Intrathecal Bupivacaine with Fentanyl versus Bupivacaine alone in Cases undergoing Elective Cesarean Section: Comparison of Hemodynamics

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ABSTRACT

Introduction: Fentanyl has been used in various doses intrathecally as an adjunct to local anesthesia in Cesarean section. It has been shown to increase the analgesic effect and prolong sensory blockade without increasing the side effects in the mother and the neonate. We conducted a study to compare hemodynamics of patients receiving 10 mcg fentanyl with 0.5% bupivacaine with those receiving bupivacaine alone.

Materials and Methods: Hundred women undergoing elective Cesarean section under spinal anesthesia were randomly divided into group F (fentanyl) and group C (control). Group F received 10 mcg of fentanyl with 2ml of 0.5% hyperbaric bupivacaine whereas Group C received 2.2ml of 0.5% hyperbaric bupivacaine. Hemodynamic parameters including blood pressure and heart rate, use of vasopressors, incidence of nausea, vomiting, pruritus, shivering, visceral pain, discomfort and neonatal outcome were recorded.

Results: There was similarity in incidence of hypotension and bradycardia before birth of baby between the two groups (Fentanyl group 69.39% vs Control group 66%, (p=0.830) and 0.02% vs 0.02%,p=1.00).The use of vasopressors (p=0.264), incidence of nausea, vomiting (p=0.318) and Apgar score at 1 and 5 minutes (p=0.919, p=0.952) were also not statistically significant. One patient in the fentanyl group complained of itching intraoperatively whereas four patients in each group complained of visceral pain during surgery. Two patients in fentanyl group experienced shivering intraoperatively.

Conclusion: Our study demonstrated that hemodynamic profile of patients undergoing elective Cesarean section under spinal anesthesia with use of 10 mcg fentanyl plus 0.5% hyperbaric bupivacaine was similar to those receiving hyperbaric bupivacaine alone.

Keywords: hemodynamics, Cesarean section, fentanyl, bupivacaine

INTRODUCTION

Neuraxial techniques are the preferred method for Cesarean deliveries over general anesthesia.[1]Rather than intermittent use of parenteral opioids, neuraxial opioids are routinely used for postoperative analgesia after neuraxial anesthesia for Cesarean section (CS).[1] Most of the anesthesiologists worldwide prefer single shot spinal anesthesia as a regional technique for the procedure.[2] Addition of different doses of fentanyl to subarachnoid bupivacaine has shown to improve surgical anesthesia and increase

the duration of sensory block.[3,4] Fentanyl in a dose as little as 10 mcg with 10mg hyperbaric bupivacaine has been demonstrated to provide adequate surgical anesthesia and analgesia with the least requirement of vasopressors and insignificant opioid related side effects.[5] Intrathecal fentanyl is thought to act synergistically with local anesthetic thereby lowering its dose and providing adequate anesthesia with decrease in episodes of hypotension and vasopressors requirement.[6] In our department, we routinely use 0.5% hyperbaric bupivacaine 11mg (2.2ml) for CS. We hypothesized that addition of fentanyl 10 mcg with 10 mg 0.5% hyperbaric bupivacaine might prove beneficial by decreasing hemodynamic side effects and improvement of overall quality of surgical anesthesia without increasing side effects in the mother and the newborn.

MATERIALS AND METHODS

After ethical clearance from Institutional Review Committee, Pokhara Academy of Health Sciences(PoAHS), Pokhara, a prospective, randomized, double blind study was carried out from August 2018 to January 2019 to compare the hemodynamics between patients undergoing elective CS under spinal anesthesia. Two groups were formed- those receiving 0.5% hyperbaric bupivacaine plus 10 mcg fentanyl (Fentanyl group–F)and hyperbaric bupivacaine alone (Control group-C).

Patient inclusion criteria were:

- ASA I and II full term singleton parturients aged 18 years to 40 years scheduled for elective cesarean section
- Height 150 -160cm
- Weight 50-90 kg

Patient exclusion criteria were:

- Parturients with cardiovascular disease, hypertensive disorders of pregnancy
- Parturients undergoing emergency CS
- Parturients with multiple gestation, hepatic disease, renal disease, endocrine disease
- Contraindications for spinal anesthesia

One hundred parturients were randomized into: Fentanyl group (F) and Control group(C)

In the waiting area, baseline blood pressure and heart rate were measured. All patients received premedication with intravenous ranitidine 50 mg and metoclopramide 10 mg which is our routine practice. Patients were co-loaded with 10ml/kg of crystalloid via 18 G intravenous catheter and monitors were attached including non-invasive blood pressure (NIBP), electrocardiogram (ECG), and pulse oximeter. Spinal anesthesia was performed in sitting position with 25 G Quincke spinal needle. Group F received 2 ml of hyperbaric bupivacaine 0.5% with 10 mcg fentanyl (0.2 ml) with total volume 2.2 ml while group C received 0.5% hyperbaric bupivacaine (2.2 ml).

After spinal block, the patients were immediately turned supine and the bed was tilted to left lateral side. Oxygen was administered via simple facemask at 4litre/ minute to all the patients.

Blood pressure, heart rate was recorded every minute after the spinal block till the delivery of baby and then after every 3 minutes till the end of the surgery. The time to reach T4 sensory block for pin prick was recorded and surgery was allowed to proceed only when T4 sensory level was reached.

Those parturients who did not achieve sensory block of T4 with pinprick till 20 minutes from the time of subarachnoid block were excluded from the study.

Maternal hypotension was defined as fall in mean blood pressure below 25% of the baseline and managed with injection mephentermine 6 mg bolus.

Bradycardia was defined as heart rate less than 50 beats per minute and managed with injection atropine 0.6 mg.

After the delivery of baby all patients received injection oxytocin 5 mg intravenous bolus and were positioned supine.

Discomfort or visceral traction pain was noted and expressed as numerical rating scale (NRS) 0-10. Patients requiring intervention with NRS more than 3 prior to delivery were excluded from the study. For patients achieving adequate anesthesia but NRS more than 3 during visceral traction were reassured and injection fentanyl 40 mcg or injection ketamine 20 mg was administered as required.

Apgar score of all babies was recorded at 1 and 5 minutes.

Any other side effects like nausea, vomiting, pruritus

and shivering was noted and managed accordingly.

Data analysis was done using SPSS version 20.0 (SPSS, Chicago, IL, USA). Continuous data were expressed as mean ± standard deviation (SD) or median (lower, upper quartile). Categorical data were presented as number (percentage). Comparison between two groups was done using independent t-test for normally distributed data and Mann-Whitney U-test for non-normally distributed data. Categorical data were analyzed using Chi-square test or Fisher's exact test or Likelihood ratio wherever appropriate. The sequential measurements of mean arterial pressure and heart rate, done in the first 22 minutes after spinal anaesthesia, were compared using analysis of variance for repeated measurements followed by pairwise comparison. P< 0.05 was considered to be statistically significant.

RESULTS

There were a total of 99 patients in our study, 49 patients in fentanyl group and 50 patients in control group, as one patient in fentanyl group was excluded due to failed spinal. The age, weight and height of patients of the two groups were similar. (Table 1)

Table 1: Patient characteristics

	Fentanyl (n=49)	Control (n=50)	p-value
Age (years)	25 (18-38)	25.5 (20-36)	0.765
Weight (kg)	65.12 ± 7.62	64.84 ± 9.195	0.868
Height (cm)	154 (150-168)	154.5 (150-165)	0.895
Data given as n, mean ± SD or median (lower - upper quartile).			

Most common cause of elective CS performed in our study population was previous CS. (Figure 1)

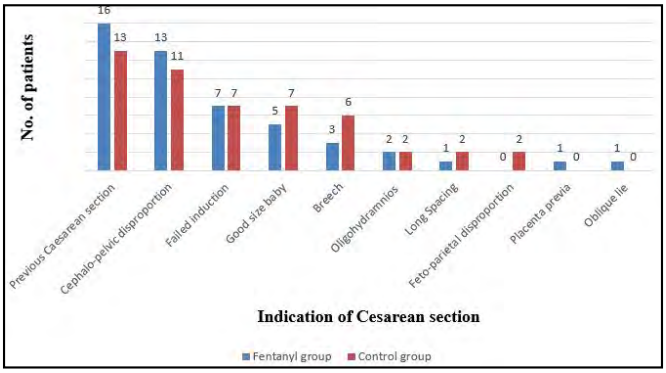

Figure 1: Indication of Cesarean section

The time required for attainment of T4 level block after spinal anaesthesia; spinal puncture to skin incision interval; spinal puncture to baby delivery interval; and the duration of surgery (interval between skin incision and skin closure) was similar in the two groups. (Table 2)

Table 2: Intraoperative characteristics

Duration (minutes)	Fentanyl (n=49)	Control (n=50)	p-value
1. Spinal puncture to T4 level block interval	5 (2-10)	4.5 (2-9)	0.655
2. Spinal puncture to skin incision interval	6 (3-13)	6 (3-11)	0.491
3. Spinal puncture to birth of baby interval	11 (6-25)	12 (5-19)	0.985
4. Skin incision to skin closure interval	32 (18-63)	28 (16-54)	0.160
Data given as median (lower - upper quartile).			

The incidence of hypotension and bradycardia was similar in the two groups. (Table 3)

Table 3: Hemodynamic Changes

	Fentanyl (n=49)	Control (n=50)	p-value
Before birth of baby			
Hypotension	34 (69.39%)	33 (66%)	0.830
Bradycardia	1 (0.02%)	1 (0.02%)	1.000
After birth of baby			
Hypotension	33 (67.35%)	29 (58%)	0.408
Bradycardia	1 (0.02%)	0	0.495
During whole surgery			
Hypotension	41 (83.67%)	42 (84%)	1.000
Bradycardia	2 (0.04%)	1 (0.02%)	0.617
Data represented as n (%)			

There was no significant difference between the two groups with respect to mean arterial pressure and heart rate.

In both the groups, the mean arterial pressure was higher at two minutes but lower after that when compared to the baseline value in the first 22 minutes after spinal anesthesia. The MAP was significantly lower at 6, 8, 10, 20 and 22 minutes in fentanyl group and 4, 6, 8, 10, 18, 20 and 22 minutes in control group.

In the first 22 minutes after spinal anesthesia, heart rate increased in both the groups when compared

to baseline value. The increase in heart rate was significant at 2 minutes in fentanyl group and at 2, 4, 16, 18, 20 and 22 minutes in control group.

The number of episodes of hypotension that occurred in the two groups before birth, after birth and during whole surgery is given in table 4.

Table 4: Number of episodes of hypotension

No. of episodes of hypotension		Fentanyl (n=49)	Control (n=50)	p-value
Before birth of baby				0.922
	0	15	17	
	1	18	16	
	2	8	11	
	3	4	4	
	4	3	2	
	5	1	0	
After birth of baby				0.277
	0	16	21	
	1	14	15	
	2	10	8	
	3	6	3	
	4	0	2	
	5	2	0	
	6	0	1	
	7	1	0	
During whole surgery				0.715
	0	8	8	
	1	6	13	
	2	13	10	
	3	7	9	
	4	6	4	
	5	4	3	
	6	2	2	
	7	2	0	
	8	0	0	
	9	1	1	
Data represented as n				

There was no significant difference in the two groups with regards to total dose of mephentermine and atropine used during surgery, the incidence of nausea and vomiting and Apgar score of the newborn at 1 and 5 minutes after delivery. (Table 5)

Table 5: Maternal hemodynamic data; dose of vasopressors, Maternal symptoms; Apgar score in New borns

	Fentanyl (n=49)	Control (n=50)	p-value
Baseline MAP	88.06 ± 7.872	87.38 ± 8.774	0.685
Baseline Heart Rate	86.69 ± 13.251	82.26 ± 10.095	0.064
Dose of			
Mephentermine	12 (0-54)	12 (0-54)	0.264
Atropine	0 (0-0.6)	0 (0-0.6)	0.617
Incidence of			
Nausea	6	3	0.318
Vomiting	3	4	1.000
Apgar Score			
At 1 minute	7 (4-8)	7 (4-8)	0.919
At 5 minute	8 (7-9)	8 (6-9)	0.952
Data given as n, mean ± SD or median (lower - upper quartile).			

Four patients in the fentanyl group and four patients in the control group complained of visceral pain during surgery. (In the fentanyl group, one patient had visceral pain before birth of baby, two patients had pain after birth of baby, and one patient had pain both before and after birth of baby. In the control group, three patients had visceral pain after birth of baby, and one patient complained of pain both before and after birth of baby.)

One patient in the fentanyl group complained of itching in the perioral region (after birth of baby). And two patients in the fentanyl group complained of shivering (after birth of baby).

For those having visceral pain during the surgery reassurance was done followed by injection fentanyl 40 mcg followed by injection ketamine 20 mg was given as rescue analgesic.

DISCUSSION

In the recent years, fentanyl is being used in various doses ranging from 10-25 mcg as an adjuvant to 0.5% heavy bupivacaine for intrathecal administration.[5] Studies have shown that addition of fentanyl has reduced the dose of bupivacaine in spinal anesthesia for CS as well, with adequate anesthesia thereby decreasing its harmful effects.[7,8] A study which compared the effect of different doses of intrathecal fentanyl with bupivacaine showed that

25 mcg fentanyl was associated with more maternal hypotension as compared to 12.5 mcg fentanyl.[9]

The aim of our study was to compare maternal hemodynamics between patients undergoing elective CS under spinal anesthesia receiving 10 mcg of fentanyl plus 10 mg 0.5% hyperbaric bupivacaine with 11mg bupivacaine alone. Subedi et al used 11mg (2.2 ml) 0.5% hyperbaric bupivacaine in fixed dose group in their study where they compared and demonstrated that adjusted dose of intrathecal hyperbaric bupivacaine will lower dose of spinal bupivacaine and reduce incidence of hypotension, nausea and vomiting.[10]

In our study, we observed that there was no significant difference in incidence of hypotension and bradycardia between the groups which is consistent with other studies.[7] A clinical study by Shashikala et al on effect of spinal fentanyl in subarachnoid block also revealed no difference in incidence of hypotension and bradycardia between study and control group.[11]

However, studies comparing different doses of fentanyl with different doses of bupivacaine have demonstrated better hemodynamics with decreasing dose of bupivacaine and addition of fentanyl.[6,8,12]In the study conducted by Kumar et al there was no difference in the incidence of bradycardia between the groups who received different doses of intrathecal fentanyl and those who received bupivacaine. However, there was significantly increased incidence of hypotension with increased dose of fentanyl.[9]

The need for vasopressors were comparable between group F and group C in our study which is similar to the results of other studies.[4,13]In the study performed by Shende et al the requirement of ephedrine was similar in both fentanyl and saline group.[4] Similarly Jain et al studied the effect of adding various doses of fentanyl with 7.5mg bupivacaine in patients with pregnancy induced hypertension.[13]The consumption of mephentermine in saline group, intrathecal fentanyl 10 mcg group and 20 mcg group were similar.[13]Whereas a study conducted by Ben David et al showed that decreasing the dose of bupivacaine and addition of fentanyl in different doses significantly reduced utilization of vasopressors.[6]

In our study, incidence of visceral pain and discomfort during surgery was comparable in both the groups revealing that addition of 10 mcg fentanyl did not offer benefits in terms of intraoperative quality of analgesia and anesthesia. On contrary, several studies have demonstrated adequate quality of surgical anesthesia and analgesia with addition of fentanyl at varying doses.[4,5,14,15,16]

However, none were excluded from the study for visceral pain or discomfort based on NRS which shows quality of anesthesia was comparable between groups. One patient in fentanyl group required conversion to general anesthesia due to failed spinal anesthesia.

We observed that incidence of nausea and vomiting was similar between the study and control group which is comparable to other studies.[16,17] Few studies have revealed significant increase in incidence of nausea and vomiting in control group in comparison to those receiving intrathecal fentanyl.[11,18]

Shivering was present in one patient in fentanyl group. In contrary, use of intrathecal fentanyl showed significant reduction in occurrence of shivering in several other studies.[11,18]

Neonatal outcome as assessed by Apgar score showed no difference between two groups as observed in other studies as well.[5,8,9,16]

CONCLUSION

Based on our study, it can be concluded that use of 10 mcg fentanyl plus 0.5% hyperbaric bupivacaine produces similar hemodynamic profile in patients undergoing elective cesarean section under spinal anesthesia to those receiving hyperbaric bupivacaine alone without increasing significant maternal and neonatal side effects.

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