluate motor block.

Patient's pain score was assessed using visual analogue scale (VAS); scored from 0–10 (where 0=no pain and 10=the worst pain imaginable) during the recovery room (T0) and at one, three, and six hours (T1, T3, and T6) in the postoperative period. If the VAS score was more than 3, a rescue dose of tramadol 100 mg was administered intravenously.

Duration of analgesia was defined and noted as the time interval between block onset and the first analgesic request. The duration of surgery was recorded. The respiratory depression (respiratory rate  $< 10$  per minute) and the incidence of nausea, vomiting, and shivering were assessed and recorded during six hours after the surgery. Moreover, Apgar scores of neonates were also evaluated at one and five minutes after delivery.

### Results

**Table 1:** Demographic Characteristics and ASA Class

Parameters	Group B-D (n=65)	Group B-F (n=65)	P-value
Age (years)	28.74 $\pm$ 5.69	30.02 $\pm$ 4.63	0.08
Weight (kg)	70.88 $\pm$ 13.03	71.79 $\pm$ 13.89	0.41
Height (cm)	161.11 $\pm$ 6.12	161.87 $\pm$ 6.87	0.11
ASA I/II	50/15	45/20	0.29

**Table 2:** Evaluation of Postoperative Pain Scores (VAS) in Two Groups

Time	Group B-D (n=55)	Group B-F (n=55)	P-value
T0	0.36±0.91	0.53±0.61	0.003
T1	1.90±1.52	2.12±0.77	0.811
T3	4.43±1.59	4.65±1.23	0.36
T6	8.55±1.74	8.76±1.28	0.81

**Table 3:** Duration of Analgesia, Motor Block and Surgery in Two Groups

Parameters	Group B-D (n=65)	Group B-F (n=65)	P-value
Duration of analgesia (min)	432.12±70.36	271.96±62.87	<0.001
Duration of motor block (min)	266.06±61.07	285.22±42.69	0.07
Duration of surgery (min)	50.98±13.75	50.73±9.67	0.15

**Table 4:** Comparison of Complications in Two Groups

Characteristics	Group B-D (n=65)		Group B-F (n=65)		P-value
	Number	%	Number	%	
Hypotension	38	58.46	47	72.31	0.15
Bradycardia	10	15.38	6	9.23	0.32
Respiratory depression	2	3.08	2	3.08	1.00
Shivering	5	7.69	12	18.46	0.12
Nausea/vomiting	4	6.15	6	9.23	0.62

Spinal anesthesia was successful in all study subjects. Demographic characteristics such as age, weight, height, ASA class were matched in two groups. (Table 1) Hemodynamic parameters (SBP, DBP, MAP, HR, and SpO<sub>2</sub>) in two groups were comparable at different time periods, and the findings revealed that there was no significant statistical difference between them ( $P>0.05$ ). Moreover, following hypotension, the mean dose of mephentermine in the B-D and B-F groups were 5.45±6.74 and 6.79±5.69mg, respectively. In this regard, the Mann–Whitney test showed that there was no significant difference between the two groups ( $P=0.78$ ). With respect to the bradycardia, the mean dose of atropine in the B-D and B-F groups were 0.12±0.28 and 0.06±0.15 mg, respectively. According to the Mann–Whitney test, in this regard, no significant difference was seen between the two groups ( $P=0.32$ ).

The results of the Mann–Whitney *U*-test indicated that the onset of block in the B-D group (97.88±32.78 seconds) was significantly faster than in the B-F group (112.03±36.68 seconds) ( $P=0.041$ ). Considering the level of sensory block, T4 level was shown in 81 (62.31%) patients, from whom 47 (58.02%) and 34 (41.98%) patients were in the B-D and B-F groups, respectively. Moreover, T6 level was observed in 49 (37.69%) patients, from whom 19 (38.78%) and 30 (61.22%) patients were in the B-D and B-F groups, respectively. Chi-squared test revealed that there was no statistically significant difference between the two groups ( $P=0.13$ ).

The pain score was measured at the first hour of arrival in the recovery (T0) as well as at one, three, and six hours (T1, T3, and T6) in the postoperative period. According to the results of the Mann–Whitney *U*-test, the mean VAS scores indicated a significant reduction during recovery time in the B-D group ( $P=0.003$ ). However, no significant difference was observed in the mean of pain intensity between the two groups at other times ( $P>0.05$ ) table 2. The mean dose of tramadol for pain relief in the post-operative period in the B-D and B-F groups was 2.81±6.97 and 4.41±10.36 mg, respectively. In this regard, there was no significant difference between the two groups in accordance with the Mann–Whitney *U*-test ( $P=0.32$ ).

In the B-D group, there was a significantly longer duration of analgesia than in the B-F group ( $P<0.001$ ). The mean duration of motor block in the B-D and B-F groups was 266.06±61.07 and 285.22±42.69 min, respectively. According to independent sample *t*-test, no significant difference was seen between the two groups ( $P=0.07$ ). Moreover, the duration of surgery was almost similar between the two groups ( $P=0.15$ ). Table 3.

The incidence of complications such as hypotension, bradycardia, respiratory depression, shivering, as well as nausea and vomiting was recorded in two groups. (Table 4) The first minute Apgar score in the B-D and B-F groups was 8.79±0.58 and 8.67±0.88, respectively ( $P=0.81$ ). Moreover, the fifth minute Apgar score of the B-D and B-F groups was 9.95±0.47 and 9.81±0.56, respectively ( $P=0.86$ ). The results of Apgar scores showed no significant difference at the time points of one and five minutes.

## Discussion

In the present study intrathecal administration of dexmedetomidine and fentanyl combined with bupivacaine compared in women undergoing cesarean section. The results showed that adding 10 µg of dexmedetomidine to bupivacaine has a better effect on postoperative pain management compared to 25 µg fentanyl.

Today, intrathecal administration of Dex has attracted considerable attention during spinal anesthesia with the aim of increasing the duration of analgesia and decreasing postoperative pain. Many studies have addressed the administration of different doses of intrathecal Dex (3µg, 5 µg, 10 µg, 15 µg) as an adjuvant to local anesthetics [14–17]. It seems that Dex induces the activation of  $\alpha_2$ -agonist receptors in the spinal cord, which leads to a decrease in the transmission of nociceptive signals such as substance P. It has also been revealed that its analgesic effects after the surgery are due to the inhibition of the intracellular potassium transport activities [18]. As Dex binds to  $\alpha_2$  receptors in the locus coeruleus, reduces norepinephrine release, and inhibits sympathetic activity; it can cause hypotension and bradycardia. Hence, evaluation of hemodynamic changes in patients was of great importance in this study. There was no significant difference between

the B-D and B-F groups in terms of SBP, DBP, HR, MAP, and SpO<sub>2</sub> at most of the studied times, which is in accordance with the results of the pre-vious studies [14, 16, 19, 20]. Moreover, the findings of this study revealed the usage of ephedrine and atropine had no sig- nificant difference between the two groups, which were similar to the other studies [19, 21, 22]. However, Contractor *et al.* showed that the probability of MAP and HR decrease was higher in the Dex group compared to the control group [23]. It is worth mentioning that in the mentioned study, the patients received intravenous Dex infusion under spinal anesthesia. The study by Shukla *et al.* also showed that although MAP was similar between groups, bradycardia was more likely in the Dex group [20]. However, the mentioned study also examined Dex and MgSO<sub>4</sub> as an adjunct to spinal anesthesia. The results of this study indicated that the onset of block in the B-D group was faster than in the B-F group. There was no significant difference between the two groups in sensory block level, which was consistent with the findings of other studies [22, 24].

Considering the pain intensity based on VAS score, the results showed that pain intensity was less in the B-D group during recovery room period (T0). However, at T1, T3 and T6 in the postoperative period, no significant difference was observed between the groups. The mentioned observation may be attributed to the effects of Dex on the inhibition of pain receptors at the spinal cord that decreased c-fiber translocation and hyperpolarization of dorsal horn neurons [21]. This finding was in agreement with the results of studies conducted by Gupta *et al.* and Mahendru *et al.* [16, 25] and was consistent with the study by Sun *et al.*, just in the first hour while at two and four hours after the surgery, patients in the fentanyl group experienced less pain [24].

Moreover, compared with the B-F group, the duration of analgesia in the B-D group was significantly longer. The mentioned findings were entirely consistent with the results of studies by Jain *et al.* and Gupta *et al.* [16, 19]. In another fascinating study, Shukla *et al.* compared the effect of adding Dex and MgSO<sub>4</sub> to intrathecal bupivacaine and found that the onset of block was faster in the Dex group and duration of analgesia also was significantly longer in Dex group [20]. The results of the present study were in contrast with those of the Khalifa *et al.* study; however, it is worth noting that the mentioned study used sufentanil 0.1 µg instead of fentanyl and did not find any significant difference between the sufentanil and Dex groups regarding the duration of postoperative analgesia. Moreover, both groups in the mentioned study had a similar analgesic course [26].

The results of this study indicated that the duration of motor block and the length of surgery were almost identical between the two groups. The findings of this study were in line and in contrast with the findings of Sun *et al.* study in terms of the length of surgery and the duration of motor block, respectively [2] which Dex group in the mentioned study had a longer duration of block, that may be ascribed to the higher dose of Dex (10 µg).

Regarding other complications such as shivering, nausea and vomiting, and respiratory depression, there were no differences between these two groups in the present study, which was in agreement with the results of other studies [25]. However, Sun *et al.* indicated that shivering, as well as nausea and vomiting, was most commonly observed in the fentanyl group [24].

In the evaluation of the neonatal outcome, Apgar scores were compared between the two groups at one and five minutes after the birth that were almost identical between the two groups. The mentioned finding was in line with the results of other studies [2, 3] although Jain *et al.* [3] evaluated neonatal outcome with fetal heart rate.

### Conclusion

Compared with fentanyl, it seems that adding 10 µg dexmedetomidine to bupivacaine has a better effect on postoperative pain management in cesarean section under spinal anesthesia.

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