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Original Research Article

COMPARISON OF FRACTIONATED DOSE VERSUS BOLUS DOSE INJECTION OF HEAVY BUPIVACAINE WITH FENTANYL IN SPINAL ANAESTHESIA FOR PATIENTS UNDERGOING ELECTIVE CAESAREAN SECTION: ONE YEAR RANDOMIZED CLINICAL TRIAL

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Abstract

Background and Aim: Maternal hypotension is the common complication encountered after subarachnoid block (SAB).
This needs attention and treatment for the better maternal and foetal outcome. Administration of SAB with bolus dose of local anaesthetic produce faster onset and precipitate maternal hypotension. Injecting fractionated dose provides dense block and haemodynamic stability. Aim of this study was to compare fractionated and bolus dose of SAB in terms of haemodynamic stability and duration of analgesia.
Methodology: Eighty parturients undergoing caesarean delivery under SAB were included in the study. They were divided into Group B or F according to computer randomization. Group B parturients received bolus dose SAB with 2ml of 0.5% hyperbaric bupivacaine and 10µg of fentanyl. Group F parturients received fractionated dose of 2ml of 0.5% hyperbaric bupivacaine and 10µg of fentanyl. In which, from the total dose two-third was given initially. After 90 sec remaining one third of the dose was injected. Haemodynamic parameters and analgesia period were analyzed using Student's unpaired *t*‾ test.
Results: The haemodynamic parameters were better in group F than group B. The number of patients required vasopressor in group F were six and group B were seventeen. There was a prolonged analgesia period in group F than group B (214.40 + 15.48 and 195.95 + 8.98 min respectively).
Conclusion: The patients in fractionated dose group were haemodynamically better with longer analgesia period than bolus dose group. It is a newer technique to prevent maternal hypotension after SAB.

Keywords: Fractionated-dose, hypotension, caesarean section

Introduction

The subarachnoid block (SAB) is the preferred anaesthetic technique used in pregnant women undergoing lower segment caesarean session (LSCS). It is the most used method because of its rapid onset and postoperative analgesia. Pregnant women have profound hypotension with spinal anaesthesia because of anatomical and hormonal changes in pregnancy. Incidence of hypotension among pregnant women is 92%-94% without any preventive measures [1]. Maternal hypotension compromises uteroplacental blood flow leading various complications

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in the foetus [2, 3].
In SAB, administration of hyperbaric bupivacaine in bolus dose cause high sympathetic block and produce profound hypotension. Whereas administration of hyperbaric bupivacaine in fractionated dose provide dense block with better haemodynamic stability [4].
In LSCS, adding opioid like fentanyl to intrathecal injection reduces the volume of hyperbaric bupivacaine and improves the intensity and quality of spinal anaesthesia. The combined effect of fentanyl and bupivacaine provides prolonged analgesia [5, 6].
The present study is to compare haemodynamic changes and postoperative analgesia of fractionated dose versus bolus dose with hyperbaric bupivacaine and fentanyl in SAB for patients undergoing elective LSCS.

Materials and Methods

After obtaining the departmental research committee and institutional ethical board approval, written informed consent was taken from 80 patients undergoing elective c-section delivery under SAB. Parturients of ASA physical status-I and II, age between 18-40 yrs and height from 140-170 cm were included into the study. Multiple pregnancy, PIH, eclampsia and contraindication for SAB were excluded from the study. They were separated into groups B and group F using a computer-generated random number table.
In preoperative holding area, 18-Gauge intravenous (IV) cannula was secured. Patient was administered with ranitidine 1mg/kg and ondansetron 0.1mg/kg. Preloading was done with ringer lactate 10-15 ml/kg. After shifting inside operation theatre standard non-invasive monitors like blood pressure (BP), pulse oximeter and ECG were attached. Baseline blood pressure, heart rate (HR) and oxygen saturation were measured.
Patient was positioned in left-lateral position. Under sterile aseptic precaution, L3-L4 intervertebral space identified. Skin was infiltrated with local injection with lignocaine 2%. Using 23 gauge Quincke spinal needle 2ml of 0.5% hyperbaric bupivacaine plus 0.2ml (10µg) of fentanyl was injected into L3-L4 subarachnoid space according to group B or group F. For group B patient drug was administered intrathecally as continuous bolus dose for 10sec. Group F patient received the drug in fractionated dose. In which from total dose two third of the drug was given initially. Patient was maintained in same lateral position with spinal needle in situ, after 90 sec remaining one third of the drug was administered. Both the doses of drug were injected at the rate of 0.2 ml/sec.
After injection of the drug, patient was put in supine position. Left uterine displacement was done by keeping pillow under right hip. Supplied with oxygen through face mask at 5L/min. The onset and level of motor and sensory block assessment were done. The sensory block level was assessed by performing pin prick test at mid axillary line. The sensory block onset was taken from the time of administration of the drug intrathecally to highest sensory level achieved. The motor block level was assessed with modified bromage scale. The motor block onset was taken as time to achieve bromage score of 3 from the time drug injected into intrathecal space.
The procedure was converted to general anaesthesia if desired sensory or motor level fails to achieve and patient was excluded from the study. The blood pressure and heart rate were recorded immediately after giving spinal anaesthesia. There after it was recorded every 2 min for 10 min and then every 5min till 50 min. Hypotension was considered if blood pressure falls more than 20% from baseline reading and was treated with IV ephedrine 6mg. For each patient, the usage of ephedrine and episodes of hypotension were noted. Bradycardia was treated with 0.6mg of IV atropine.
Immediately after baby delivery, 10U of IM oxytocin was given and another 10U of IV oxytocin was given in 500 ml of normal saline. Apgar score was noted at 1 and 5 min after baby delivery. Developments of side effects like shivering, pruritus, respiratory depression, nausea, vomiting and urinary retention were observed.
Post operatively, vitals were recorded. The duration of motor, sensory block and analgesia were noted. The sensory block duration was considered from the time drug was injected

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intrathecally to S2 segment regression. Motor block duration was taken from the time drug was injected into subarachnoid space till the time to achieve bromage score zero. Visual analogue scale (VAS) was used assess the pain. Duration of analgesia was time interval from local anaesthetic injected into subarachnoid space till the requirement of rescue analgesia. Intravenous 75mg of diclofenac was used as rescue analgesia.

Results

Table 1: Mean of age, height, weight

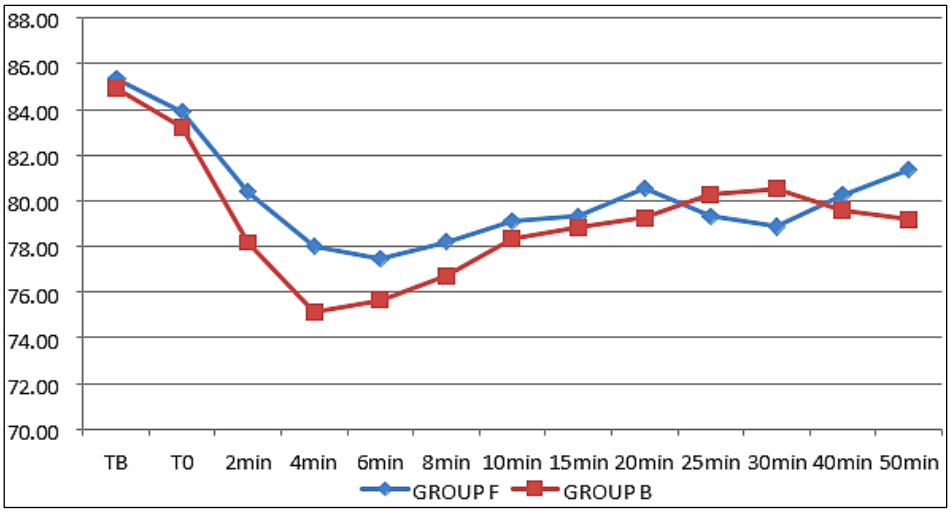
	GR	OUP F	G	ROUP B	P Value
	Mean	Standard Deviation	mean	Standard Deviation	
Age (Years)	27.48	3.77	26.65	3.45	0.3105
Height (cm)	152.85	3.68	151.80	3.11	0.1721
Weight (kg)	60.38	5.24	60.65	6.07	0.8289

The demographic profiles among the both groups were comparable. Group F patients, onset of sensory block was earlier than group B patients (3.45 $\pm$ 0.96 min and 5.66 $\pm$ 0.69 min respectively).

This was statistically significant with P value of < 0.001. Motor block onset in group F was 4.70 $\pm$ 0.80 min and in group B was 7.80 $\pm$ 0.78 min ($p<0.001$). Patients in group F were haemodynamically stable than group B. The mean arterial pressure values in group F were on higher range than group B but they were statistically not significant. The number of patients requiring intraoperative ephedrine in group F and group B were 6 and 17 respectively with P= 0.0066. The time taken for sensory and motor block regression in group F (182.93 $\pm$ 6.34 min and 172.25 $\pm$ 7.86 min) were delayed than group B (174.85 $\pm$ 8.36 min and 165.95 $\pm$ 8.27 min) with was highly significant. Group F and group B had duration of analgesia of 214.40 + 15.48 and 195.95 + 8.98 min respectively ($p<0.0001$). APGAR score at 1 and 5 min was not statistically significant in both the group. The adverse effects like respiratory depression, pruritus and headache were not observed in both the groups.

Table 2: Characteristics of sensory and motor block

	Group F		Group B		
	Mean	Standard Deviation	Mean	Standard Deviation	P Value
Onset of sensory block (min)	3.45	0.96	5.66	0.69	<0.001
Onset of motor block (min)	4.70	0.80	7.80	0.78	<0.001
Sensory regression (min)	182.93	6.34	174.85	8.36	<0.001
Motor regression (min)	172.25	7.86	165.95	8.27	0.0008



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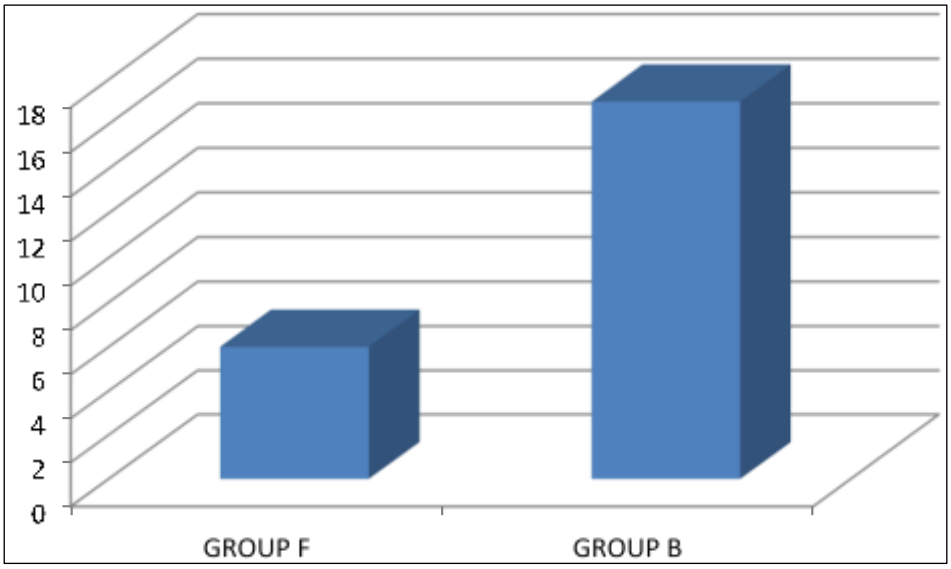
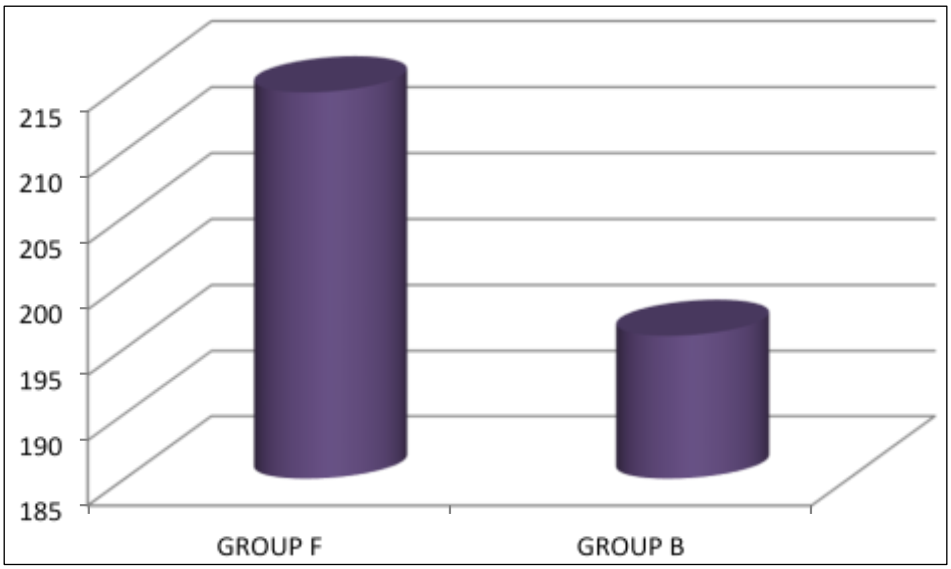
Graph 1: Comparison of Mean arterial pressure (MAP) at different time intervals (mm of Hg)



Graph 2: Number of patients requiring ephedrine



Graph 3: Duration of analgesia (min)

Discussion

The subarachnoid block is the anaesthetic method of choice for pregnant women undergoing LSCS. It provides a quicker onset of action with adequate sensory and motor block. But the main disadvantage of this technique is maternal hypotension with adverse neonate outcome. Various non-pharmacological and pharmacological methods were studied to prevent hypotension in the mother after SAB [7].

Our study was conducted to analyze the haemodynamic stability with single bolus dose of bupivacaine in SAB to the divided dose (fractionated dose) of bupivacaine along with fentanyl for pregnant women undergoing LSCS and the quality of sensory and motor block among them.

Badheka JP *et al.* [8] conducted a study comparing fractionated and bolus dose injection of spinal anaesthesia in pregnant women. He found that patients in fractionate group were haemodynamically more stable than bolus dose group patients. Five patients required

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vasopressor in fractionated group whereas fourteen patients needed the same in bolus dose group. The study concluded that giving bupivacaine in divided dose provides dense block leading to haemodynamic stability in fractionated group.

In a study conducted by Monika Gandhi *et al.* [9] haemodynamic parameters were analyzed between fractionated and bolus dose injection of bupivacaine in SAB. They concluded that patients were haemodynamically more stable in fractionated group than bolus dose group. The numbers of people requiring vasopressor in fractionated and bolus dose group were 15 and 39 respectively. Another randomized control trial was conducted by Ramasali Manjula V *et al.* [10] compared haemodynamic parameters like HR, BP and MAP between fractionated group and bolus dose group. The study was done on 60 patients undergoing elective LSCS. They concluded that HR, BP and MAP of the patients in fractionated group were on a higher range than bolus group.

Fahmy *et al.* [4] conducted a study comparing circulatory effect and duration of analgesia in divided dose and single-dose subarachnoid block. From the study, they obtain that patient in divided dose group have a better circulatory effect than single-dose group. The duration of analgesia was longer in fractionated group.

In our study, pregnant women in fractionated group were haemodynamically more stable than in bolus dose group. Even though it was not statistically significant, the blood pressures in fractionated group were on higher range. Six persons required vasopressor in fractionated group whereas in bolus group seventeen persons required the same. Injecting local anaesthetic in divided dose into subarachnoid space provides dense block. This explains the haemodynamic stability in fractionated group.

The onsets of sensory and motor block were faster in our study. The onset of sensory block in fractionated and bolus dose was 3.45 ± 0.96 min and 5.66 ± 0.69 min respectively. The onset of motor block was 4.70 ± 0.80 and 7.80 ± 0.78 min in fractionated and bolus dose group respectively. This result correlates with the study performed by Monika Gandhi *et al.* [9] The onset of sensory block was early in fractionated group (71.53 ± 5.66 sec) than bolus group (88.950 ± 4.51 sec). The onset of motor block was also early in fractionated group than bolus group (88.95 ± 4.51 sec and 116.20 ± 2.56 sec respectively).

The time taken for sensory regression in our study was 182.93 ± 6.34 min in fractionated group which was delayed than bolus group (174.85 ± 8.36 min). In Badheka JP *et al.* [8] study, the sensory regression was delayed in fractionated group (236 ± 42 min) than bolus dose group (161 ± 29 min). In another study conducted by Deepak K *et al.* [11] found a delay in sensory regression in fractionated group than bolus group which was significant statistically ($p<0.00001$).

In a study conducted by Nugroho AM *et al.* [12] haemodynamic effect and the level of sensory block were compared between fractionated and single-dose SAB for patients with hypertension associated with pregnancy. No difference was found in the MAP between the groups. The level of sensory block in fractionated group and single dose group were 52.4% and 42.9% respectively (not significant). This was explained by excessive vasoconstriction and vascular resistance in preeclampsia patients due to increased activation of inflammatory cytokines. In these patients, BP was maintained by excessive vasoconstriction despite of sympatholytic activity after SAB. So fractionated dose effect was limited here.

Adding adjuvant like an opioid to bupivacaine in SAB provides longer duration of analgesia. It even reduces the dose of bupivacaine and maintains the volume of drug to achieve an adequate level of block. 10 to 25 µg of intrathecal fentanyl produce prolong sensory block and analgesia [13]. Bupivacaine and fentanyl produce synergic action on intrathecal injection [5]. Fentanyl blocks the nociceptive impulse by acting on a specific opioid receptor in the spinal cord. It modulates the C and A-delta fibers by opening potassium channel and causes hyperpolarization. Bupivacaine acts by blocking Na^+ channel in the axon. The combined action of these drugs on nerve fibers produce an enhanced sensory block and increase the duration of analgesia with minimal side effects. This also reduces the volume of bupivacaine and produce haemodynamic stability [13].

In our study, adding fentanyl to bupivacaine in both the groups increased the duration of

analgesia. In fractionated group, the duration of analgesia was longer than bolus dose group (214.40 ± 15.48 min vs 195.95 ± 8.98 min respectively). The longer duration of analgesia in the fractionated group was explained by the combined action of dense block produced by fractionated dose and intrathecal fentanyl. Lakshmi sowmya N *et al*. [13] compared duration of analgesia in fractionated and bolus dose group patients undergoing lower limb surgery. They found that fractionated group had prolonged duration of analgesia than bolus dose group. Sowmya N *et al*. [15] conducted a study, comparing two different doses (10 µg and 15 µg) of fentanyl with 10mg of heavy bupivacaine for caesarean section. They concluded that 15µg of intrathecal fentanyl produce the quicker onset of sensory block and prolonged analgesia. In our study, we decided to use 10µg of intrathecal fentanyl to avoid possible adverse effects related to them.

In a study done by Jain K *et al*. [16] compared different dose of fentanyl with bupivacaine in pregnant women with pregnancy induced hypertension (PIH). The longer duration of analgesia was found in the group which received 20µg of intrathecal fentanyl. The side effects like respiratory depression, pruritis, nausea and vomiting were less in both 10µg and 20µg of intrathecal fentanyl. In our study, no side effects occurred to 10µg of intrathecal fentanyl.

There was no difference in the Apgar score at 1 and 5min between the groups, in our study. This was supported by the study conducted by Maayan-Metzger A *et al*. [17]. They studied the effects of maternal hypotension on the fetal outcome and found no difference in the outcome of the fetus born to a hypotensive mother. This assures that hypotension for a short duration does not have any effect on the newborn.

Conclusion

To conclude, this study demonstrated that giving subarachnoid block in fractionated dose is better than single-bolus dose for pregnant women undergoing elective caesarean section delivery in terms of providing better haemodynamic parameters like HR, blood pressure, MAP and faster onset of motor and sensory block. Adding opioid like fentanyl to bupivacaine increases the analgesia period. It provides prolongs postoperative pain-free periods and decreases the need for rescue analgesia. This newer technique is better than the usual method in preventing maternal hypotension after spinal anaesthesia.

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