

A Comparative Study of Intrathecal Versus Intravenous Fentanyl in Cesarean Section under Subarachnoid Block

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Abstract

Background: The use of neuraxial opioid has gained popularity over the last few years. The dose calculation of local anesthesia for intrathecal block is difficult due to hormonal and mechanical factors of pregnant women along with neonatal outcome. **Aim:** This study was undertaken to compare the effects on outcome of newborn and peri-operative maternal analgesia with intrathecal versus intravenous fentanyl in lower segment cesarean section under subarachnoid block. **Materials and Methods:** The ASA I and II pregnant women were randomly allocated into 2 Groups (30 patients each). Group A received 1.7 ml of 0.5% hyperbaric bupivacaine along with 25 mcg fentanyl (0.5 ml), Group B received 1.7 ml of 0.5% hyperbaric bupivacaine along with saline (0.5 ml) 1 mcg/kg body weight of intravenous fentanyl immediately after SAB. Umbilical arterial blood gas analysis was sent immediately after baby extraction and Apgar score noted. The sensory and motor level achieved, hemodynamic changes, post-operative maternal analgesia and side effects were recorded. **Results:** Apgar score of newborn was normal in both the groups. Patients in Group A had statistically significant prolonged maternal analgesia than a patient in Group B ($p < .0001$). There was statistically significant ($p = 0.002$) decreased incidence of nausea and vomiting in Group A. **Conclusion:** Intrathecal and intravenous fentanyl achieves quality anesthesia with good Apgar score of neonate, while intrathecal fentanyl has added benefit of prolonged peri-operative maternal analgesia with minimal side effects.

Keywords: Fentanyl; Bupivacaine; Intrathecal; Intravenous; Spinal anesthesia.

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Introduction

For cesarean section subarachnoid block has been the best method since long-time with a quick onset of sensory and motor block with complete muscle relaxation.¹ Neuraxial administration of adjuvants like opioids along with local anesthetics improves the quality of intra-operative analgesia and also provides good quality anesthesia with post-operative pain relief for longer duration.²

The morphine is the first hydrophilic opioid used intrathecal in cesarean section.³ However, this hydrophilic opioid has a late onset of action that often precludes any intra-operative analgesic effect and potentially serious late respiratory depression.⁴ Fentanyl is a synthetic lipophilic opioid commonly used in obstetrics anesthesia, with rapid onset and short duration of action, and it lacks active metabolites. Fentanyl increases analgesic effect of bupivacaine during cesarean section. Fentanyl does

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not tend to migrate to fourth ventricle in sufficient concentration to cause delayed respiratory depression when administered intrathecal.

Neonatal outcome is assessed by blood gas analysis of umbilical cord vessel and Apgar scores. In this more sensitive tool was Umbilical cord blood gas analysis of the neonate. This provide important information about the past, present and possibly the future condition of the infant and are recommended in high risk pregnancies. Fentanyl when given during induction of cesarean section (1 mcg/kg) and as hourly I.V. injections (50–100 mcg) for labor analgesia showed no increase in the incidence of respiratory depression or low Apgar scores.⁵ The neonatal neurological and adaptive capacities after delivery were normal when fentanyl is used for cesarean section.

In the above scenario, this study was undertaken to compare the efficiency of intrathecal fentanyl versus intravenous fentanyl on neonatal outcome and to compare the maternal analgesia during post-operative period for cesarean section in both the groups.

Materials and Methods

It is a Prospective Randomised double blind comparative study. The sample size is calculated as 30 in each group, considering difference of 2 in mean HCO₃ and SD in each group as 2.3, 90% power, and 5% alpha.

Inclusion criteria include the patient willing to give consent, pregnant women with no co-morbidities and patients in term pregnancy. Exclusion criteria include pregnant women prolong labor, Fetal distress (based on NST, CST and FHR), Preterm fetus, fetal anomaly or congenital syndrome, Fetus exit time > 8 mins and any factor Contraindication to spinal anesthesia.

After obtaining Institutional ethical committee clearance, informed written consent was taken. Pre-anesthetic evaluation done and baseline investigations noted. Anesthetic protocol explained to the patient. 60 pregnant women were randomly selected and divided with the help of computer generated random number tables into two groups:

Group A received 25 mcg of intrathecal fentanyl with 1.7 ml of 0.5% hyperbaric bupivacaine (8.5 mg) with total volume of 2.2 ml for spinal anesthesia and 2 ml of normal saline I.V.

Group B received 1.7 ml of 0.5% hyperbaric bupivacaine (8.5 mg) with 0.5 ml of normal saline with total volume of 2.2 ml for spinal anesthesia

and 1 mcg/kg body weight of I.V. fentanyl after spinal anesthesia.

Each patient was hydrated with 500 ml of Ringer lactate solution I.V. and placed in the left lateral position. Pre-medication's Inj. Ranitidine 50 mg I.V. and Inj. metaclopramide 10 mg I.V. was given. Electrocardiogram, pulse oximetry, and non-invasive blood pressure were monitored.

Spinal anesthesia was performed by using a 27 gauge needle at the L2-3 to L3-4 intervertebral space. Immediately after the intrathecal injection the pregnant woman is placed supine with left uterine displacement. Oxygen 5 L/min was given via a face mask during the surgery. The highest level of sensory and motor sensory blockade was recorded after spinal anesthesia. The degree of motor block was assessed with the Bromage Scale (BS) and sensory by pin prick.

Intra-operative blood pressure (measured by a non-invasive blood pressure monitor), saturation, heart rate, every 3 minutes for first 10 mins and at 5 min intervals for next 20 mins and then at 15 mins interval until the end of the surgery and hourly for 6 hours. Whenever Systolic Blood Pressure (SBP) was less than 100 mm Hg or 20% below the baseline (defined as hypotension), ephedrine 5 mg was administered I.V. If HR < 50 min, Inj. Atropine 0.6 mg I.V. was given. In the event of respiratory depression (RR < 8 or SpO₂ < 95%), oxygen supplementation and respiratory support were given when required.

Immediately after delivery of the fetus umbilical cord was clamped and the umbilical arterial blood was collected in a heparinized syringe and arterial blood gas analysis was done immediately. The Apgar scores of the infant were assessed at 1 and 5 min. Following a delivery, Fetal Heart Rate (FHR) was monitored and FHR of 120–160 bpm was considered normal and baseline variability of ≥ 6 bpm was considered normal.

The occurrence of the side effects like pruritus, respiratory depression etc. was assessed at the same time. Vomiting was treated with I.V. 4 mg Ondansetron. Pruritus was treated with Inj. Chlorpheniramine 10 mg I.V. Rescue analgesia was given as paracetamol 12–15 mg/kg body wt. I.V. when VAS was greater than 3. Pain scores were recorded using a 10 cm visual analog score (VAS) (0 cm = no pain, 10 cm = worst pain imaginable).

Statistical Analysis

Chi-square and independent *t*-test as test of significance. *p* - value of < 0.05 was considered significant. Continuous data:

Represented as mean and standard deviation;

Data entered into Microsoft excel data sheet and was analysed using SPSS 22 version software.

Results

The mean age, weight, height, ASA physical status was comparable in both groups and statically insignificant as shows in Table 1.

The onset of bupivacaine induced spinal block was similar in both the groups. The time interval (duration) for sensory level to regress to L1 dermatome were prolonged in Group A whereas the duration of motor blockade was similar in both groups as shown in Table 3.

There was no difference in the number of patients experience of bradycardia (HR < 60 min), hypotension in both the groups (fall off systolic BP < 20% from base level). Respiratory depression (RR < 8 breaths/min), desaturation (SpO₂ < 90%) in both the groups shown in Table 3.

The neonatal outcome from Patients in both groups showed no significant difference with a mean pH of 7.28 in Group A and 7.29 in Group B in ABG. The Apgar score showed no neonatal depression, 8 score in 1 minute at 70% in Group A and 73.3% in Group B and a score of 9 at 5 minutes in both the groups shown in Table 2.

Patients in Group A had statistically significant prolonged maternal analgesia than patients in Group B ($p < 0.001$). The vas score is also significantly lower in Group A compared to Group B at 2nd hour which is also statistically significant ($p < 0.001$), as shown in Table 4. The time for the first request of post-operative analgesia was significantly longer in the Intrathecal Fentanyl (Group A) than in the I.V. Fentanyl (Group B) (.234 ± 54 min versus 145 ± 7.1 min) Table 3.

There was statistically significant ($p = 0.002$) decreased incidence of nausea and vomiting in Group A when compare to Group B. Purities were seen in 26.7% of cases in Group A, whereas purities in Group B were 3.4% shown in Table 5.

Demographic Data

Table 1: Age, weight, height, ASA physical status

	Group 1	Group 2
Age	22.8 ± 2.5	23 ± 2.4
Height	149 ± 3.7	151 ± 2.3
Weight	58.2 ± 5.9	60.2 ± 5.5
BMI	25.97 ± 2.885	26.40 ± 2.630

Table 2: Apgar score

	Group 1	Group 2	p Value
Apgar Score-1'	8.3 ± 0.3	7.8 ± 0.6	0.421
Apgar Score-5'	9	9	NS

Table 3: Comparison of Different variables in both groups

Variables	Group A	Group B	p Value
Heart rate at 5 min	92.20 +/- 13.7	93.30 +/- 13.7	0.660
Systolic blood pressure at 5 min	101.37 +/- 4.8	99.37 +/- 7.3	0.216
Diastolic blood pressure at 5 min	61.07 +/- 6.9	57.60 +/- 6.3	0.48
Onset of sensory blockade	1.5	2.1	0.32
Onset of motor blocked	3.1	4.1	0.23
2 segment regression	180.3 +/- 2.2	122.2 +/- 3.5	0.001
Duration of post-op analgesia	234 +/- 54	145 +/- 7.1	0.001

p value < 0.001

Table 4: VAS Score of both the Groups at 2nd hour

VAS at 2 hr	Group	
	1	2
0	30	0
1	0	7
2	0	14
3	0	9

p value < 0.001

Table 5: Side Effects

Side Effects	Group 1	Group 2	P Value
Nausea	2	12	0.002
Vomiting	0	5	0.02
Bradycardia	2	1	0.302 (NS)
Hypotension	3	1	0.556 (NS)
Pruritus	5	1	0.085 (NS)

Discussion

In obstetric the most preferred mode of anesthesia is subarachnoid block [SAB] for elective lower segment cesarean section [LSCS]. SAB has high efficiency, involves less dose, minimal depression of neonate and minimal incidence of aspiration pneumonia. But SAB as its own limitation like fixed duration of anesthesia, less control of block height, intra-operative hypotension and lack of post-operative analgesia.⁶ In view of above advantages and disadvantages of the SAB for LSCS with plain bupivacaine, the addition of opioid to SAB is carried out as it is already practiced in surgical and orthopedic cases.

Initially morphine in low dose was used for SAB along with bupivacaine due to its hydrophilic property, it caused complications like nausea, vomiting and potentially serious late respiratory depression. In the present study, we are comparing intrathecal fentanyl and intravenous along with bupivacaine for SAB for LSCS. The Ben-David B *et al.* study used 5 mg of isobaric bupivacaine with 25 mcg fentanyl, the neonatal outcome was good but maternal analgesia was in-adequate.⁷ Himabindu GV *et al.* used 7.5 mcg hyperbaric bupivacaine with 25 mcg of intrathecal fentanyl and observed significant post-operative analgesia.⁸ Hence, in the present study, we used 8.5 mg of hyperbaric bupivacaine with 25 mcg of fentanyl.

The studies available for intravenous fentanyl for LSCS under SAB are few. The Maziyar *et al.* documented that no alteration in Apgar score was noted when intravenous fentanyl was used in doses of 1 mcg/kg body wt., 3 min before induction of anesthesia for LSCS under GA.⁹ Saha MK *et al.* conducted the study with a single dose of 12.5 mcg of intravenous fentanyl for LSCS under SAB with normal Apgar at 1 min and 5 min.¹⁰ In the present study, we are using fentanyl 1 mcg per kg per body wt. immediately after SAB.

In the present study, the achievement of T6 level was fastest in Group A compared to Group B shows in Table 3, but it is not statistically significant, which correlates with a study conducted by Turkmen A *et al.*¹¹ There is no difference noted in motor block in both the Groups which is similar to the study conducted by Choi D H *et al.*¹² In intra-operative period quality of anesthesia was excellent with dense block in Group A compared to Group B. Which is similar to study conducted by Manullang TR *et al.*¹³

In the present study, in both the Groups patients are hemodynamically stable throughout the intra-operative period, which is similar to the study conducted by Gajanan C *et al.* and Sowmya N *et al.* with different doses of fentanyl intrathecal.^{14,15}

The time taken for sensory regression to T12 is prolonged in Group A was 180.3 ± 2.2 , while Group B it was 122.2 ± 3.5 as shows in Table 3. It concurred with a study done by Abhina AV *et al.* (183 min) and Biswas *et al.* (151 min).^{16,17}

In our study, blood gas analysis of umbilical cord arterial blood did not reveal a significant difference in pH, PaO₂ and SpO₂ between the two groups. This is due to the rapid metabolism of fentanyl when it is given by intravenous route. Thus the minimal amount of fentanyl enters the fetal circulation and will not affect the fetus.

Chopra G *et al.* noted no difference in Apgar scores when fentanyl used intrathecal and intravenous for cesarean section.¹⁸ In present study, Apgar score at 1 min and 5 min was same in both the groups, which coincide with the study done by Goyal *et al.* and biswas *et al.* with different doses of intrathecal fentanyl for LSCS shows in Table 4.^{19,17}

Biswas *et al.* indicated that by increasing the dose of intrathecal fentanyl and reducing dose of bupivacaine there was a decrease in incidence of hypotension but poor outcome of neonates.¹⁷

The vas score at the end of 2nd hour was zero in all patients in Group A, whereas most of the patients of Group B are at 2 or 3 score of VAS at the same time shows in Table 4, which is statically significant ($p < 0.001$).

The prolonged analgesia has been explained with intrathecal fentanyl dose of 6.25 and 12.5 mcg by Biswas *et al.* and Bogra J *et al.*¹⁷⁻²⁰ In our study, post-operative analgesia was prolonged in Group A *i.e.*, 234 ± 54 min compared to Group B *i.e.*, 145 ± 7.7 min shows in Table 3, which is statically significant ($p < 0.001$). Which is similar to study conducted by weigi w *et al.* and Shashekala TR *et al.* with similar doses of fentanyl intrathecal post-operative analgesia was 240 min and 248 min respectively.^{21,22} This action is due to synergetic effect of lipophilic property of fentanyl with bupivacaine has been explained by Dhupal PR *et al.*²³

In present study, intra-operative nausea and vomiting was significantly reduced in Group A compared to Group B ($p = 0.002$). Intra-operative nausea and vomiting is commonly seen in LSCS due to traction of uterus and exteriorization of uterus. Muhammad AS *et al.* in their study concluded that intrathecal fentanyl at 25 mcg causes dense spinal block and leads to less nausea and vomiting in peri-operative period in LSCS.²⁴ Pallab R *et al.* documented that lipophilic fentanyl has board spectrum anti-emetic effect when it is given intrathecal.²⁵

In present study, pruritus was more in intrathecal fentanyl compared to intravenous fentanyl, which is similar to study conducted by the Himabintu GV *et al.* and Cowan CM *et al.*^{8,26} Abhina AV *et al.* demonstrated that if an intrathecal fentanyl dose is more than 25 ug causes more pruritus shows in Table 5.¹⁶

Conclusion

In a present comparative study of intrathecal versus intravenous fentanyl for cesarian section under

spinal anesthesia, intrathecal fentanyl achieve excellent intra-operative anesthetic condition and stable hemodynamic with prolonged pre-operative maternal analgesia with minimal side effect and with good Apgar scores of neonates.

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