Original Article

Role of Fentanyl With Bupivacaine During Spinal Anaesthesia for Caesarean Section in Reducing Hypotension

Col Md. Al Mamun[1], Lt Col Md Rabiul Alam[1] Maj Suraya Akter[1], Brig Gen Mozibul Haque[2]

[1]Classified Anaesthesiologist, Combined Military Hospital, Dhaka; [2]Adviser Anaesthesiologist, CMH, Dhaka

Corresponding Author: E-mail: mamun720@gmail.com

Abstract:

Background and Objectives: *The hypotension following spinal anaesthesia is a common problem in caesarean section. The combination of reduced dose of local anaesthetics with intrathecal opioids makes it possible to achieve adequate spinal anaesthesia with minimum hypotension. We investigated whether this synergistic phenomenon could be used to provide less frequent hypotension while incurring adequate spinal anaesthesia for caesarean section.*

Methods: *Sixty women scheduled for caesarean delivery (thirty in each group) were divided into two groups of patients who received a spinal injection of either 12.5 mg of hyperbaric bupivacaine or 10 mg of hyperbaric bupivacaine with 25 μg fentanyl added. Each measurement of a systolic blood pressure less than 95 mmHg or a decrease in systolic pressure of greater than 25% from baseline was considered as hypotension and treated with a bolus of 5 to 10 mg of intravenous ephedrine. The quality of surgical anaesthesia was evaluated also.*

Results: *Spinal block provided excellent surgical anaesthesia in almost all patients. Peak sensory level was higher (D_{2-3} vs. D_{4-5}) and motor block was more intense in the hyperbaric bupivacaine group; the patients from bupivacaine group were more likely to require treatment for hypotension (75% vs. 15%) and had more persistent hypotension (4.6 vs. 1.0 hypotensive measurements per patient) than patients in the reduced bupivacaine-fentanyl group. Mean ephedrine requirements were 15.0 mg and 3.5 mg, respectively. Patients in the bupivacaine group also complained of emetic effects more frequently than patients in the reduced dose bupivacaine-fentanyl group.*

Conclusions: *Bupivacaine 10 mg plus fentanyl 25 μg provided spinal anaesthesia for caesarean delivery with less hypotension and vasopressor requirements while ensuring excellent perioperative surgical anaesthesia.*

Key words: *Caesarean delivery; spinal anaesthesia; bupivacaine, fentanyl.*

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Introduction

A spinal anaesthesia for caesarean section has become increasingly popular and the recent decade has been the preferred technique for the majority of anaesthesiologist. This is primarily due to increased maternal mortality with general anaesthesia and benefits conveyed to the mother. But, spinal anaesthesia is associated with major or minor complications in the pregnant patient, the commonest being maternal hypotension. It is believed to occur in up to 95% of the patients and may lead to a reduction in utero-placental perfusion resulting in foetal acid-base abnormalities[3]. How important is this and what should we be doing to prevent it? Local anaesthetics plus opioids administered together intrathecally have been shown to have a synergistic analgesic effect[4,5,9]. Intrathecal opioids increase the quality of analgesia and reduces local anaesthetic requirements, with some studies showing favourable effects on haemodynamic stability[6,7,9,10]. Therefore, it may be possible to achieve spinal anaesthesia with less hypotension, by using a reduced (low) dose of local anaesthetic in combination with fentanyl. The

aim of this study was to test a reduced dose intrathecal bupivacaine in combination with intrathecal fentanyl for caesarean delivery both in terms of its feasibility as an anaesthetic and as its potential to minimize maternal hypotension.

Methods

The study included 60 ASA I healthy parturients between 18 and 40 years of age with similar demographic characteristics, scheduled for elective, semi urgent or urgent caesarean section. Complicated pregnancies such as multiple pregnancy, serious pregnancy induced hypertension, and placenta previa patients were excluded; patients with cardiac, renal, or other organ-system disease were also excluded from the study. Each patient received 10 mg metoclopramide intravenously before spinal block and a rapid intravenous infusion of 500 mL of saline solution were given in the operating room via an 18-gauge intravenous catheter. In addition to the loading dose of IV fluids, patients received a further saline solutions during the remainder of the operation. Only minimal sedative medications were administered during the operation (midazolam1-2 mg). Standard continuous electrocardiogram monitoring and pulse oximetry was included. Baseline maternal heart beat and blood pressure values were established before the lumbar puncture. The lumbar puncture was performed at the L2–3 (mostly patients with bupivacaine-fentanyl injection) or L3–4 interspace, with a 26-gauge B Braun needle, with the parturients in the sitting position. After confirming the correct placement of the spinal needle by aspiration of the cerebrospinal fluid (CSF) and after completion of the injection (the spinal volume was injected over 20–25 seconds) the patients were immediately returned to the supine position with 15 to 20 degrees of left uterine displacement breathing oxygen via face mask. The patients were randomly assigned into two groups defined by the spinal injection. They received either 12.5 mg (2.50 ml) of hyperbaric (0.5% bupivacame in the first group or 10 mg of hyperbaric bupivacaine plus fentanyl 25 μg (2.25 ml) of volume in the second group. Blood pressures were measured via the non-invasive blood pressure (NIBP) monitor at 3 minute interval during the first 15 minutes after the spinal injection and every 5 minutes thereafter. Whenever systolic blood pressure was lower than 95 mm Hg or 20% below the pre-induction level (defined as hypotension), ephedrine 5 mg intravenously dosage was administered. The number of hypotensive measurements and total ephedrine use for each patient were recorded. Patients who complained of pain were given 50 μg increments of IV fentanyl. Pain scores were summed across the following sequential intervals during the procedure: skin incision, delivery until uterine exteriorization, uterine replacement and start of facial closure and skin closure. The visual analogue scale (VAS) was used if pain (analgesia) persists. The protocol allowed for conversion to general anaesthesia as deemed necessary. The degree of motor block was assessed using Bromage Scale (BS): BS0, 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 BS 3. The level of sensory block was tested with method of touch sensation. All of these time variables were measured from the beginning of the spinal injection. The newborns' Apgar scores at 1 and 5 minutes were recorded immediately after delivery. Emetic effects- nausea or vomiting were registered; other side effects were evaluated if needed.

Statistical analysis was performed using statistical tests included Student's t-test, Fisher exact test and contingency table analysis. Results were considered significant at a p value of 05.

Results

There were 30 patients in each group of total 60 patients, and were similar with respect to age, weight, and height among the groups (Table I).

Table I *Demographic characteristics of the patients undergoing caesarean section*

Indices	Plain bupivacaine	Reduced bupivacaine+ fentanyl
Patients (n)	30	30
Previous caesarean section	10	12
Age (yr)	23.0 ± 5.5	24.2 ± 3.7
Weight (kg)	68.5 ± 10	67.5 ± 8.5
Height (cm)	160 ± 4	161 ± 5
Initial systolic BP (mmHg)	128 ± 10.2	127 ± 11.5
Initial diastolic BP (mmHg)	75.4 ± 9.	76.6 ± 8.5.
Duration of the operation (min)	60.5 ± 9.5	62.5 ± 8.5

Block onset times of sensory block (to T5) was slightly faster in the hyperbaric bupivacaine group (5.5 min versus 7 min), but it was not significantly different from bupivacaine plus fentanyl group. Peak median cephalad sensory block to touch sensation was significantly higher (by at least 2 dermatome) in the hyperbaric bupivacaine group with the highest level of anaesthesia occurred at the fifth cervical dermatome in the same group (Table II). Sensory block was sufficiently intense in both groups to provide surgical anaesthesia for all patients although one patient from bupivacaine plus fentanyl group required conversion to general anaesthesia (GA) because of inadequate surgical anaesthesia. Pain: 2 of the 30 patients (2/30) in each group, 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 anaesthetic at the end of the procedure. There was the sole exception of one patient needed general anaesthesia, which was at the time of the delivery until uterine exteriorization. No patient in hyperbaric bupivacaine group required conversion to general anaesthesia. Dissatisfaction because of nausea, not from anaesthesia, was noted by 3 women in the bupivacaine group. Most of the patients in the plain bupivacaine group developed and vanished significantly faster and more intense motor block (Bromage score 2, 3, $p < 0.05$) compared with patients from bupivacaine+ fentanyl group, (Table II).

Hemodynamic effects and neonatal outcomes: With regard to hypotension, there were pronounced and significant differences between the groups. 14/30 patients developed hypotension in the bupivacaine group compared with only 14/30 patients in the bupivacaine-fentanyl group; furthermore, other 13/30 patients with bupivacaine injection developed severe hypotension with transient respiratory or conscience disturbances. In the bupivacaine-fentanyl group, only 3 patient required treatment for hypotension versus 15/30 patients (50%) of the patients in the hyperbaric bupivacaine group. There was a difference between groups in the frequency, severity, and persistence of the hypotension also. No patient in the bupivacaine fentanyl group required more than 10 mg of ephedrine, whereas in the hyperbaric bupivacaine group the median dose was 22.0 (range 0–65 mg) (Table-III). Nausea and vomiting were more pronounced in the hyperbaric bupivacaine group, occurring in 40% of patients as opposed to none of patients in the bupivacaine-fentanyl group. As noted, mostly patients express dissatisfaction with their anaesthesia in the hyperbaric bupivacaine group. Interestingly, patient dis-satisfaction stemmed from the unpleasant sensation (nausea) rather than from pain. Nausea and unpleasant feeling occurred mostly at the end of exteriorization of the uterus and manipulation of the peritoneum.

Table II *Intervertebral space used for spinal puncture; characteristics of sensory and motor spinal block and number of patients required additional analgesia or GA; patient comfort satisfaction.*

Intervertebral space forpuncture	Hyperbaric bupivacaine only (n = 30)	Bupivacaine+ fentanyl (n =30)
L2–3	9	18
L3–4	20	12
L4-5	1	0
Peak sensory levelmedian, range	T2, 3 (C5–T5)	T4,5 (2-6)
Motor block (Bromage scale) (0–1–2–3)	0-0-4-16	0-6-12-2
Pain during surgery, (requiring fentanyl)	2/30	2/30
Pain during surgery,(requiring GA)	0/30	1/30
Nausea/Vomiting	8/30	0/30
Satisfaction with anaesthesia	3-0-17	1-0-19
(1–4, 5–7, 8–10) 3–0–17 1–0–19		

Table III *Spinal block and hypotension; ephedrine requirements; neonatal outcome during surgery*

Variables	Hyperbaric bupivacaine (n=30)	Reducedbupivacaine+ fentanyl (n=30)
Hypotension < 95 mmHg	14	13
Severe hypotension < 80 mmHg	3	1
Number of measurements ofhypotension (mean ± SD)	4.6 ± 3	1.0 ± 1.2
Required treatment of hypotension	15	3
Ephedrine total dose(mean ± SD), range	22.0 ± 18.4(0–65)	3.5 ± 3.4(0–10)
Apgar score, 1 min	8.5 ± 0.5	8.8 ± 0.8

Neonatal outcome parameters Apgar scores were similarly excellent in both groups, and there were no significant differences between the groups.

Discussion

The principal finding of this study was that the combination of reduced (low) dose of bupivacaine -10 mg with opioid (fentanyl) provides excellent spinal anaesthesia for caesarean delivery with significantly less hypotension than standard dosage of bupivacaine alone. Nowadays, textbooks of anaesthesia recommend large (standard) doses of bupivacaine still, even though clinical experience favour small doses combined with opioids. Often, dosages between 12–15 mg of hyperbaric bupivacaine are recommended, but hypotension could be very often complication with such dosages. Further, unacceptable high spinal anaesthesia has been reported with doses larger than 12 mg of bupivacaine in patients undergoing caesarean section, although the problem seems not to be often[8,21]. Thus, the appropriate dosage of bupivacaine seems to be under re-evaluation[8]. Hypotension is perhaps the most common complication of standardized bupivacaine spinal anaesthesia. If no preventive measures are taken during this manoeuvre, the incidence of hypotension is reported as 92% and 94%.[15,18] The variety of ways have been tried to minimize the hypotension during this anaesthetic procedure. Measures to prevent hypotension include the administration of fluids (colloids or crystalloids) before the regional anaesthesia, left uterine displacement and administration of a prophylactic vasopressor. But, adding colloids as preloading protocol may counteract hypotension; the infusion of prophylactic ephedrine may be associated with umbilical pH values under 7.20 in some newborns[4,11,22]. The concept of using a reduced (low) dose of local anaesthetic with opioid to minimize hypotension has received an attention.[1,5] The combination of reduced (low) dose of local anaesthetic plus lipophilic opioid, over traditional higher-dose local anaesthetic spinal anaesthesia, has increased in recent years, producing clear benefits: less hypotension and better perioperative analgesia. Vercauteren et al. used a combination of sufentanyl with low-dose bupivacaine (6.6 mg) for spinal anaesthesia in caesarean section and found a lower incidence of hypotension;[26] spinal administration of fentanyl, may potentiate the local anaesthetics analgesia and be associated with a decreased incidence of hypotension also, faster onset of block and motor recovery, and shorter time to micturition[7]. Bruce Ben-David et al. concluded that spinal anaesthesia using very low doses (as 5 mg) of isobaric bupivacaine plus 25 ìg fentanyl, is associated with significantly less hypotension and vasopressor requirements than 10 mg of isobaric plain bupivacaine, but they have evaluated non representative number of patients.[3] Other clinical experiences with doses between 5–10 mg bupivacaine are valuable and report about similar findings.[5,10,13,17] Definitely, the reduced local anaesthetic doses (bupivacaine) play role in getting less severe hypotension together with the mechanism by which intrathecal opioids decrease hypotension. Intrathecal fentanyl have a very selective spinal cord site of action; it acts synergistically with bupivacaine to enhance the

effect on the efferent pathways but without an effect on sympathetic pathways, thus producing no hypotension.[20,25] Even more, it appears that the addition of intrathecal fentanyl to bupivacaine spinal anaesthesia, potentiates the surgical analgesia for somatic and visceral pain, thus making the patients from bupivacaine-fentanyl anaesthesia more satisfied with their anaesthetic (Table II). It is likely that complex mechanisms along with potency, lipophilicity, and drug concentration all play a role in the local anaesthetic actions of spinal opioids[16]. Furthermore, studies in gravid animal models suggest hormonal milieu may also contribute to opioid effectiveness. Jayaram and Carp found that spinal progesterone potentiated the analgesic effect of spinal opioids in rats.[19] Adequate spinal anaesthesia for caesarean section which provides sympathetic blockade up to T4 causes a minimal reaction of hypotension compounded with reflex increase in heart rate. Most patients in the bupivacaine-fentanyl group reached lower median peak sensory level (T4), compared with patients from other group, but it seems this sensory level was quite enough to reach adequate surgical anaesthesia. The normal blood pressure compounded with this median peak sensory level, was associated with a reduction in the mean ephedrine requirement; in fact, most patients in the bupivacaine – fentanyl group required no ephedrine. It seems, that peak sensory level above those segment, affects the cardiac sympathetic innervation, thereby attenuating the compensatory mechanism and so high spinal block may further reduce the heart rate and produce a hypotension with more ephedrine requirement (Table II). Maintenance of normal maternal blood pressure during spinal caesarean section is key factor for adequate neonatal outcome, too. The mature placenta is high capacitance organ with no auto regulatory ability, so uteroplacental perfusion pressure is dependent on systemic blood pressure. The patients in the bupivacaine-fentanyl group experienced significantly less nausea than patients in the plain bupivacaine group. The decreased incidence of emetic effects after supplementation of spinal anaesthesia with intrathecal fentanyl in our study has also been reported by other investigators.[27] The finding of less nausea in the bupivacaine-fentanyl group may be surprising in that nausea is generally considered a side effect of intrathecal opioids. Palmer et a1. found a lower incidence of perioperative nausea and vomiting when 15 μg fentanyl was added to lignocaine spinal anaesthesia for caesarean delivery;[16] Dahlgren et al. found that either fentanyl or sufentanyl added to the spinal anaesthetic for caesarean delivery led to reduced need for intraoperative antiemetic.[7] The increased emetic effects in the bupivacaine group may be secondary to the increased incidence of hypotension, because effects were relieved when the blood pressure was increased after the administration of ephedrine. It has been our observation that rare hypotension in bupivacaine-fentanyl group occurs in the absence of nausea and vice versa. These findings and observations suggest about a protective effect of the intrathecal fentanyl, rather than from the more stable haemodynamics.

Conclusion

The findings of this study suggest that spinal anaesthesia for caesarean delivery using 10 mg hyperbaric bupivacaine plus 25 μg fentanyl is associated with significantly less hypotension, vasopressor requirements and nausea than spinal anaesthesia with 12.5 mg of bupivacaine, without untoward effects. This combination has been shown to improve the quality of spinal anaesthesia for caesarean delivery. But, further large study is warranted to verify a reliable minimum dose of bupivacaine-fentanyl for spinal anaesthesia in caesarean delivery.

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