

Effect of Intrathecal Fentanyl with Bupivacaine on Maternal Hemodynamics and Fetal Outcome during Cesarean Section: A Comparative Study with Two Different Doses

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Abstract

Introduction: Intrathecal opioids to increase analgesic effect of bupivacaine during cesarean section are being used worldwide. Fentanyl a short-acting synthetic opioid is particularly suited for this purpose in doses from 10 to 30 µg.

Materials and Methods: Total of 120 parturients of American Society of Anaesthesiologists Grades I and II scheduled for cesarean section were randomly allocated to receive either 10 mg of 0.5% injection bupivacaine (Group B, $n = 40$) or 0.25 ml (12.5 µg) fentanyl with 10 mg of 0.5% injection bupivacaine (Group BF1, $n = 40$) or 0.50 ml (25 µg) fentanyl with 10 mg of 0.5% injection bupivacaine (Group BF2, $n = 40$). The total volume of drug was made 2.5 ml in every group by adding distilled water, and maternal hemodynamic parameter was assessed every 5 min for first 15 min, then at 15 min interval for remainder of operation, thereafter at 30 min interval for 2 h postoperatively.

Results: Four patients (10%) in Group B had intraoperative discomfort and required ketamine supplementation while none in the fentanyl groups complained of pain. About 19 patients (47.50%) in Group BF2, 11 patients (27.50%) in Group BF1 and eight patients (20%) in Group B required vasopressors ($P < 0.05$ between Group B and Group BF2 and BF1 and BF2 group and $P > 0.05$ between Group B and Group BF1).

Conclusion: There was no significant difference in neonatal Apgar and neurological and adaptive capacity scores score among any of the group. There was no significant difference in adverse effects among the three study groups. 25 µg fentanyl intrathecally causes significantly more hypotension as compared to 12.5 µg fentanyl.

Key words: Fentanyl, Maternal hypotension, Neonate

INTRODUCTION

The subarachnoid blockade is the most frequent anesthetic technique for caesarian section. However, local anesthetics alone are usually insufficient to provide uniform block despite the high sensory level of anesthesia.^{1,2}

The epidural or subarachnoid administration of opioids to increase analgesic effect of bupivacaine during caesarean section is being used widely. The use of hydrophilic agents such as morphine was associated with prolonged duration of action and delayed respiratory depression.³ To overcome these drawbacks newer agents, such as fentanyl were introduced. Fentanyl has a rapid onset of action and does not tend to migrate to fourth ventricle in sufficient concentration to cause delayed respiratory depression when administered intrathecally.⁴

It has been used in doses ranging from 10 to 30 µg for supplementing subarachnoid block during caesarean delivery.^{5,6}

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This study was designed to evaluate the effect of 2 different doses of fentanyl (12.5 µg and 25 µg) on the maternal hemodynamic status and neonatal outcome.

MATERIALS AND METHODS

The study was conducted on 120 primigravida as well as multigravida patients belonging to American Society of Anaesthesiologists Grades I and II, between the ages of 18-30 years. After obtaining approval from the Institutional Ethical Committee, written informed consent was obtained from all the patients. Beside general contraindications to regional anesthesia during cesarean section, patients with fetal heart rate (FHR) >160 or <100 were excluded from the study.

Patients were randomly allocated to receive either 10 mg of 0.5% injection bupivacaine (hyperbaric) (Group B, $n = 40$) or 10 mg of 0.5% injection bupivacaine and 12.5 µg fentanyl (Group BF1, $n = 40$) or 10 mg of 0.5% injection bupivacaine and 25 µg fentanyl (Group BF2, $n = 40$). All the study agents were introduced intrathecally and the total volume of agents administered was made equal (2.5 ml) by adding distilled water.

In the operating room, after establishing an intravenous (IV) line, patients were premedicated with injection metoclopramide and injection ranitidine IV and were preloaded with 15 ml/kg ringer lactate solution. Pulse rate, blood pressure, respiratory rate (RR), SpO₂, and FHR were recorded before giving spinal anesthesia.

Under all aseptic precautions, lumbar puncture was performed with 25 gauge Quinckes needle in L₃L₄ space in left lateral position and study drug were injected as per group of patients according to random assignment. The patient was turned in supine position, table was tilted to 15° head down position, and a wedge was placed under the right hip of the patient. All patients received oxygen supplementation (3-4 L/min) via ventimask immediately after administration of spinal anesthesia. FHR were noted for any bradycardia. Pulse rate, blood pressure, rate of respiration, tidal volume, SpO₂, and side effects such as pruritus, nausea, vomiting and shivering were recorded every 5 min for first 15 min and then at 15 min interval for remainder operation and thereafter at 30 min interval for 2 h postoperatively.

The decrease in systolic blood pressure (more than 20% from baseline values and/or <90 mmHg) after spinal injection was treated by increasing the rate of IV fluid administration, by exaggerating the uterine shift and by injecting ephedrine 5-10 mg IV.

10 U of oxytocin was given intravenously after delivery of baby. Neonatal Apgar score was recorded at 1 and 5 min after delivery of baby and neurological and adaptive capacity scores (NACS) scoring (Table 1) was performed at 15 min and 2 h interval.

Data were analyzed by using one-way analysis of variance test.

RESULTS

The study groups were comparable with respect to age, weight, height, parity and gestational age (Table 2) and operative management (Table 3).

The level of anesthesia was considered sufficient for the surgical procedure because no patient had a sensory level below T₆. None of the patient in the study experienced respiratory depression, (RR <9 breaths/min), desaturation (SpO₂ <90%), or significant decrease in tidal volume. 8 patients (20%) in bupivacaine group, 11 patients (27.50%) in 12.5 µg fentanyl group and 19 patients (47.50%) in 25 µg fentanyl group had hypotension and required ephedrine administration. The difference was statistically significant between bupivacaine group and 25 µg fentanyl group and 12.5 µg and 25 µg fentanyl group ($P < 0.05$) while it was insignificant between BF1 and B group. Maximum fall from baseline in mean blood pressure was seen 10 min after block in Group B, 20 min after block in Group BF1 and 5 min after block in Group BF2 (Table 4). 4 patients in Group B had intraoperative pain and were given ketamine 30 mg. No patient in fentanyl groups had pain. 5 patients in bupivacaine group (12.5%), 3 patients in 12.5 µg fentanyl group (7.5%) and 1 (2.5%) patient in 25 µg fentanyl group had intraoperative nausea ($P < 0.05$). No patient in either of the group had bradycardia, hypoxia or pruritis. 5 (12.50%) patients in bupivacaine group, 2 patients (5.0%) in 12.5 µg fentanyl group and 3 patients (7.50%) in 25 µg fentanyl group had shivering ($P > 0.05$). There was no significant difference in neonatal Apgar or NACS score among the three groups.

DISCUSSION

Opioids added to local anesthetics for spinal anesthesia was the first introduced into clinical practice in 1979. Morphine was the first opioid used intrathecally⁷ but problem with morphine was its slow onset of action and delayed respiratory depression. To overcome these drawbacks, newer agents such as fentanyl and sufentanil were

Table 1: Neurological and adaptive capacity scores

NACS scoring	0	1	2
Adaptive capacity			
Respond to sound	Absent	Mild	Vigorous
Habituation of sound	Absent	7-12 stimuli	<6 stimuli
Response to light	Absent	Mild	Brisk blink
Habituation to light	Absent	7-12 stimuli	<6 stimuli
Consolability	Absent	Difficult	Easy
Passive tone			
Scarf sign	Encircles the neck	Elbow slightly passes midline	Elbow does not reach midline
Recoil of elbow	Absent	Slow, weak	Brisk
Popliteal angle	>100	100-110	<90°
Recoil of lower limbs	Absent	Slow, weak	Brisk
Active tone			
Active contraction of neck flexors	Absent	Difficult	Good
Active contraction of neck extensors	Absent	Difficult	Good
Palmar grasp	Absent	Weak	Good
Response to traction	Absent	Lifts part of body weight	Lifts all body weight
Supporting reaction	Absent	Incomplete	Strong
Primary reflexes			
Automatic walking	Absent	Difficult to obtain	Perfect
Moro reflex	Absent	Weak	Perfect
Sucking	Absent	Weak	Perfect
General assessment			
Alertness	Coma	Lethargy	Normal
Crying	Absent	Weak, excessive	Normal
Motor activity	Absent	Diminished	Normal

Table 2: Patients demographics

Demographics	Group B	Group BF1	Group BF2	P value
Age (years)	23.19±5.62	24.22±5.96	24.36±3.56	>0.05
Height (cm)	152.3±4.81	152.5±6.44	150.63±11.22	>0.05
Weight (kg)	60.96±6.20	62.06±6.79	62.43±7.62	>0.05
Multiparous (n)	15	16	17	>0.05

Table 3: Operative management

Parameters	Group B	Group BF1	Group BF2	P value
Induction-delivery interval (min)	11±5.6	12±3.2	11±4.2	>0.05
Skin incision-delivery interval (min)	6.4±2.3	6.6±3.1	6.5±3.6	>0.05
Uterine incision-delivery interval (s)	40±15	37±20	39±22	>0.05
Duration of surgery (min)	45±6.8	47±7.2	44±6.4	>0.05

Table 4: Changes in mean arterial blood pressure

Mean arterial blood pressure (mmHg)	Group B	Group BF1	Group BF2
Pre-operative	80.03±12.60	83.13±15.61	85.89±16.20
Just after block	79.46±12.04	81.54±13.60	78.65±12.20
At 5 min	74.17±11.18	76.78±12.56	70.32±10.42
At 10 min	70.19±11.34	74.68±12.40	72.39±11.56
At 20 min	73.66±8.40	73.08±13.45	74.16±12.50
At 30 min	77.18±8.34	74.60±10.72	78.79±9.86

introduced. Because of high lipid solubility of fentanyl, only a small proportion of the administered dose tends to

migrate cephalad to the cervical region or 4th ventricle⁸ so there is no respiratory depression. An additional advantage is rapid onset of action, analgesia occurs within 5-10 min following intrathecal administration.

A wide range of doses of fentanyl is being used as adjuvant to bupivacaine for intrathecal administration during cesarean section, ranging from 10 to 30 µg.^{5,9} This study was conducted to find most appropriate fentanyl dose which has minimum hemodynamic side effects and is sufficient to provide good analgesia during cesarean delivery.

The result of this study showed that fentanyl 25 µg causes significantly higher incidence of hypotension (47.50%) as compared to 12.5 µg fentanyl (27.50%) when used as adjuvant to bupivacaine for LSCS.

Incidence of nausea did not differ significantly among the study groups and no patient had vomiting in any of the group (Table 5). This may be because of the use of injection metoclopramide and injection ranitidine as premedication to all patients.

10% patient in bupivacaine group complained of intraoperative discomfort while non in the fentanyl groups had intraoperative discomfort. The site of action of intrathecal fentanyl is substantia gelatinosa in spinal cord. Neuraxial opioids act by inhibiting release of substance P in this region of spinal cord.¹⁰

No significant difference was there in incidence of shivering among the 3 groups. No patient in either of the group had hypoxia or respiratory depression. This may be due to highly lipophilic nature of the drug limiting its rostral spread.

Neonatal condition was assessed by both Apgar score and NACS score. We used NACS score also because it was designed specifically to study effects of maternal drug administration on fetus.¹¹ Results of study revealed that fentanyl in doses of 12.5 µg and 25 µg have no adverse effect on neonatal Apgar score or NACS scoring (Table 6) which is in agreement with other studies.¹²

Table 5: Maternal side effects (n=40)

Side effects	n (%)		
	Group B	Group BF1	Group BF2
Nausea	5 (12.5)	3 (7.5)	1 (2.5)
Vomiting	0 (0)	0 (0)	0 (0)
Hypotension	8 (20.0)	11 (27.50)	19 (47.50)
Bradycardia	0 (0)	0 (0)	0 (0)
Hypoxia	0 (0)	0 (0)	0 (0)
Shivering	5 (12.50)	2 (5.00)	3 (7.50)
Pruritis	0 (0)	0 (0)	0 (0)
Complaint of discomfort by patient	4 (0.0)	0 (0)	0 (0)

Table 6: Neonatal outcome

Parameters	Group B	Group BF1	Group BF2	P value
Apgar score				
1 min	8.00±0.77	7.83±0.74	8.06±0.77	P>0.05
5 min	9.26±0.73	8.86±0.99	9.23±0.80	P>0.05
NACS				
15 min	37.93±1.80	37.73±1.96	37.56±2.01	P>0.05
2 h	35.92±1.40	39.16±1.20	38.96±1.67	P>0.05

NACS: Neurological and adaptive capacity scores

CONCLUSION

We conclude that fentanyl in doses of 12.5 and 25 µg although equally safe from neonatal prospective but, 25 µg fentanyl added to 10 mg bupivacaine for SA during cesarean section causes significantly higher incidence of hypotension in mother as compared to 12.5 µg fentanyl without any additional benefit, so ideal dose of fentanyl as adjuvant to bupivacaine during SA for cesarean section should be 12.5 µg.

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