

## Comparative study of intrathecal low dose bupivacaine-fentanyl versus conventional dose of bupivacaine in parturients undergoing cesarean section

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### Abstract:

**Objectives:** To compare effectiveness of low-dose bupivacaine-fentanyl versus conventional dose of bupivacaine in parturients undergoing cesarean section and the frequency of hypotension in two regimens.

**Study design:** Randomized clinical study

**Place and duration of study:** Anesthesiology Department and Surgical Intensive Care Unit and Pain Management, Civil Hospital, Dow University of Health Sciences, from July to December 2019.

**Material and methods:** 52-women undergoing cesarean section were randomly allocated into two groups; 26-patients in group-A were given 10 mg bupivacaine, and 26 in group-B, 5 mg bupivacaine-25µg fentanyl. Blood pressure (BP) and heart rate were recorded. Intra-operative pain assessment was done using visual analog scale (VAS). Duration of effective analgesia was taken from the time of intra-thecal injection to a VAS score  $\geq 4$ . Systolic BP (SBP)  $< 20\%$  of pre-operative value was labelled as hypotension. Data was analyzed with SPSS 19.

**Results:** Mean age was  $26.19 \pm 4.31$  years. There was no significant difference among age, weight, height and ASA of patients in two groups ( $p=0.65, 0.052, 0.19, \text{ and } 0.39$ , respectively). Mean baseline SBP, diastolic blood pressure (DBP), and heart rate were not significantly different. Mean final SBP was significantly different ( $p = 0.006$ ), while no significant difference was seen in DBP and heart rate and duration of surgery ( $p=0.23, 0.42, 0.23$ , respectively). The duration of analgesia was more prolonged in group-B ( $p < 0.001$ ), and hypotension was significantly higher in group-A ( $p=0.005$ ).

**Conclusion:** Low-dose intra-thecal bupivacaine and fentanyl provides more effective spinal anesthesia for cesarean section with less hypotensive episodes.

**Keywords:** Spinal anesthesia, hypotension, bupivacaine-fentanyl, cesarean section

### Introduction:

Spinal anesthesia is the preferred method for caesarean section, because of simplicity, low cost and quick onset of anesthesia and complete muscle relaxation.<sup>1</sup> It carries high efficiency, involves less drug doses, minimal neonatal depression,<sup>2</sup> awake mother and lesser incidence of aspiration pneumonitis. General anesthesia is associated with higher mortality rate in comparison to regional anesthesia. Hence, the spinal anesthesia is very popular for caesarean section now-a-days, when possible.<sup>3</sup>

However, spinal anesthesia is not without risks. Morbidity and mortality in regional anesthesia are primarily related to excessively high regional block and toxicity of local anesthetic solution. It also produces fixed duration anesthesia,<sup>4</sup> post-dural puncture headache, hypotension and bradycardia.<sup>5</sup> The most common of these complications is hypotension with reported incidence of 80%.<sup>6</sup> Hypotension is related to the extent of sympathetic blockade, which is responsible for a decrease in systemic arteriolar and venous tone, resulting in decreased venous return leading to

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a fall in cardiac output.<sup>7</sup> Reduction in dose and improvement in technique to avoid higher block levels and heightened awareness to the toxicity of local anesthetic solution has contributed to the reduction of complications related to regional anesthesia.<sup>8</sup>

Hypotension is usually defined as a systolic blood pressure of less than 100 mmHg, or a decline of 20% from baseline.<sup>9</sup> Spinal anesthesia with a single dose of bupivacaine up to 5 mg for patients undergoing hip surgery yielded only a moderate incidence of hypotension but in 15% of patients, this low dosage did not provide an adequate level of sensory block.<sup>9</sup> Therefore, although the use of a single-shot low dosage local anesthetic for spinal block may limit hypotension, it may not provide acceptable anesthesia. Opioids and local anesthetics administered together intrathecally have a potent synergistic analgesic effect. Intra-theal opioids enhance analgesia from sub-therapeutic doses of local anesthetics and make it possible to achieve successful spinal anesthesia using otherwise inadequate doses of local anesthetics.<sup>9</sup> Previously reported frequency of hypotension in parturients treated with bupivacaine was 94% and in patients treated with bupivacaine-fentanyl, it reduced to 34%.<sup>10</sup>

The objective of this study was to compare effectiveness of low-dose bupivacaine-fentanyl versus conventional dose of bupivacaine in parturients undergoing cesarean section and to determine the frequency of hypotension in two regimens. According to our knowledge, no published data is available on this subject in Pakistan, so this study will help us to devise guidelines for prevention of these common and distressing complications not only in our country but also internationally.

#### **Material and Methods:**

This study was conducted after the approval of Ethical Committee of Dow University of Health Sciences, Karachi. All patients were selected from pre-operative anesthesia assessment clinic on fulfilling the inclusion criteria, which included age range of 18-35 years, weight of 50 to 70

kg, ASA status I and II, and no prior history of complications during previous spinal anesthesia. Patients who did not give consent for spinal anesthesia, un-cooperative patients, any infection at site of lumbar puncture, anatomic abnormality of vertebral column, complicated pregnancies like multiple pregnancies, pregnancy-induced hypertension and placenta previa, and history of coagulopathy were excluded from the study. Written informed consent was obtained. Two groups were made by balloting method by making equal numbers of chits bearing group-A and group-B. After application of standard monitoring of non-invasive blood pressure (BP), electrocardiogram (ECG), and pulse oximetry and two 18 G intravenous lines, all patients were preloaded with 15 ml/kg Ringer's Lactate solution over 10 minutes and then placed in sitting position. Pre-operative systolic BP, diastolic BP and heart rate were recorded before spinal anesthesia. All aseptic measures were taken. Local infiltration with 2% Lidocaine was done at the L3-L4 vertebral interspace and spinal needle of 25 G (Quincke) was inserted in midline at 90° and after aspiration of cerebrospinal fluid, parturients in two groups received following drugs over 5 seconds: Group-A received 10 mg bupivacaine, 0.5% and group-B, 5mg bupivacaine, 0.5% plus 25µg fentanyl.

Patients were immediately placed supine with 15° left lateral tilt position using wedge under right buttock. Medium-sized pillow was placed under head and both legs. Oxygen inhalation (6 l/min) with face mask was given immediately after the block. BP and heart rate were recorded at every 5-minute interval for 3 hours in both the groups. Hypotension was defined if systolic BP was <20% of pre-operative value. Intra-operative pain assessment will done using visual analog scale (VAS) as 0-10, where, 0 = no pain and 10 = worst pain. Post-operative pain was also assessed using the VAS scale. Duration of effective analgesia was taken from the time of intra-theal injection to a VAS score  $\geq 4$ . This was taken as a surrogate marker of effective analgesia. Apgar score of new born was recorded at 1 min and 5 min.

Table 1: Age and Healing time of the patients of Group I and Group II

Variables	Group A n=26	Group B n=26	P-Values
Age (Years)	25.92±4.25	26.46±4.43	0.65
Weight (kg)	59.65±6.26	62.73±4.75	0.052
Height (cm)	153.27±6.65	155.62±6.08	0.19
ASA status	I/II (18/8)	I/II (14/12)	0.39
APGAR Score	8/9	8/9	0.50
Baseline Systolic BP (mmHg)	111.38±11.06	113.23±13.99	0.60
Baseline Diastolic BP (mmHg)	78.73±8.79	77.12±9.91	0.53
Baseline Heart Rate (beats/min)	87.12±15.72	84.16±11.33	0.061

Table 2: A comparison of hemodynamic parameters, duration of surgery and analgesia between two groups

Variables	Group A n=26	Group B n=26	P-Values
Final Systolic BP (mmHg)	108.04±8.46	115.69±15.54	0.006
Final Diastolic BP (mmHg)	72.77±6.38	68.96±9.38	0.232
Final Heart Rate (beats/min)	90.04±15.77	93.19±11.8	0.42
Duration of surgery (min)	46.35±8.66	49.09±7.48	0.23
Duration of analgesia (min)	72.12±9.61	140±14.1	<0.001

Table 3: A comparison of effectiveness of drug between two groups

Variables	Group A n=26	Group B n=26	Total	P-Values
Yes	10(38.5%)	20(76.9%)	30(57.7%)	0.005
No	16(61.5%)	6(23.1%)	22(42.3%)	

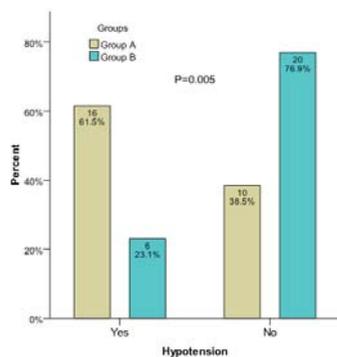


Figure 1: Bar graph showing comparison of hypotension between two groups

Data analysis procedure: Statistical Packages for Social Sciences (SPSS-19) was used to analyze data. Relevant descriptive statistics were used. Frequency and percentages were computed for qualitative variables like ASA status and effectiveness of drug. For quantitative variables such as age, weight, height, systolic and diastolic BP, heart rate, duration of analgesia and duration

of surgery were summarized by mean and standard deviation (SD). Effect modifiers were controlled by stratification like age, weight, height to observe effect on outcome variable (effectiveness of drug). The comparison of variables among two groups was performed by t-test and chi-square test and a p value < 0.05 was taken as significant.

### Results:

A total of 52-women undergoing elective cesarean section were included in this study. The mean age of all patients was 26.19±4.31 years. There was no statistically significant difference among age, weight, height and ASA status of the patients between two groups as shown in table-1 (p= 0.65, 0.052, 0.19 and 0.39, respectively). Mean baseline systolic BP, diastolic BP, and heart rate were also not significant between the groups as shown in table-2. Among mean final systolic BP, diastolic BP, heart rate (recorded at an interval of 40 minutes post-procedure) and duration of surgery, systolic BP was significantly different between two groups (p=0.006), while no significant difference was seen in diastolic BP, heart rate and duration of surgery (p=0.232, 0.42, and 0.23, respectively) as shown in table-2. Table-3 shows that effectiveness of combination of drugs (group-B) was significantly higher than the singular drug (group-A) (76.9% vs. 38.5%; p=0.005).

Hypotension was observed in 61.5% (16/26) patients in group-A and 23.1% (6/26) patients in group-B. Hypotension was significantly higher in group-A than group-B (p=0.005) as shown in figure 1.

### Discussion:

The prevention and treatment of maternal hypotension associated with spinal anesthesia for cesarean section remains a difficult problem with no consensus as to the optimal mode of management. This lack of consensus is probably due to the causes of hypotension. As hypotension is pre-dominately due to venous, arterial and arteriolar vasodilatation secondary to sympathetic blockade, the dose of local anesthetic is an important part of the etiology of the hypoten-

sion.<sup>11</sup> It has been reported that increasing the dose of local anesthetics increases the incidence of maternal hypotension. Intra-theal opioids enhance analgesia without altering the degree of sympathetic blockade when added to sub-therapeutic doses of local anesthetics.<sup>12</sup>

In this study, we compared both the effectiveness and the frequency of hypotension with low-dose bupivacaine-fentanyl spinal anesthetic versus a conventional dose of spinal bupivacaine in parturients undergoing cesarean section. The results showed that low-dose intra-theal bupivacaine and fentanyl, in comparison with conventional dose of bupivacaine, provided a marked decrease in the incidence of hypotension and associated side effects such as nausea and vomiting, without reducing the anesthesia quality in cesarean section patients.

Spinal anesthesia offers many advantages for cesarean section, including simplicity, rapid onset, and dense neural blockade.<sup>13</sup> The combination of bupivacaine with fentanyl for cesarean section has been shown to improve the quality of spinal anesthesia without unwanted effects. Decreasing the bupivacaine dose can lead to decreased incidence of maternal hypotension, ephedrine requirements, nausea, and time to discharge from the recovery room.<sup>14</sup>

Spinal anesthesia is popular for its rapid onset and profound neuromuscular blockade of high quality. After the injection of local anesthetic, absorption depends upon blood flow, which, in turn, is determined by injection site, presence of vasoconstrictor and the type of local anesthetic agent.<sup>15</sup> Our results indicated that 5mg bupivacaine, 0.5% plus 25µg fentanyl could be used safely and effectively for spinal anesthesia in caesarean section. The use of intra-theal fentanyl provided a more intense sensory block and allowed lower bupivacaine doses. Limiting the bupivacaine dose has been advocated with goals of decreasing maternal hypotension, vasopressor requirements, nausea and time of discharge from the recovery room and maternal satisfaction.<sup>16</sup> Our results also concur with the above observations.

The administration of intrathecal opioid carries a risk of respiratory depression.<sup>17</sup> Varrassi et al, noted that administration of 25µg fentanyl during spinal anesthesia in non-premedicated elderly patients did not alter respiratory rate, end-tidal carbondioxide tension, minute ventilation, respiratory drive, respiratory timing or ventilatory response to carbondioxide.<sup>18</sup> This is in agreement with our study as the respiratory rate and the oxygen saturation did not change from the baseline rate. Also none of the new borns had 5 min APGAR score <7. Similar observations were made by Biswas et al, indicating that the dose of fentanyl may not have significant effect on the new borns.<sup>19</sup> The incidence of other side effects, i.e., nausea, vomiting was significantly lower in bupivacaine-fentanyl group than the bupivacaine only group.<sup>19</sup>

The most important determinant of both successful surgical anesthesia and time until recovery is the dose of local anesthetic drug.<sup>20</sup> Low dose of spinal anesthetic has the advantage of providing cardiovascular stability and it is advocated that 8 mg of 0.5% bupivacaine is the optimal dose for cesarean section.<sup>21</sup> Our study demonstrates that cesarean section can be completed with low-dose bupivacaine and fentanyl. The synergistic action of fentanyl and local anesthetic in central neuraxial block improves the quality of intra-operative analgesia and also prolongs the post-operative analgesia.

A number of studies have used 25µg of intrathecal fentanyl as adjunct to the anesthetic agent with good results. A few studies have used intrathecal fentanyl in <25µg, but most studies have shown that 25µg of fentanyl provides maximum duration of post-operative analgesia with minimal side effects (respiratory depression and pruritus).<sup>22</sup> Another study on parturients for cesarean delivery found that the peak sensory level was higher and motor block more intense in patients receiving 5 mg isobaric bupivacaine with 25µg fentanyl.<sup>16</sup>

Atallah and colleagues reported that the incidence of clinically relevant bradycardia and hypotension was 8.5% and 11%, respectively

in the whole study population.<sup>23</sup> Similar results have been reported in previous investigations, in which low dose spinal anesthesia has been shown to reduce the effects of spinal block on heart rate and blood pressure when small doses of hyperbaric bupivacaine 0.5% are used.<sup>24</sup>

In agreement with previous investigations, bupivacaine–fentanyl combination produced good intra-operative and post-operative analgesia and better patient satisfaction without prolonging recovery room stay.<sup>25</sup>

### Conclusion:

In conclusion, this study showed that low-dose intra-thecal bupivacaine and fentanyl provides good spinal anesthesia for cesarean section with less hypotensive episodes. It has advantages of lower dose of bupivacaine and good hemodynamic profile as compared to conventional bupivacaine dose.

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**Funding source:** None

### Role and contribution of authors:

Dr. Shakil Malik, collected the data, references and did the initial write up.

Dr. Rajeev Kumar Chawla, collected the data and helped in introduction writing.

Dr. Sagar Khurana, collected the references and helped in discussion writing.

Dr. Shaheera Shakil, critically review the article and made final changes.

Dr. Rahma Rashid, went through the article and advised useful changes.

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