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Comparison Between Hyperbaric Bupivacaine with and Without Fentanyl in Reducing Visceral Pain During Cesarean Delivery Under Spinal Anaesthesia

Rashmi Thapa,[1] Pooja Paudyal,[2] Bishwas Pradhan,[3] Megha Koirala,[1] Bashu Dev Parajuli[1]

[1]Department of Anesthesiology, Tribhuvan University Teaching Hospital, Maharajgunj Medical Campus, Institute of Medicine, Tribhuvan University, Kathmandu, Nepal, [2]Department of Obstetrics and Gynaecology, Tribhuvan University Teaching Hospital, Kathmandu, Nepal, Department of Cardiothoracic and Vascular Anesthesiology, Manmohan Cardiothoracic Vascular and transplant Centre, Teaching Hospital, Kathmandu, Nepal.

ABSTRACT

Background: Visceral pain occurred during cesarean delivery during spinal anesthesia can be decreased with a higher dose of bupivacaine. However, larger doses of bupivacaine increases the risk of high sensory block. We hypothesized that addition of fentanyl to bupivacaine intrathecally could intensifies the sensory block and improves the quality of intraoperative analgesia. The aim of this study is to compare incidence of visceral pain between hyperbaric bupivacaine with or without fentanyl during cesarean delivery under spinal anesthesia.

Methods: In this prospective randomized controlled trial, 72 term parturient with ASA PS II undergoing cesarean delivery under spinal anesthesia were randomly distributed into two groups. Group B received 2.2ml (11mg) of 0.5% hyperbaric bupivacaine while Group BF received 2 ml (10mg) of 0.5% hyperbaric bupivacaine and 0.2ml (10µg) of fentanyl intrathecally. Incidence of intraoperative visceral pain, maternal hemodynamics, side effects and APGAR score were compared.

Results: During exteriorization of uterus, 11% of parturient in Group BF and 44% parturient in Group B complained of intraoperative visceral pain with significant difference between two group (p=0.002). The intraoperative rescue analgesia was given in 22 % parturient in Group BF and 33% parturient in Group B (p= 0.29). Maternal vital parameters like blood pressure, heart rate, oxygen saturation and respiratory rate were comparable between two groups. APGAR score was similar in both groups.

Conclusion: Addition of intrathecal fentanyl to hyperbaric bupivacaine was effective in reducing intraoperative visceral pain during cesarean delivery with stable maternal hemodynamics and without neonatal side effects.

Keywords: Bupivacaine; cesarean delivery; fentanyl; spinal anesthesia; visceral pain

INTRODUCTION

Spinal anesthesia is the preferred technique for cesarean delivery.[1] The most frequent preparation used for spinal anesthesia is hyperbaric bupivacaine.[2] A larger dose of bupivacaine (12-15mg) is required to obliterate the visceral pain caused due to traction on the peritoneum and intraperitoneal organs during cesarean deliveries.[3] Sensory block was obtained above T4 with hyperbaric bupivacaine doses of 7.5-10 mg; yet, almost all of the patients who underwent surgery needed supplemental intraoperative analgesics.[3] When the dose of bupivacaine was increased, visceral pain seemed to be reduced, but larger doses were associated with a higher level of sympathetic blocks. Fentanyl, when given intrathecally, has a potent synergistic analgesic effect and can decrease the incidence of intraoperative visceral pain during cesarean delivery without causing a sympathetic block.[4] It can augment the analgesia with a lower dose of local anesthetics and make it possible to achieve successful spinal anesthesia with minimal side effects.[1] At our centre, we conduct cesarean section under subarachnoid block using hyperbaric bupivacaine with addition of fentanyl in most of the cases. At our centre, the surgeon usually exteriorize the uterus after the delivery of the baby, which can cause the discomfort and pain in the epigastric region. The addition of fentanyl could lower the incidence of the peritoneal

Correspondence: Dr Bashu Dev Parajuli, Department of Anesthesiology, Tribhuvan University Teaching Hospital, Maharajgunj Medical Campus, Institute of Medicine, Tribhuvan University, Kathmandu, Nepal. Email: bashuparajuli2012@gmail.com, Phone: +9779851179038.

stretch pain during exteriorization. The objective of this study was to evaluate the effect 10µg fentanyl with bupivacaine in reducing the intraoperative visceral pain and compared it with bupivacaine alone group during cesarean delivery under spinal anesthesia.

METHODS

This was a prospective, randomized controlled trial conducted in operation theatre in TUTH hospital from April 2023 to April 2024. Approval was taken from Institutional Review Committee (IRC) and Nepal Health Research Council (NHRC) and trial was registered in clinicaltrails.gov.np (NCT05491187). Total sample size of 72 was calculated based on the observation of a 30% incidence of intraoperative visceral pain in a routinely used dose of 11mg of hyperbaric bupivacaine in TUTH and incidence of pain (0-3.7%) in previous studies who had included bupivacaine with fentanyl group[5, 6] with power of 80% and type I error of 0.05. ASA PS II parturient above 18 years age and height ≥150 cm with gestational age ≥37 weeks undergoing elective cesarean delivery under spinal anesthesia were included in this study. Parturient with contraindication to spinal anesthesia and with communication problems were excluded from the study. The study variable were age, weight, height, parity, gestational age, level of sensory block, grade of motor block, incidence of visceral pain, the need of rescue analgesia (IV Fentanyl), duration of surgery, intraoperative vitals and maternal side effects like nausea, vomiting, pruritus, sedation and APGAR score.

After pre-anesthetic evaluation, patients were distributed in the two groups in a 1:1 ratio using computer-generated numbers (https://www.random.org/lists/) to receive either 2.2ml (11 mg) of 0.5% hyperbaric bupivacaine (Group B) or 2 ml (10 mg) of 0.5% hyperbaric bupivacaine plus 0.2ml of fentanyl (10µg) (Group BF) intrathecally, which was prepared in 5ml syringe. Primary investigator and the patients were blinded to the study drugs. The primary investigator did assessment of the patient prior to, during and after the operation and also collected the data. Numerical rating scale (NRS) was explained to each patient during preoperative evaluation. Patients were premedicated with oral Pantoprazole 40mg and Metoclopramide 10 mg, evening before surgery and in morning of surgery. In the pre-anesthetic room, an 18 G IV cannula was secured, and each patient was preloaded with ringer lactate 10 ml/kg IV 20 minutes before giving spinal anesthesia. Heart rate and blood pressure were recorded every 3 minutes following spinal anesthesia for 15 minutes or until delivery of a baby and thereafter every 5 minutes till the end of surgery. Saturation and ECG were monitored continuously throughout the study period. The level of sensory block was assessed by a cold spirit swab bilaterally along the midclavicular line. The test was performed every 2 min from "time zero" for the first 10 min, then every 5 min till peak sensory block level was confirmed up to 25 min.[7] Motor block was assessed based on the Modified Bromage Scale and recorded. Surgery was allowed once the bilateral sensory block height at T6 was achieved. The inability to achieve the sensory block up to the T6 level within 25 minutes from "time zero" was considered a failure.

Hypotension (decrease in systolic blood pressure of more than 20% from the baseline or to less than 90 mmHg)[8] was promptly treated with intravenous fluid bolus (200 ml), Mephentermine 6mg IV, which was repeated as necessary. Bradycardia (heart rate less than 50 bpm)[9] was treated with Atropine 0.6 mg IV. Intraoperative pain was assessed in terms of Numerical Rating Scale (NRS) (0-10).[10] Assessment of visceral pain was mainly done during delivery of baby, exteriorization of the uterus, handling of other intraperitoneal organs like bowels and adnexa, placement of uterus back to abdominal cavity and peritoneal suturing. Each time if NRS was four or more, fentanyl 25 µg IV was given. If pain still persisted, then fentanyl 1 µg/kg IV was provided, followed by ketamine 0.5 mg/kg IV if the pain did not subside. The occurrences of adverse events like hypotension, bradycardia, pruritus, nausea, and vomiting, itching and level of sedation were monitored, treated and recorded. The neonatal APGAR score at 1 minute and 5 minutes was evaluated and recorded.

Statistical analysis was done by using a statistical package for the social sciences (SPSS) software version 16. Mean ± SD was used to present continuous data; median ± quartiles were used to present ordinal data, and raw data with percentage was used to present categorical data. An independent t-test was used to compare the mean between two groups. Differences in categorical variables were compared using a chi-square test and Fisher's exact test according to the suitability of data.

RESULTS

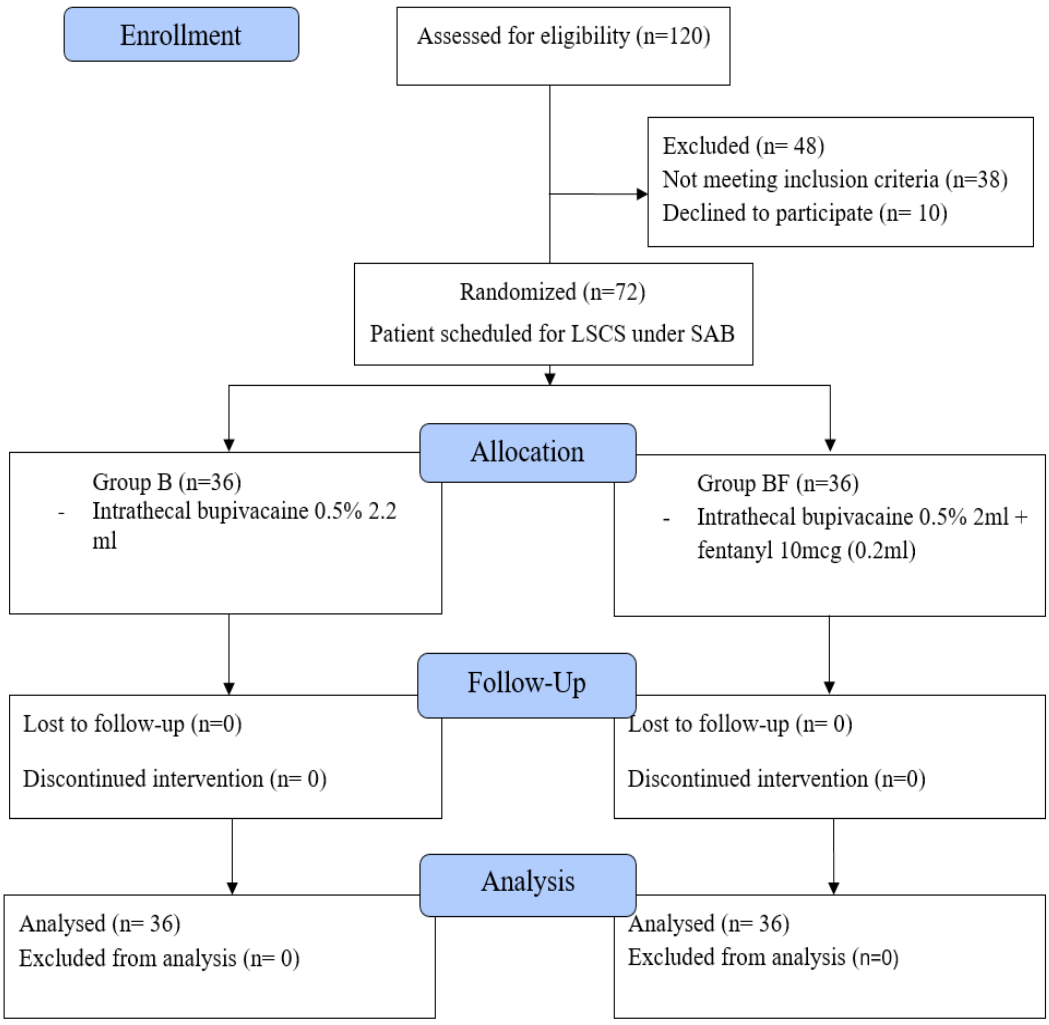

Figure 1. Consort flow diagram.

The mean age, weight, height and BMI were comparable between two groups as presented in the table 1.

Table 1. Demographic comparison.

	Group BF		Group B		p value
	Mean	SD	Mean	SD	
Age (years)	30.3	3.2	30.6	4.4	0.784
Wight (kg)	73.1	10.5	71.4	9.8	0.486
Height (cm)	154.8	3.7	156	4.3	0.212
BMI (kg/m²)	30.4	3.8	29.4	3.8	0.271

The visceral pain occurred during exteriorization of uterus in 11% in BF group while it was 44% in B group which was statistically significant (p value 0.002) while the visceral pain occurred was not statistically significant during the delivery of baby, during handling of intraperitoneal organ, during placement of uterus in situ, during suturing of peritoneum was comparable between two groups as shown in the figure 2.

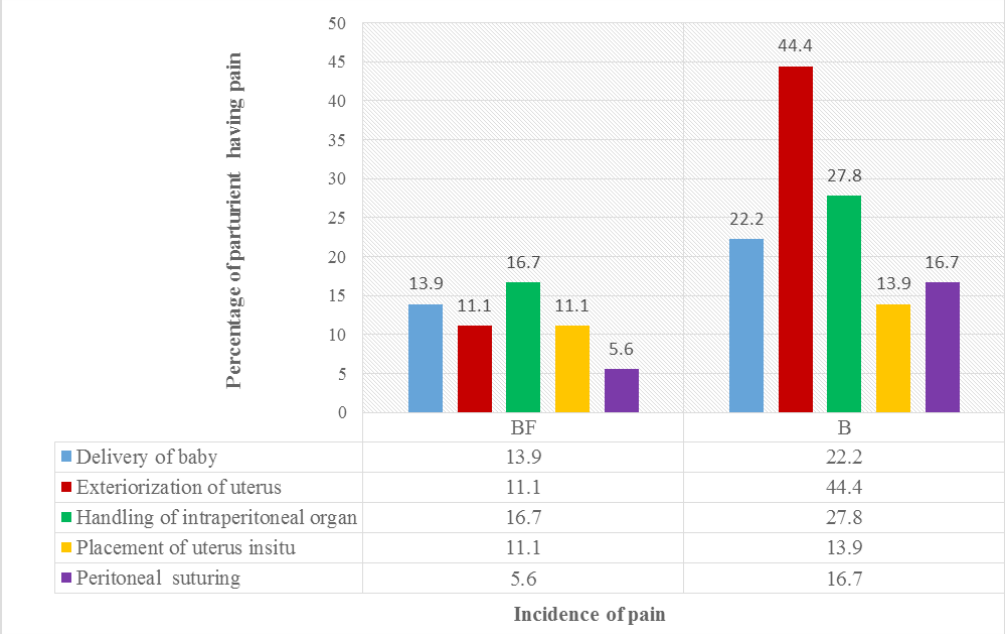

Figure 2. Graphical representation of overall pain assessment between two groups.

The intraoperative rescue analgesia was given in 22.2 % parturient in Group BF and 33.3% parturient in Group B with p value of 0.29. The use of rescue analgesics was comparable between the two groups.

The mean systolic blood pressure, diastolic blood pressure, mean arterial blood pressure, heart rate, SPO2, respiratory rate was comparable between two groups with no significant differences.

There was no significant difference in maternal side effects like nausea vomiting, pruritus, sedation between two groups as shown in the figure 3.

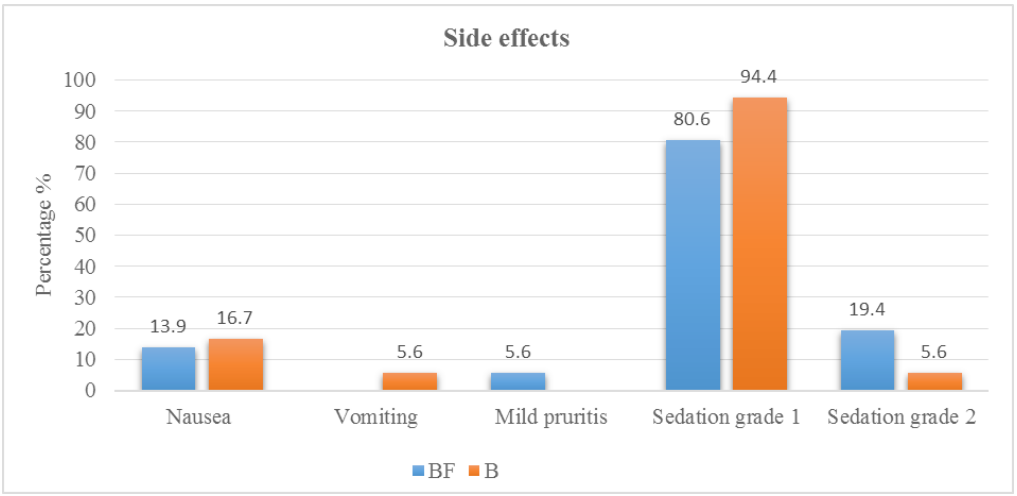

Figure 3. Comparison of overall side effects between two groups.

All neonate had normal APGAR score with median score of 7 at 1 minute and 8 at 5 minutes of birth.

DISCUSSION

In our study, the addition of intrathecal fentanyl to hyperbaric bupivacaine during cesarean delivery reduced intraoperative visceral pain during exteriorization of the uterus with favorable hemodynamics, without any significant maternal and neonatal adverse events.

Intrathecal opioids are now routinely utilized to prolong and enhance the action of spinal anesthesia during cesarean sections while decreasing systemic and central side effects compared to opioids administered systemically.[11] It enhances analgesia during surgery and extends the duration of anesthetic block without compromising the clinical status of newborns.[8, 12] Additionally, it decreases the dose of hyperbaric bupivacaine when used as an adjunct during spinal anesthesia.

In our study, the two groups were well-matched to compare demographic profiles (Table 1). Assessment of intraoperative visceral pain during cesarean delivery was done by using the numerical rating scale (NRS). There was a significant reduction of visceral pain during exteriorization of the uterus in parturient receiving intrathecal fentanyl, with an incidence of 11.1% in group BF and 44.4% in group B, showing a statistically significant difference (p value of 0.002). Similarly, during the time of delivery of the baby, handling of intraperitoneal organs, placement of uterus in situ, and peritoneal suturing, it was observed that the incidence of pain was comparatively lower in bupivacaine with fentanyl group than in the bupivacaine alone group. However, the difference wasnot statistically significant.

With these findings, our study showed that there was an overall reduction of visceral pain in the parturient who had received intrathecal fentanyl with bupivacaine than those who had received bupivacaine only. Since no previous research studies have assessed and quantified the pain during these specific intraoperative periods, our study could aid in gathering more detailed information in terms of the occurrence of visceral pain and the effects of study drugs in reducing this pain during cesarean delivery under spinal anesthesia.

These finding of our study was as per the study done by Ali et al.[6], in which out of 81 parturient receiving 10µg intrathecal fentanyl with 10mg bupivacaine, 3.7% had intraoperative pain and needed analgesics. However, there was no significant difference in the quality of surgical analgesia provided by this dose and the higher doses of fentanyl (15 and 25 µg). This finding suggests that increasing the amount of intrathecal fentanyl to more than 10 µg did not add to the quality of surgical anesthesia. In study done by Ferrarezi W.P.P et al.[12], they studied the different doses of intrathecal fentanyl (15 µg, 10 µg, and 7.5 µg) with bupivacaine and compared it with bupivacaine alone group. Eighty percentage of parturient receiving 10 µg fentanyl reported satisfactory analgesia wheras in bupivacaine only group, 28% parturient reported satisfactory analgesia. There was a significant difference between the groups that received fentanyl when compared to the control group ($p < 0.001$).

In our study, 33% parturient of Group B and 20% parturient of Group BF needed rescue analgesics However, there was no statistically significant difference. Similar finding was found in the study done by Ferrarezi W.P.P et al.[12] in which 20% parturient of group receiving 10µg fentanyl reported unsatisfactory analgesia and needed rescue analgesia whereas 72% parturient needed rescue analgesia in bupivacaine only group. The addition of intrathecal fentanyl increased the block quality and duration reducing the requirement of the rescue analgesic.

Choi et al.[5] included the different doses of intrathecal bupivacaine (8mg, 10mg, and 12mg) and compared it with the addition of 10µg fentanyl in each group. Their study showed that none of the parturients in the bupivacaine with fentanyl group had complained of intraoperative pain.This finding of the study by Choi et al. did not completely match the result of our study on the reduction of visceral pain, as 20% parturients receiving intrathecal fentanyl complained of pain.

In our study, there was no significant difference between the two groups regarding the motor and sensory blocks due to spinal anesthesia. The incidence of hypotension was higher in the bupivacaine only group than in the bupivacaine with fentanyl group (33% in Group B and 19 % in Group BF). Similarly, a study done by Acharya et al.[8], found that hypotension was more common in bupivacaine only group than compared to bupivacaine with fentanyl group with a statistically significant difference. Three parturient in each group of our study had bradycardia intraoperatively. The addition of 10 µg fentanyl with the bupivacaine wont change much hemodynamic.[1,8]

The side effects observed in this study were pruritus, nausea, vomiting, and sedation. Two parturient in group BF and none of the parturient in Group B complained of pruritus. This low incidence of pruritus may be due to the use of low doses of fentanyl. In the study done by Ali et al.[6], where they compared three different doses of fentanyl (10 µg, 15 µg, 25 µg) with 10 mg of bupivacaine, the incidence of pruritus was highest in the 25µg fentanyl group (38%) whereas 7% in 10 µg fentanyl group. The result of this study supports our study finding that decreasing the dose of fentanyl is associated with a lower incidence of pruritus. There was no significant difference in the incidence of nausea and vomiting among the two groups. This finding was consistent with a study done by Choi et al.[5] The APGAR

score was above 7 in the 1st and 5th minutes and these finding was consistent with other previous studies.[6, 12] The result confirms the safety of the association of drugs that were used in our study.

This was a single-centered study. The effect of the study drug was assessed by calculating APGAR score only. Measuring pH could have been a better parameter to evaluate neonatal outcome and neonates werenot followed beyond immediate postnatal period. Aditionally, we had included ASA PS II parturients undergoing elective cesarean delivery, so this study cannot be generalized in emergency cases or parturients with ASA PS III and IV.

CONCLUSIONS

From this double-blind, randomized, prospective study, it was concluded that addition of intrathecal fentanyl 10 µg to hyperbaric bupivacaine was effective in reducing intraoperative visceral pain during cesarean delivery while maintaining stable maternal hemodynamics with no significant risk to the mother or the newborn.

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CONFLICT OF INTEREST

There is no any potential conflict of interest concerning this paper.

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