

Addition of Fentanyl to Hyperbaric Bupivacaine in Spinal Anesthesia for Caesarian section Effect on Dose of Local Anesthetic and Duration of Postoperative Analgesia - A Randomized Comparative Study

Ghulam Mohammed Mir, MD.,¹ Mohammed Abdul Haadi, MD²
Madina Maternity and Children Hospital, KSA

ABSTRACT

Background : Spinal anesthesia is commonly used for caesarian section for its reliability and ease of administration. However, it is limited by fixed duration of anesthesia, hypotension and lesser control of block height. The combination of reduced dose of local anesthetic agent with intrathecal opioid makes it possible to achieve adequate spinal anesthesia with minimum hypotension and prolonged postoperative analgesia. The study aims to monitor the effect of intrathecal fentanyl and bupivacaine on reduction of higher blocks and simultaneously improving the quality and avoiding higher doses of local anesthesia agents.

Methods: Forty patients scheduled for elective caesarian section were divided in to two groups of twenty each. Group I patients received Bupivacaine 12.5 mg (0.5%) for spinal anesthesia and group II patients received combination of Bupivacaine 8.5 mg (0.5%) with fentanyl 25 mcg. Patients were observed for hypotension, bradycardia, nausea, pruritus, quality of surgical anesthesia and duration of postoperative analgesia.

Results: All the patients had adequate surgical anesthesia for the procedure and in no patient conversion to general anesthesia was required. Peak sensory level was higher (T2-T3 vs T4-T6) and motor block was more intense in the regular dose bupivacaine group of patients. More patients in bupivacaine only group developed hypotension and the requirement of vasopressors was significantly higher than the low dose bupivacaine with fentanyl group. Also the Visual analogue scale score for pain was less in the bupivacaine-fentanyl group, who received less postoperative analgesics for first twelve hours.

Conclusions: We conclude that combination of low dose bupivacaine (8.5mg) with fentanyl provides adequate surgical anesthesia for caesarian section and with low incidence of hypotension and nausea. Also, addition of fentanyl helps in prolongation of postoperative analgesia. JMS 2017; 20 (2):62-68

Keywords: spinal anesthesia, bupivacaine, fentanyl, Cesarean Section, hypotension, Vasopressors

INTRODUCTION

Caesarian Section (CS) is the most common surgical procedure performed in Obstetric anesthesia. Spinal anesthesia (SA) has become an established technique, being simple to perform, economical and produces rapid onset of anesthesia and complete muscle relaxation. Maternal hypotension is believed to complicate up to 95% of these patients and may result in fetal acid-base abnormalities through reduction in utero-placental perfusion¹. Various local anesthetics and opioids have been used, either alone or in combination, for SA. Bupivacaine, an amide type of local anesthetic, has high potency, slow onset (58 minutes) and long duration of action (1.52 hours). For CS intrathecal dose

of hyperbaric bupivacaine is 12 to 15 mg². With higher doses of hyperbaric bupivacaine, incidence of intra-operative visceral pain associated with higher blocks is reduced^{3,4}. Smaller doses of local anesthetics supplemented by intrathecal opioids have been recommended for spinal anesthesia in parturient undergoing CS delivery^{5,6}. Intrathecal opioids increase the quality of analgesia and reduce local anesthetic requirements, with some studies showing favorable effects on hemodynamic stability especially hypotension⁷⁻¹⁰.

Acute postoperative pain management is challenging and also a major concern in lower abdominal surgeries¹¹. The usual methods of pain control often do not provide an adequate analgesia in half of the patients and postoperative pain can delay patient's recovery¹².

Anesthetic technique appears to be effective in postoperative pain¹³.

Correspondence

Ghulam Mohammed Mir, MD
Madina Maternity and Children Hospital, KSA
email: tikkamir@yahoo.com

Different sites of action of local anesthetics and opiates with differences in blocking central sensitization may contribute to a pre-emptive effect¹⁴. Lipophilic opioids such as Fentanyl when added to local anesthetic agent for intrathecal administration enhances sensory effects of SA without prolonging motor blockade and provides postoperative pain relief¹⁵.

The aim of this study was to compare the effectiveness of hyperbaric Bupivacaine, with or without Fentanyl, administered intrathecally in patients undergoing CS, we also looked to monitor the effect of bupivacaine-fentanyl on reduction of higher block incidence, simultaneously improving the quality and avoiding the complications of higher doses of local anesthetics. We tested the hypothesis that SA with hyperbaric bupivacaine 8.5 mg (0.5%) with fentanyl 25 mcg is superior to bupivacaine 12.5 mg (0.5%) alone in terms of avoiding high spinal anesthesia blockade and reducing the postoperative pain and analgesic consumption after CS.

METHODS

After approval by the Hospital Ethics Committee and written informed consent, we included 40 full term parturients (ASA I and II) with uncomplicated pregnancies. Patients were randomly allocated into two groups of 20 patients each. Group I patients received Bupivacaine 12.5 mg (0.5%) and group II patients received Bupivacaine 8.5 mg (0.5%) with preservative free fentanyl 25mcg. Preoperative evaluation in both study groups included a detailed history, physical examination, and review of antenatal care, including laboratory investigations such as the complete blood count, renal and liver function tests, and coagulation profile. All women were given intravenous (IV) ranitidine (50 mg) and metoclopramide (10 mg) one hour before the procedure and cefazolin sodium (1 g) as a prophylactic antibiotic just before shifting to the holding area. Prior to spinal anesthesia all the patients received 500ml of Ringer's Lactate solution via 18 gauge venous catheter. Women in both groups were placed in the left 15° lateral tilt position until delivery to protect against supine hypotension syndrome. After preoperative assessment and randomization, all patients received standard continuous monitoring of their electrocardiograph in lead II, heart rate, arterial oxygen saturation (measured by pulse oximetry), and noninvasive blood pressure.

Spinal anesthesia was administered in sitting position; for lumbar puncture, 25 gauge Quincke needle was introduced

at L3-L4 interspace. Immediately after the block the parturient was positioned with 10 cm wedge under right hip. Heart rate and noninvasive blood pressure were measured every 5 minutes for the first 30 minutes and thereafter every 10 minutes. Hypotension was defined as systolic blood pressure below 90 mm Hg or 20% below the pre spinal anesthesia value, IV boluses of 40 mcg phenylephrine were used as vasopressor support. The number of hypotensive episodes and total phenylephrine used was recorded. Pain scores were recorded at the time of skin incision until uterine replacement.

Total analgesic drug consumption was recorded. Sensory block was assessed by pinprick testing at the left mid-clavicular line till the block reached T6 when the surgical incision was allowed. The degree of motor block was assessed using Bromage Scale (BS): BS 0, full flexion of knees and feet, 1. just able to move knees, 2. able to move feet only, 3. unable to move feet and knees, and complete motor block was defined as BS3.

Intra-operative pain was scored whenever the parturient complained of discomfort or pain during operation and expressed as Visual Analogue Scale (0 cm no pain to 10 cm, worst pain imaginable) by the parturient. Occurrence of nausea, vomiting, pruritus and the onset of postoperative pain was recorded. All the time variables were measured from the beginning of the spinal injection. Post operatively all women were interviewed by an independent observer for pain at 2, 6, 8, 12 and 24 hours. When patient was discharged from recovery, if visual analogue scale (VAS) score was more than 4, intravenous 0.15mg/kg morphine was given; if the score did not reduce within 15 minutes an additional 0.1mg/kg morphine was administered and total consumption of analgesic was recorded. Statistical analysis included Students' t-test, Fisher exact test and contingency table analysis. Results were considered significant at a p value less than 0.05.

RESULTS

There were no significant differences in the baseline demographic variables between the two groups (Table 1). Block on set time of sensory block (upto T6 level) was slightly faster in the bupivacaine only group (6 min versus 7 min), but it was not significantly different from bupivacaine plus fentanyl group (Table 2). Sensory block was sufficiently intense in both groups to provide surgical anesthesia for all patients. No patient in either group had analgesia inadequate to warrant General anesthesia.

Table 1: Demographic characteristics of patients undergoing Caesarian section

Demographic variable	Group I Bupivacaine (12.5mg)	Group II Bupivacaine (8.5mg)+ Fentanyl 25 mcg
n	20	20
Age (yrs)	23±7.6	25±4.3
Weight (kg)	77±5.2	79±7.4
Height (cm)	158±5	154±3
Initial Systolic Blood pressure (mm of Hg)	124±9.5	128±11.5
Initial Diastolic Blood Pressure (mm of Hg)	68±6.1	72±6.5

Table 2- Block characteristics in the two patient groups

Block characteristics	Group I	Group II	p-value
Time to reach peak sensory block (minutes)	6.4±1.3	7.3±0.45	>0.05
Time to reach Peak motor block (minutes)	7.4±0.9	8.9±1.2	<0.05
Peak level of sensory block (Thoracic)	T2-T3	T5-T6	-

Table 3: Comparison of Visual Analog Scale score in the postoperative period

Postoperative period (hours)	Group I (VAS Score)	Group II (VAS Score)	p value
2	3.3±1.5	1±0.5	<0.05
4	4.5±1.1	1.4±0.6	<0.05
6	5.1±0.8	1.9±1.5	<0.05
8	4.6±1.2	2.4±1.2	<0.05
12	3.7±1.1	2.9±1.6	>0.05
24	2.8±0.9	2.5±1.0	>0.05

Table 4: Comparison of total dose of morphine used in first 24 hours of postoperative period

Variable	Group I	Group II	p value
Total morphine in milligrams for first 8 hours of postoperative period	10.5± 4.3	2.5±0.9	<0.05
Total morphine in milligrams used from 9 - 24 hours of postoperative period	13.59±3.2	12.45±4.5	>0.05

Table 5: Changes in systolic blood pressure during first 30 minutes after administration of spinal anesthesia

Systolic Blood Pressure	Group I	Group II	p value
Immediately after Block	127.12±15	126.34±14.4	>0.05
After 5 minutes	118.39±24.90	122.25±12.6	>0.05
After 10 minutes	92.34±7.9	118.15±10.3	<0.05
After 15 minutes	88.76±4.8	114.23±6.9	<0.05
After 20 minutes	91.84±7.8	120.14±4.6	<0.05
After 25 minutes	100.76±9.3	117.64±3.9	<0.05
After 30 minutes	106.63±6.8	114.54±6.5	>0.05

Patients in the bupivacaine only group developed motor blockade significantly faster and the blockade was more intense (Bromage score^{2,3}, $p < 0.05$) compared with patients from bupivacaine fentanyl group (Table 2).

The VAS score at 2, 4, 6 and 8 hours after the surgery (Table 3) and also the total morphine consumption (Table 4) during the first 8 hours after surgery in Group-II patients was statistically lower than Group-I, but there were no significant differences between the two groups regarding 8-24 hour postoperative pain scores and analgesic requirements ($p > 0.05$). Two patients in Group-II noted transient pressure or stretching or mild operative pain at the time of delivery, but all patients from bupivacaine - fentanyl group reported a High level of satisfaction with their anesthesia at the end of the procedure. Dissatisfaction because of nausea and transient respiratory disturbance was noted by 4 women in the bupivacaine only group.

Significant hypotension developed in 12/20 patients in the bupivacaine alone group compared with only 1/20 patients in the bupivacaine - fentanyl group (Table 5), furthermore, other 2/20 patients with bupivacaine injection developed severe hypotension with transient respiratory or conscience disturbances. In the bupivacaine-fentanyl group, only 2 patients required treatment for hypotension versus 12/20 of the patients in the plain bupivacaine group. There was a difference between groups in the frequency, severity, and persistence of the hypotension so. No patient in the bupivacaine - fentanyl group required more than 40 mcg of phenylephrine, whereas in the bupivacaine only group the median dose of phenylephrine was 250 mcg. Nausea and vomiting were more pronounced in the bupivacaine only group, occurring in 40% of patients as opposed to none of the patients in the bupivacaine-fentanyl group. As noted, mostly patients expressed dissatisfaction with their anesthesia in the bupivacaine only group. Nausea and unpleasant feeling occurred mostly at the end of exteriorization of the uterus and manipulation of the peritoneum.

DISCUSSION

Spinal anesthesia provides effective surgical anesthesia and postoperative analgesia and by ensuring minimal maternal and neonatal side effects, has been reported to be more advantageous than general anesthesia for CS^{16,17}. However, regional anesthesia is not without risk, deaths in regional

anesthesia are primarily related to excessive high regional blocks and toxicity of local anesthetic agents. Reduction in dose to avoid higher block level and increased awareness to the toxicity of local anesthetic agents have contributed to the reduction of complications related to regional anesthesia¹⁸.

The concept of using a reduced dose of local anesthetic with opioid during spinal anesthesia to minimize adverse effects has received attention^{19,20}. The addition of opioid to local anesthetic agent reduces the dose of local anesthetic and the incidence of adverse effects, due to the synergistic effects of opioids with local anesthetics, without causing a sympathetic block^{21,22}. It also ensures the occurrence of the effect in a shorter time and prolongs the duration of postoperative analgesia^{23,24}. Use of local anesthetic agent alone has been reported to be inadequate in preventing visceral pain and nausea during uterine manipulation and closure of the visceral peritoneum^{25,26}. The addition of lipophilic opioids to the local anesthetics during spinal anesthesia increases the quality of the anesthesia without prolonging the duration of the motor block. The disappearance rate of motor block increases with such combinations²⁷. In our study although motor blockade in most of the patients in the bupivacaine only group developed significantly faster and was more intense, (Bromage Score 2, 3; $p < 0.05$) compared with patients from bupivacaine-fentanyl group, no patient in either group had analgesia inadequate to warrant general anesthesia, which goes in concurrence with findings of Dahl JB et al, who observed that the addition of fentanyl increases the spread of anesthesia, slows its regression, and enhances and prolongs intra-operative and postoperative analgesia²⁸. We demonstrated low pain score at 2, 4, 6 and 8 hours after surgery and also reduced total morphine consumption during the first 8 hours after surgery in bupivacaine-fentanyl group which was statistically lower than bupivacaine only group, but there were no significant differences between the two groups beyond 8 hours relating to postoperative pain and consumption of morphine ($p > 0.05$).

The use of combination of low dose of local anesthetic plus lipophilic opioid, has increased in recent years, demonstrating clear benefits less hypotension and better peri-operative analgesia. Vercautere et al, used a combination of sufentanil with low-dose bupivacaine

(6.6mg) for spinal anesthesia in CS and found a lower incidence of hypotension²⁹. Intrathecal administration of fentanyl 1 with bupivacaine during CS was found to potentiate the analgesic effect of local anesthetic and be associated with a decreased incidence of hypotension, faster onset of block and motor recovery, and shorter time to micturition¹⁰. Unacceptably high spinal anesthesia has been reported with dose larger than 12mg of bupivacaine in patients undergoing CS. Measures to prevent hypotension during spinal anesthesia for CS include the administration of fluids (colloids or crystalloids) before the regional anesthesia, left uterine displacement and administration of prophylactic vasopressor. The use of reduced local anesthetic dose together with direct effects of intrathecal opioid results in low incidence of hypotension. The principal finding of our study was that the combination of reduced dose of bupivacaine- 8.5 mg with opioid (fentanyl) provided excellent spinal anesthesia for caesarean delivery with significantly less hypotension than standard dosage of bupivacaine alone. Bradycardia during spinal anesthesia results from blockade of sympathetic cardio-accelerator fibers and decreased venous return to the heart. In our study 4 patients in group I, developed bradycardia, while no patient in group II developed bradycardia as use of low-dose bupivacaine causes a lower incidence of bradycardia as a result of lesser sympathetic blockade. Fentanyl supplementation reduces the incidence of extremely high-block formation, and accelerates the onset of the motor block. Adverse effects of intrathecal opioids may include respiratory depression in the mother, nausea, vomiting, and itching^{23,30}.

Intrathecal fentanyl has a very selective interaction, it acts synergistically with bupivacaine to enhance the effect on the efferent pathways but without an effect on sympathetic pathways, thus preventing hypotension^{31,32}. Even more, it appears that the addition of intrathecal fentanyl to bupivacaine during spinal anesthesia potentiates the surgical analgesia for somatic and visceral pain, thus making the patients more satisfied with their anesthetic. It is likely that complex mechanisms along with potency, lipophilicity, and drug concentration play a role in the local anesthetic actions of spinal opioids³³. Most patients in the bupivacaine-fentanyl group reached lower median peak sensory level (T6), which was quite enough to reach

adequate surgical anesthesia, compared with patients from other group where the sensory level reached up to T2. The normal blood pressure compounded with peak sensory level, was associated with a reduction in the mean phenylephrine requirement; In fact, only two patients in the bupivacaine-fentanyl group required phenylephrine. Pruritus is the commonest complication of intrathecal opioids³⁴. In our study 30% of the patients developed mild pruritus although no patient demanded treatment for the same.

CONCLUSIONS

We conclude that addition of fentanyl 25 mcg to low dose hyperbaric bupivacaine 8.5 mg (0.5%) for spinal anesthesia provides adequate and reliable satisfactory anesthesia for patients undergoing CS. It is associated with significantly less hypotension and vasopressor requirement. Also addition of fentanyl increases duration of postoperative analgesia. Overall by using combination of bupivacaine and fentanyl there was improvement in quality of spinal anesthesia for CS and we were able to reduce the dose of bupivacaine, which did not produce hemodynamic instability.

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