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Fractionated Dose Vs Conventional Method of Drug Administration in Spinal Anesthesia for Pregnant Women Undergoing Cesarean Section: A Comparative Study

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Abstract

Background: Spinal Anesthesia (SA) is the routine and safe method of administering anesthesia for performing Elective or emergency cesarean sections. SA with conventional (bolus dose) method of injection provides rapid onset of action with high spinal blockade leading to hypotension, compromised the uteroplacental circulation and fetal acid-base imbalance. Our study aimed to compare, low dose bupivacaine injection by conventional to fractionated method to achieve the desired level of anesthesia with stable hemodynamic in SA. Onset of sensory and motor blockade, and duration of analgesia were monitored in patients undergoing elective Lower Segment Cesarean Section (LSCS). *Methods:* Sixty pregnant women undergoing elective Lower Segment Cesarean Section (LSCS) were included in the study and they were randomly allocated into two Groups. Group C patients received bolus dose of bupivacaine (0.5%) heavy by conventional method and Group F received the same dose of Bupivacaine in fractionated manner with two third of it initially followed by remaining one third dose after 30 secs. The hemodynamic monitoring consisted of Mean Arterial Pressure (MAP), Heart Rate (HR). Other variables recorded were time of onset, duration of analgesia, and regression of sensory and motor blockade. The vasopressor required as rescue drug for hypotension when fall of MAP below 20% of the basal value were observed and noted. *Results:* The hemodynamics were statistically comparable in both the Groups. The onset of sensory block was slightly delayed (2.50 ± 0.68 vs 3.47 ± 1.53), duration of analgesia was prolonged (141.10 ± 24.32 vs 166.80 ± 52.11) and the vasopressor requirement was less (5.33 ± 3.93 vs 2.20 ± 4.02) in Group F as compared to Group C and these results were statistically significant. The Apgar scores between the two Groups ($p > 0.05$) were not significant. *Conclusion:* SA in pregnant women for LSCS by fractionated technique of drug injection provided slightly slower onset of only sensory blockade with prolonged duration of analgesia. The statistically significant less vasopressor requirement in the study group was observed as compared to the conventional group which in turn concludes the hemodynamics more stable in the study group.

Keywords: LSCS; Fractionation; Conventional bolus dose; SA block; Hemodynamics.

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Introduction

Elective and emergency Lower Segment Cesarean Section (LSCS) under spinal anesthesia is the safe and most adopted technique for day to day practice. The required dosage of effective block for LSCS has been associated with maternal arterial hypotension of 60–90% with maternal and neonatal

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morbidity.[1] Maternal hypotension and subsequent consequences are reduced to some extent by various measures like preloading or coloading of crystalloids or colloids, low dose bupivacaine, left uterine displacement, prophylactic use of vasopressors etc but with less benefit.[2-4]

Intensity and duration of spinal block is influenced by numerous factors like anatomical and physiological changes associated with pregnancy, height, weight, and dose of local anesthetic drug.[5] The SA related hypotension can be prevented by possible and relevant technique by modifying the dose administration of the hyperbaric local anesthetic drug intrathecally.[6-8] hemodynamic stability and prolonged duration of analgesia were observed by injecting the local anesthetic drug in divided doses in to the subarachnoid space.[8,9]

The present study was done to compare the spinal anesthetic blockade (onset and recovery of sensory and motor blockade, highest sensory block and duration of analgesia) and hemodynamic (HR and MAP) parameters, vasopressor requirement and APGAR score with modification of dose injection by fractionationvs conventional method.

Materials and Methods

The present study was carried out in our hospital after the Institutional ethics committee approval in sixty pregnant women (thirty in each group).

Study population

As the hemodynamic parameters were recorded repeatedly the sample size was calculated for repeated measures of ANOVA, taking Cohen's effect size of f = 0.20 with alpha = 0.05 and 1-beta (power) = 0.99, total sample size was 54, however to compensate for the dropout cases total of 60 cases (30 in each group) were considered.

The study was done in our hospital as a prospective randomised double blinded controlled study. Singleton pregnant women posted for elective LSCS under SA with American Society of Anesthesiologists' (ASA) physical status I–II, age between *18* and *35 years* and height between *145* and *175 cm* were included. The women with pregnancy induced hypertension, preexisting cerebrovascular or cardiovascular disease, any contraindication to SA, weight less *than 50 kg* or more than *110 kg*, taller than *175 cm* or shorter than *140 cm*, severely altered mental status, uncooperative patients, and history of spine surgery or spine deformities were excluded from the study.

Study Procedure

All the pregnant women coming for Cesarean section had undergone preanesthetic checkup day before surgery. On the day of surgery premedication was given with pantoprazole *40 mg* IV after securing the intravenous line. In the operation theatre the monitoring consisted of electrocardiogram (ECG), pulse oximeter (SpO_2) and Noninvasive Blood Pressure (NIBP) for all the patients. The baseline blood pressure and Heart Rate (HR) were recorded. Preloading was done with *10 ml/kg* Ringer's Lactate (RL) solution over period of *10 min*. Procedure of spinal anesthesia was done in sitting position using all aseptic precautions with 25 G quincke spinal needle through L3–L4 space. Bupivacaine 0.5% heavy *2 ml* (*10 mg*) was injected intrathecally after free flow of CSF. Randomization into two Groups was done using computer generated sequential number and placed in sealed envelopes to be opened only before the study. The study was double blinded so that, the women and the assessor were unaware of the group. Only the attending consultant administering the SA knew the group allocation.

Group C - received the drug injection in conventional method over *10 second*.

Group F - received the drug injection in fractionation method [two thirds of the drug was injected initially and the remaining one third was given after *30 seconds*].

The drug was injected with *5 ml* syringe. In Group C, all received the bupivacaine injection in the conventional manner over the period of *10 seconds*. Where as in Group F, two thirds of the dose was given initially followed by the remaining dose after *30 seconds*. The syringe was kept in situ for remaining *30 seconds* to avoid the CSF leak before the full dose is injected. Immediately after the injection all women were made supine with a wedge under the right hip in both the Groups and were supplemented with oxygen by Hudson mask at *5 L/min*.

Continuous ECG, HR, NIBP and SpO_2 were monitored intraoperatively. The HR and BP were monitored at base line, just before subarachnoid block, then at *2, 4, 6, 8, 10, 15, 20, 30, 40, 50,* and *60 minutes* after giving SA.

Hypotension was treated with injection mephentarmine *6 mg* IV whenever mean arterial pressure (MAP) decreased to ≤ 20% of baseline and repeated as and when required. Atropine *0.6 mg* was given for episodes of bradycardia (HR of < *50 beats/min*). The amount of these two drugs given were recorded in both Groups.

Time of onset, highest level and two segment regression of sensory and motor block were assessed and hemodynamic (MAP and HR) parameters were recorded. Loss of sensation to pinprick was considered as the level of sensory block. Modified Bromage scale was used to assess the motor blockade. These tests were performed every min till the achievement of maximum sensory and motor block (Bromage scale 3) and every *30 minutes* later on postoperatively until the recovery of sensory and motor blockade returned back to normal. The onset time of sensory or motor blockade was defined as the interval between intrathecal administration and time to achieve T10 and a modified Bromage score of 3 respectively.

Onset of sensory block was considered with loss of sensation to pinprick at T10 from the start of drug injection. Time from the highest level of sensory blockade to two segment regression was considered as duration of sensory blockade and fromthe onset of motor block to the complete motor recovery or achievement of modified Bromage scale zero (0) as duration of motor blockade. Time for first request to rescue analgesic demand from the start of drug injection is taken as duration of analgesia.

Motor block was assessed by Modified Bromage scale: Grade 0 – No motor block, Grade 1 – Inability to raise an extended leg, able to move knees and feet, Grade 2 – Inability to raise an extended leg, unable to move knees but able to move feet and Grade 3 – Complete motor block of lower limb.

Surgery was allowed only when the sensory blockade reached at least T6 dermatome level and Bromage scale of three or more. Those requiring conversion to general anesthesia were excluded from the study. After the baby delivery, IV oxytocin 5 IU IV slowly and 15 IU in *500 ml* RL was given. Episodes of nausea, vomiting, respiratory distress, shivering, pruritus, urinary retention were monitored and recorded postoperatively for *24h* and treated accordingly. Apgar scores were assessed at *1, 5* and *10 minutes* and noted.

Visual Analog Scale (VAS) [*0 to 10 cm* where 0 = no pain and 10 = worst pain ever felt] was used to assess pain postoperatively. Pain was assessed every *30 min* initially for the first *2 hrs* and then hourly for *6 hrs*. VAS score ≥ 4 was considered as the rescue analgesic demand. Diclofenac sodium *75 mg* IM/IV was used as rescue analgesic in our study.

Statistical Analysis

Kolmogorov-Smirnov test was used to confirm the normal distribution of the data recorded. The continuous data was displayed by mean and standard deviation and discrete data as Median and Interquartile Range (IQR). Unpaired *t* - test was used to compare continuous data. ANOVA (repeated measures) was performed for hemodynamic parameters. The discrete data Apgar score was compared by using Mann-Whitney *U* test. The Fischer test was performed for numerical discrete data. Results with *p* - value < 0.05 were considered statistically significant.

Results

Demographic observations (age, height and weight) were comparable in two Groups (Table 1).

Table 1: Demographic data in two groups

Demographic data	Group C (Mean ± SD)	Group F (Mean ± SD)	*p* - values
Age in *years*	24.1 ± 3.61	24.67 ± 3.37	0.532
Height in *cm*	156.73 ± 4.89	154.76 ± 5.81	0.057
Weight in *kg*	61.97 ± 8.85	65.6 ± 7.56	0.084

p - values < than 0.05 is statistically significant

Table 2: Characteristric of the Spinal block both the Groups

Observations	Group C Mean ± SD	Group F Mean ± SD	*p* - values
Onset of sensory block (*min*)	2.5 ± 0.68	3.47 ± 1.54	0.002
Onset of motor block (*min*)	4.97 ± 1.57	5.23 ± 1.89	0.556
Sensory block level (number of patients)			
T2	6 (20%)	1 (3.33%)	0.001
T4	8 (26.67%)	4 (13.33%)	
T5	5 (16.67%)	6 (20%)	
T6	11 (36.67%)	19 (63.33%)	
Two segment regression of sensory block (*min*)	97.13 ± 24.85	93.87 ± 32.81	0.665
Motor Recovery (*min*)	180.0 ± 26.73	192.57 ± 53.04	0.251
Duration of Analgesia (*min*)	141.1 ± 24.31	166.80 ± 52.10	0.017
Vasopressors Required (*min*)	5.33 ± 3.92	2.2 ± 4.01	0.003
APGAR score (*IQR*)	8.3 ± 10	8.5 ± 5	0.259

p - values < than 0.05 is statistically significant

The onset of sensory block (2.50 ± 0.68 *vs* 3.47 ± 1.53 *min*) was delayed in the Group F than the control group (conventional method). Similarly the duration of analgesia was significantly prolonged (141.10 ± 24.32 *vs* 166.80 ± 52.11) in Group F as compared to Group C ($p < 0.05$). The vasopressor requirement was much less (5.33 ± 3.93 *vs* 2.20 ± 4.02) in Group F in comparison to Group C and is statistically significant (Table 2). Our results showed that hemodynamic parameters (Table 3) were comparable in both the groups and this may be because of the increased requirement of vasopressor in the conventional method. Onset of motor blockade, two segment regression of sensory and motor recovery were statistically insignificant ($p > 0.05$). APGAR scores were same in both the Groups (Table 4).

Table 3: Heart Rate changes (beats/min) in both the groups

Heart rate	Group C Mean ± SD	Group F Mean ± SD	*p* - values
BL	99.17 ± 15.59	92.8 ± 15.59	0.096
SAB	99.4 ± 14.41	94.17 ± 13.35	0.151
2 min	100.07 ± 19.11	91.54 ± 14.68	0.057
4 min	95 ± 17.43	89.7 ± 16.51	0.229
6 min	87.8 ± 17.49	89 ± 17.04	0.789
8 min	80.77 ± 15.72	80.84 ± 17.22	0.102
10 min	84.73 ± 15.84	87.33 ± 15.28	0.522
20 min	90.37± 13.31	91.6± 14.79	0.735
30 min	92.87± 16.74	91.37± 12.91	0.699
40 min	91.23 v 14.21	91.03 ± 13.21	0.955
50 min	88.5 ± 11.96	86.43 ± 12.42	0.514
60 min	85.86 ± 9.81	85.5 ± 12.76	0.901

p - values < than 0.05 is statistically significant

Table 4: Mean Arterial Pressure (mm of Hg)

Map	Group C Mean ± SD	Group F Mean ± SD	*p*-values
BL	84.9 ± 9.58	82.13 ± 6.06	0.187
SAB	83.53 ± 12.65	81.33 ± 7.97	0.424
2 min	74.43 ± 17.14	75.57 ± 9.31	0.751
4 min	75.3 ± 11.91	73 ± 9.71	0.329
6 min	68.03 ± 13.67	70.03 ± 9.51	0.513
8 min	71.5 ± 13.24	69.73 ± 11.63	0.585
10 min	74.27 ± 13.23	73.57 ± 9.37	0.814
20 min	70.83 ± 12.67	72.6 ± 9.02	0.536
30 min	71.27 ± 10.72	71.87 ± 10.95	0.831
40 min	71.7 ± 9.89	73.5 ± 7.69	0.435
50 min	74.87 ± 10.22	76.23 ± 8.73	0.581
60 min	75.93 ± 9.22	75.43 ± 8.35	0.827

p - values < than 0.05 is statistically significant

Discussion

Subarachnoid block is the most preferred technique of anesthesia because of its safety and economical purpose for both elective and emergency Lower Segment Cesarean Section (LSCS). Maternal hypotension, impaired uteroplacental circulation with maternal and neonatal morbidity[1] are common side effects with conventional method of SA. A large variety of dosage regimes (National survey at UK) were in use for SA to improve the neonatal outcome by maintaining normotension during LSCS. The incidence of hypotension is reported to be 60–90% of cases, if preventive measures (preloading or coloading of crystalloids or colloids, low dose bupivacaine, left uterine displacement, prophylactic use of vasopressors etc) are not taken.[2,11]

Height[5] and weight[12] are considered to be significant variables in predicting the level of spinal blockade. Dose adjustment as per height and weight proved to be having less maternal hypotension as compared to the fixed dose.[13] Pregnancy itself (hormonal changes alter the action of neurotransmitters and permeability in the spinal column).[14,15]

Use of opioid as an additive to the local anesthetics in SA proved to have faster onset of sensory blockade, stable hemodynamics and longer duration of analgesia,[16] (Fig. 1).

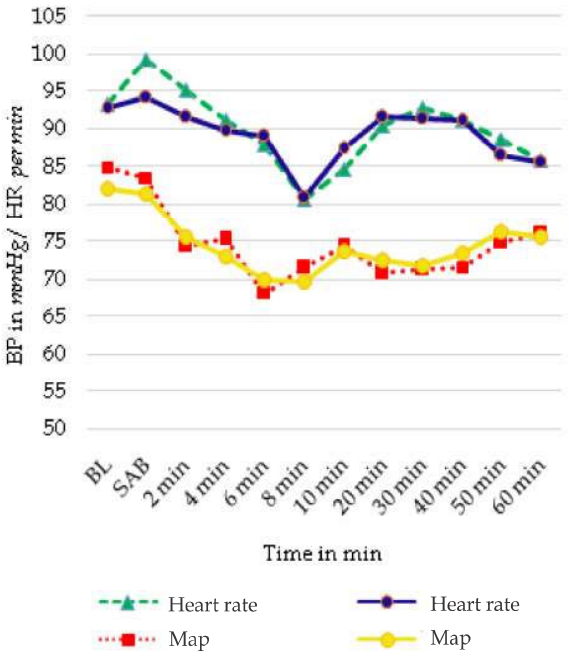

Fig. 1: Hemodynamic changes

Fractionated [initial two thirds of the dose injection followed by one third dose after *90 sec* of bupivacaine heavy (0.5%)] dose was compared with bolus dose in SA for elective LSCS by Badheka Jigisha *et al*.[8] and found to have stable hemodynamics, longer duration of analgesia and dense blockade with fractionated dose injection method. Similar method was used in PIH patients by Bina Patel *et al*.[17] giving the second half of the drug after after *90 secs* in sitting position and observed stable hemodynamics, dense block and longer duration of analgesia in the fractionated method. In another study, fractionated dose of one third of the remaining total drug injection after sixty seconds proved to have stable hemodynamics with longer duration of analgesia compared to bolus dose injection.[9]

As per our hospital settings, to get higher level of sensory blockade we reduced the waiting time (*30 seconds*) in fractionation method.

Onset of sensory blockade was slightly delayed with the fractionated method in comparison to the conventional method of SA in our study. Same results were observed with the study of Agarwal N *et al*.[18] Essam E *et al*.[19] concluded that in their study in pregnant women undergoing LSCS the onset of sensory blockade was faster in the conventional method than the patients kept sitting for longer time. Fractionated method of SA by injecting the remaining one third of the drug after *60 sec*. also showed delayed onset of sensory block.[9] Our study results are in concurrent with the above studies. In contradiction to our study results Bina Patel *et al*.[17] and Bhadeka Jigisha *et al*.[8] had faster onset of sensory block in the fractionated method.

Studies have shown that with the fractionated method of drug injection for SA, sensory and motor blockade and recovery was delayed in the fractionated method of SA.[8,9,17] In contrast our study results had no difference in both the two Groups in regards to two segment sensory regression, onset of motor blockade and motor recovery. This explains that shorter duration of time fractionation of drug injection does not alter much in the above said characteristics.

Paramaters of MAP were comparable in both the Groups throughout the study, probably because the BP were maintained with the use of mephenteramine. Whereas other studies proved to have statistically significant stable hemodynamics in fractionated group than the control group.[8,20] As compared to the single bolus dose of SA in LSC Sby Bina Patel *et al*.[17] showed stable hemodynamics and less vasopressors requirement with fractionated dose SA. In another study with titrated dose of Bupivacaine in patients undergoing hip fracture surgery, safe, efficient and better cardiovascular stability was observed than with a single bolus dose.[21]

Studies have observed stable HR with fractionated method of administration of bupivacaine in SA.[8,9,20] in contrast our study did not show significant difference between the two Groups because of the lesser time duration of fractionated (*30 sec*) drug injection. Our study results are in concurrence with the study of Agrawal N *et al*.[18] who concluded that sitting position for *30 seconds* after spinal anesthesia helps to prevent high spinal and gives better hemodynamic stability.

The fractionated dose of Bupivacaine prolonged the duration of sensory and motor blockade in the study of Fahmy and colleagues[20] and this not in agreement with our study results of insignificant difference between the two groups. Our observations are in concurrence with the various other studies[8,9,17] with regard to prolonged duration of analgesia and the first rescue for analgesic requirement. Even with lesser time duration of fractionation of drug injection, the prolonged duration of analgesia was observed in our study which was be very much useful in postoperative period decreasing the total analgesic requirement and patient comfort.

Apgar scores were comparable in both the groups in our study and the results of Bhadeka Jigisha *et al*.[8] and Bina Patel *et al*.[17] were similar to observations of our study.

Conclusion

Fractionated dose method of spinal anesthesia technique proved to have adequate spinal anesthetic blockade, stable hemodynamics and better outcome in terms of uteroplacental circulation in comparison to the conventional method in patients undergoing LSCS. Profound hypotension and high level spinal block can be avoided by using this method where ever hemodynamic stability is desired. This makes the fractionated dose method as safe alternative and acceptable technique of local anesthetic drug injection for SA in pregnant women undergoing LSCS.

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