

ORIGINAL RESEARCH

## **Comparative study of adding fentanyl or dexmedetomidine or morphine as adjuvant for intrathecal bupivacaine for caesarean sections**

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### **ABSTRACT**

**Background:** Caesarean section is one of the most commonly performed surgical procedures worldwide and 80–90% of them are performed under spinal anaesthesia. Adding adjuvants drugs to intrathecal local anaesthetics improves quality and duration of spinal blockade, and prolongs postoperative analgesia. The aim of our study was to compare the efficacy of using intrathecal Fentanyl, morphine and Dexmedetomidine as adjuvants to Bupivacaine in patients undergoing caesarean section at a tertiary hospital.

**Material and Methods:** Present study was comparative study, conducted among pregnant women, 20-35 years age, ASA grade I/II, posted for elective Caesarean section. Patients received either Fentanyl or Morphine or Dexmedetomidine as adjuvants with Intrathecal Bupivacaine (H) 0.5% 10mg (2ml) with as a standard dose.

**Results:** In present study, 99 pregnant women, equally allotted (33 each) to each group (i.e. Group BF, Group BM & Group BD). Mean age & duration of surgery was comparable among all 3 groups & difference was not statistically significant ( $p > 0.05$ ). Onset of action (Group BD-  $43.3 \pm 10.22$  secs < Group BF -  $50.15 \pm 10.56$  secs < Group BM -  $51.4 \pm 9.46$  secs) & Duration of analgesia (Group BD-  $460.2 \pm 40.27$  mins > Group BM -  $326.2 \pm 32.92$  mins > Group BF -  $292.8 \pm 34.61$  mins) was significantly better in dexmedetomidine group as compared to fentanyl group & morphine group, difference was statistically significant ( $p < 0.05$ ). Maternal vitals (pulse rate, systolic blood pressure & diastolic blood pressure) were stable throughout surgery & early postoperative period among all 3 groups, difference was not statistically significant ( $p > 0.05$ ).

**Conclusion:** Intrathecal dexmedetomidine as an adjuvant to bupivacaine has early onset of action, prolonged post-operative analgesia combined with minimal side effects.

**Keywords:** Cesarean section; Dexmedetomidine; Fentanyl; morphine, Spinal anesthesia

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## INTRODUCTION

Caesarean section is one of the most commonly performed surgical procedures worldwide and 80–90% of them are performed under spinal anaesthesia.<sup>1</sup> Because of the risks related to airway oedema, difficulty with the airway or failed intubation, hypertensive response to direct laryngoscopy and aspiration pneumonitis; general anaesthesia is associated with more untoward outcomes.<sup>2</sup>

Spinal anaesthesia is comparatively safer, simple, fast in onset with uniform sensory and motor blockage and cost effective. The main disadvantage in using spinal anaesthesia is postoperative analgesia is short and more requirement of analgesics postoperatively.<sup>3</sup> The use of adjuvants intrathecally has become a common practice as an effective method of analgesia. Adding adjuvant drugs to intrathecal local anaesthetics improves quality and duration of spinal blockade, and prolongs postoperative analgesia.<sup>4</sup>

Fentanyl and morphine are preferred for their fast onset of action, good postoperative analgesia and minimal side effects.<sup>5</sup> Dexmedetomidine are Alpha 2-adrenergic receptor agonist which are proved to have good analgesia, sedation, peri operative sympatholytic, anaesthetic-sparing and hemodynamic stabilizing property.<sup>6</sup> The aim of our study was to compare the efficacy of using intrathecal Fentanyl, morphine and Dexmedetomidine as adjuvants to Bupivacaine in patients undergoing caesarean section at a tertiary hospital.

## MATERIAL AND METHODS

Present study was comparative, interventional study, conducted under department of anesthesiology & department of obstetrics & gynaecology, at Andaman and Nicobar Islands Institute Of Medical Sciences, Port Blair, India. Study duration was of 1 year (January 2021 to December 2021). Study approval was obtained from institutional ethical committee.

### Inclusion criteria

- Pregnant women, 20-35 years age, ASA grade I/II, posted for elective Caesarean section, willing to participate in present study

### Exclusion criteria

- Pregnant women with co-morbidities (hypertension, heart disease, renal disease, liver disease, psychiatric diseases),
- Pregnant women with fetal compromise and/or anomalies,
- Pregnant women with contraindication to spinal anaesthesia
- Pregnant women required additional general anaesthesia
- Pregnant women not consented for participation

Study was explained to patients in local language & written consent was taken for participation & study. Patient details such as demographic information, obstetric/medical/surgical history, clinical examination findings, laboratory investigations (CBC, urine routine and microscopic examination, KFT, LFT, FBSL) were noted. All patients underwent preanesthetic examination, after fitness patients were posted for surgery. One day prior to the surgery, written consent for surgery was obtained.

In operation theatre, the standard monitoring was done & baseline parameters (maternal pulse rate, non-invasive blood pressure, oxygen saturation, and respiratory rate) were recorded. Patients received either Fentanyl or Morphine or Dexmedetomidine as adjuvants with Intrathecal Bupivacaine (H) 0.5% 10mg (2ml) with as a standard dose. Patients were randomly divided into 3 groups by computer generated numbers.

- Group BM - Bupivacaine (H) 0.5% 10mg (2ml) and Morphine 150mcg (0.5ml)
- Group BF - Bupivacaine (H) 0.5% 10mg (2ml) and Fentanyl 25mcg(0.5ml)
- Group BD - Bupivacaine (H) 0.5% 10mg (2ml) and Dexmedetomidine 5mcg (0.5ml)

After preloading with 10 mL/kg Ringer lactated solution, spinal anaesthesia was administered under all aseptic precautions, through midline approach. Intraoperatively

patient's hemodynamic parameters were periodically recorded. Patients were observed intraoperatively at baseline and at 5, 10 and 15 min respectively, then at interval of 15 min up to 1 h and at 30 min till patient is shifted from operation theatre to PACU.

Standard postoperative care was provided. Variables measured were duration of effective analgesia (from the time of intrathecal drug administration to the time of first supplementation with rescue analgesic), postoperatively blood pressure, pulse rate, intensity of pain, spO<sub>2</sub>, adverse effects such as hypotension, bradycardia, respiratory depression were recorded.

Data was collected and compiled using Microsoft Excel, analysed using SPSS 23.0 version. Frequency, percentage, means and standard deviations (SD) was calculated for the continuous variables, while ratios and proportions were calculated for the categorical variables. Difference of proportions between qualitative variables were tested using chi-square test or Fisher exact test as applicable. P value less than 0.5 was considered as statistically significant.

## RESULTS

In present study, 99 pregnant women, equally allotted (33 each) to each group (i.e., Group BF, Group BM & Group BD). Mean age & duration of surgery was comparable among all 3 groups & difference was not statistically significant ( $p > 0.05$ ). Onset of action (Group BD-  $43.3 \pm 10.22$  secs  $<$  Group BF -  $50.15 \pm 10.56$  secs  $<$  Group BM -  $51.4 \pm 9.46$  secs) & Duration of analgesia (Group BD-  $460.2 \pm 40.27$  mins  $>$  Group BM -  $326.2 \pm 32.92$  mins  $>$  Group BF -  $292.8 \pm 34.61$  mins) was significantly better in dexmedetomidine group as compared to fentanyl group & morphine group, difference was statistically significant ( $p < 0.05$ ).

**Table 1: General characteristics**

Characteristics	Group BF	Group BM	Group BD	P value
Mean age (mean $\pm$ SD)	$25.68 \pm 3.56$	$25.79 \pm 3.69$	$25.44 \pm 3.35$	0.34
Onset of action (seconds)	$50.15 \pm 10.56$	$51.4 \pm 9.46$	$43.3 \pm 10.22$	0.02
Duration of surgery (mins)	$62.5 \pm 9.25$	$59.1 \pm 10.13$	$58.2 \pm 11.45$	0.47
Duration of analgesia (mins)	$292.8 \pm 34.61$	$326.2 \pm 32.92$	$460.2 \pm 40.27$	$<0.001$

Maternal vitals (pulse rate, systolic blood pressure & diastolic blood pressure) were stable throughout surgery & early postoperative period among all 3 groups (dexmedetomidine group, fentanyl group & morphine group), difference was not statistically significant ( $p > 0.05$ ).

**Table 2: Maternal vitals**

Characteristics	Group BF	Group BM	Group BD	P value
Systolic blood pressure				0.56
Baseline	$126.8 \pm 11.4$	$128.9 \pm 12.2$	$125.3 \pm 10.3$	
At 5 minutes	$119.5 \pm 8.3$	$121.0 \pm 8.9$	$118.5 \pm 8.3$	
At 10 minutes	$115.8 \pm 9.1$	$116.1 \pm 8.3$	$113.7 \pm 8.6$	
At 15 minutes	$115.0 \pm 8.9$	$113.8 \pm 9.2$	$112.2 \pm 8.8$	
At 30 minutes	$112.3 \pm 8.2$	$113.9 \pm 9$	$111.4 \pm 9.1$	
At 45 minutes	$112.5 \pm 8.5$	$114.7 \pm 8.4$	$110.9 \pm 8.3$	
At 60 minutes	$112.7 \pm 8.9$	$114.7 \pm 8.3$	$111.7 \pm 9.3$	
Diastolic blood pressure				0.63
Baseline	$81.3 \pm 8.4$	$80.1 \pm 9.1$	$78.7 \pm 8.8$	

At 5 minutes	72.3 ± 8.1	74.6 ± 8.2	73.7 ± 8.6	
At 10 minutes	71.5 ± 9.1	70.6 ± 8.4	70.9 ± 8.2	
At 15 minutes	69.5 ± 9	69.6 ± 8.6	68.0 ± 8.4	
At 30 minutes	69.8 ± 7.9	68.4 ± 8.6	68.2 ± 8.1	
At 45 minutes	68.3 ± 8.1	68.8 ± 8.3	67.6 ± 8	
At 60 minutes	67.8 ± 8.4	69.8 ± 8.4	69.3 ± 8.2	
Pulse rate				0.43
Baseline	92.5 ± 8.8	83.8 ± 8.7	83.9 ± 8.9	
At 5 minutes	89.0 ± 8.5	80.2 ± 8.6	80.3 ± 8	
At 10 minutes	83.6 ± 7.7	78.6 ± 8.3	77.2 ± 7.7	
At 15 minutes	81.3 ± 7.3	76.3 ± 8.2	75.3 ± 8.6	
At 30 minutes	82.8 ± 8	75.7 ± 7.8	73.7 ± 7.2	
At 45 minutes	81.0 ± 7.2	76.4 ± 8.2	73.0 ± 8.4	
At 60 minutes	81.1 ± 6.4	77.5 ± 8	73.6 ± 8.2	

Minor intra-operative complications were noted among dexmedetomidine group (1 bradycardia, 1 hypotension), fentanyl group (2 PONV) & morphine group (1 PONV, 1-pruritis, 1 bradycardia, 1 hypotension), all were managed medically. No respiratory depression, incomplete block, morbidity or mortality noted.

**Table 3: Complications**

Complications	Group BF	Group BM	Group BD
PONV	2 (6.06 %)	1 (3.03 %)	
Pruritis		1 (3.03 %)	
Bradycardia		1 (3.03 %)	1 (3.03 %)
Hypotension		1 (3.03 %)	1 (3.03 %)

## DISCUSSION

Hyperbaric Bupivacaine is the local anaesthetic used most commonly used drug worldwide for spinal anesthesia in Caesarean sections. But dose dependent usage of Bupivacaine can cause hypotension, bradycardia, vomiting, respiratory depression and shivering Low dose diluted bupivacaine limits the distribution of spinal block and yield a comparably rapid recovery, but may not provide an adequate level of sensory block.<sup>7</sup> Adjuvants decrease dose of local anaesthetic and their side effects. (Myocardial depression, hypotension, bradycardia, heart block, and ventricular arrhythmias) & to prolong intraoperative and postoperative analgesia.<sup>8</sup>

Opioids (fentanyl & morphine) are the most popular used adjuvants added to bupivacaine in spinal blockade to obtain a sufficient intraoperative visceral analgesia and increase the duration and quality of postoperative analgesia, with less sympathetic block and hemodynamic effect.<sup>9</sup> Morphine injected intrathecally results in analgesia by acting on opioid receptors in the dorsal horn of the spinal cord. Analgesia is adequate and long-lasting due to its hydrophilicity, decreased systemic absorption, cephalad spread in the cerebrospinal fluid, and slow rate of clearance from the opioid receptors.<sup>10</sup>

Dexmedetomidine (Dex), a new selective  $\alpha_2$ -agonist, is being introduced as an adjuvant to local anesthetics with significant analgesic, sympatholytic and sedative properties.<sup>11</sup> Intrathecal dexmedetomidine has been found to be ten times more potent analgesic and anaesthetic as compared to intrathecal clonidine and five times more potent than opioids like intrathecal fentanyl.<sup>12,13</sup>

In study by Rastogi K et al.,<sup>14</sup> duration of sensory and motor blockade was significantly prolonged ( $p < 0.001$ ) in Group LD as compared to Group LF or L. Onset of sensory and

motor blockade was earlier in Group LF as compared to Group LD and L ( $p < 0.001$ ). Time to first rescue analgesia was prolonged in Group LD than Group LF and L ( $p < 0.001$ ). Intrathecal dexmedetomidine produces prolonged motor blockade as well as postoperative analgesia than fentanyl when used as an adjuvant to 0.5% isobaric levobupivacaine in elective cesarean section.

Tufail AS et al.,<sup>15</sup> noted that 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) ( $P=0.041$ ). Compared with fentanyl, it seems that adding  $10\mu\text{g}$  dexmedetomidine to bupivacaine has a better effect on postoperative pain management in cesarean section under spinal anesthesia. Similar findings were noted in present study.

Sinha M et al.,<sup>16</sup> noted that time for the first analgesic request was  $320.80 \pm 41.75$  min in the dexmedetomidine group as compared to the morphine group ( $451.63 \pm 38.55$  min). The analgesic requirement in the first 24 h was significantly higher in Group D as compared to Group M. Adverse effects were similar in both the groups, except pruritus which was seen only in Group M. Use of intrathecal morphine as an adjuvant to isobaric levobupivacaine provides better analgesia than intrathecal dexmedetomidine; however, adverse effects such as nausea and pruritus may be seen. Similar findings were noted in present study.

In a systematic review and meta-analysis of randomized controlled trials ShuJun S et al.,<sup>17</sup> noted that compared to fentanyl, Dex as local anesthetics adjuvant in spinal anesthesia prolonged the duration of spinal anesthesia, improved postoperative analgesia, reduced the incidence of pruritus, and did not increase the incidence of hypotension and bradycardia.

The incidence of side effects like nausea and vomiting, hypotension, bradycardia, respiratory depression, shivering and pruritus were not significantly different among the groups. Limitations and shortcomings of present study were small sample size, for elective surgery patients only and from single hospital. Studies with larger number of participants are required to generalise the results and also the patient-to-patient variability of pain perception.

## CONCLUSION

Intrathecal dexmedetomidine as an adjuvant to bupivacaine seems it to be an attractive alternative to fentanyl and morphine for caesarean section procedures due to its early onset of action, prolonged post-operative analgesia combined with minimal side effects.

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