Original Article

Comparison between Fractionated Dose versus Bolus Dose of Intrathecal Hyperbaric Bupivacaine Injection in Spinal Anesthesia for Patients Undergoing Elective Caesarean Section

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Abstract

Background: *Spinal anesthesia (SA) with bolus dose has rapid onset but may causes hypotension. When we inject local anesthetic in fractions with a time gap, it provides more hemodynamic stability an. We aimed to compare fractionated dose with bolus dose in SA for hemodynamic stability in patients undergoing elective lower segment caesarean section (LSCS).*

Objectives: *To find out whether the fractionated dose of spinal local anesthetics could reduce the incidence of hemodynamic changes in comparison to bolus dose of spinal local anesthetics.*

Methods: *After clearance from the Institutional Ethics Committee, the study was carried out in 80 patients undergoing elective LSCS. Patients were divided into two groups. Group B patients received single bolus SA with injection bupivacaine heavy (0.5%) and Group F patients fractionated dose with 2/3rd of the total dose of injection bupivacaine heavy (0.5%) given initially followed by 1/3rd dose after 90 s. The intraoperative hemodynamics were recorded and analyzed with chi- square test Student's t-test.*

Result: *Intraoperative mean blood pressure of group –F were higher than those of Group-B patient and showed statistically significant difference. Mean heart rate of group –F were higher than those of Group-B patient and showed statistically significant difference.*

Conclusion: *Fractionated dose of SA provides greater hemodynamic stability compared to bolus dose.*

Key Words:
Fractionated dose vs. Bolus dose, Intrathecal hyperbaric bupivacaine, Spinal anesthesia

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Introduction

Spinal anesthesia with local anesthetics (LA) such as bupivacaine is routinely used to provide anesthesia for both elective and emergency caesarean section. Spinal anesthesia has a rapid onset of action but at the same time it causes hypotension as well as nausea, vomiting due to sudden sympathetic block by LA agent. Maternal hypotension may cause decrease the uterine and placental blood flow resulting in acid base abnormalities in fetus.[1]

To prevent the hypotension there are various methods and techniques are used such as administration of either colloid or crystalloid fluid before or at the time of spinal anesthesia, use of prophylactic vasopressor such as ephedrine, mephentamine and left lateral uterine displacement. The

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incidence of hypotension is high if no preventive measures are taken to reduce hypotension.[2,3] Dose of hyperbaric bupivacaine depend on many factor such as weight,[4] heights,[5] anatomy of spine and pregnancy. It has been shown that minimal effective dose of hyperbaric bupivacaine heavy for spinal anesthesia in patient undergoing caesarean section is average 0.06mg/cm height.[5]

Although bolus dose of intrathecal LA causes rapid onset of action but sometime it precipitates hypotension specially the patient with hypovolemic state, patient who suffer hypertension during pregnancy, pre-eclampsia, eclampsia etc.

The fractionated dose of spinal bupivacaine heavy, in which total dose was not given at a time rather than two third of total calculating dose was given initially followed by remaining one third was given after ninety-second-time interval which achieved adequate spinal anesthesia and with more hemodynamic stability.[6]

So, the aims of this prospective randomized control study was to compare the fractionated dose versus bolus dose in spinal anesthesia for hemodynamic change in patient undergoing elective lower segment caesarean section.

Materials and methods

This randomized controlled trial study was carried out in the department of Anesthesia, Intensive care & Pain medicine of Shaheed Suhrawardy Medical College Hospital (ShSMCH), Dhaka, January 2018 to June 2018.Prior to the commencement of the study, the research protocol was submitted to the ethical review committee of ShSMCH. Study population was the patient with female sex, ASA grade I &II, whose body weight was 50-75 kg, height from 140-170 cm, who was admitted for elective caesarian section under spinal anesthesia in ShSMCH, Dhaka. In this study total number of patient was 80 were aged between 18-35 years, had given informed written consent, randomly selected and divided in to two group (Group B -40 and Group F 40) by odd number and even number basis.

Hypotension was defined as a mean blood pressure decreased d" 20% of baseline blood pressure. Bradycardia was defined as heart rate ≤60 b/min.

After reaching to the operation room IV cannula with 18 – gauge was inserted in a peripheral vein and the patient was infused with ringer's lactate solution @ 50 ml/min.

Patient's baseline vital data was recorded by using non-invasive blood pressure (NIBP), pulse oximeter (for O_2 saturation), ECG.

SA was given in sitting position with 25-gauge Quincke spinal needle in L_3–L_4 interspace after skin infiltration with lignocaine (1ml, 2%). After aspiration of cerebrospinal fluid, injection bupivacaine 0.5% heavy was injected according to respective groups, B and F. Total dose of SA was calculated as 0.06 mg/cm of the height of the patient.

The patients were randomly divided into two groups. Group B patients were receiving a single bolus dose of bupivacaine over 15 second. Group F patients was received fractionated dose of bupivacaine with two-third of the total calculated dose was give initially followed by one-third dose after 90 s, both doses were given at a rate of 0.2 ml/s.

After injection of initial two-third dose, the syringe was kept attached to the spinal needle for remaining 90 s, after which remaining one-third dose was administered.

Patients were turned into the supine position with a wedge under the right hip in both groups. Supplemented oxygen was given with the nasal cannula at 3 L/min. The patients were randomly divided into two groups using computer-generated sequential number. Assessed and recorded time of onset, level and regression of motor and sensory block. Confirmation of sensory block was assessed by loss of sensation to pinprick.

Motor blockage was assessed by a modified Bromage scale. The onset time of sensory or motor blockade was defined as the interval between intrathecal administration and time to achieve maximum block height or a modified Bromage score of 3, respectively.

The surgical incision was allowed when loss of pinprick sensation was reaches the T_6 dermatome level bilaterally and when Bromage scale of three was achieved. Patients with inadequate sensory blockade and requiring conversion to general anesthesia were excluded from the study. Intra-operatively, patients were monitor with continuous ECG, HR, NIBP and SpO_2. Hypotension was treated when mean arterial pressure (MAP) decreased d"20% of baseline with injection ephedrine 5 mg IV and repeated when needed. The number of hypotensive episodes and ephedrine used was recorded for each patient. Treated bradycardia if any (HR of < 60 beats/min) with IV atropine 0.6 mg.

The duration of sensory blockade was defined as the interval from intrathecal administration of local anesthetic to S_2 segment regression. The duration of motor blockade was defined as the time interval from the onset of motor block to the time of achievement of modified Bromage scales zero (0).

After delivery, IV oxytocin 5 IU IV slowly and 20 IU in 1000 ml RL. The incidence of nausea, vomiting, respiratory distress, shivering, purities, and urinary retention was noted for 24 h post-operatively and treated accordingly. The attending pediatrician assessed APGAR scores at 1 and 5 min.

All the observations were recorded, and all the results were analyzed statistically. Statistical analyses were carried out by using the Statistical Package for Social Sciences version 16.0 for Windows (SPSS). The mean values were calculated for continuous variables. The quantitative observations were indicated by frequencies and percentages. The chi- square test and student "t" test was used to analyze the significance level of $p < 0.05$.

Results

Group B= Single bolus dose

Group F= Fractionated dose

Table-I

Distribution of the study patients by age (n=80)

Age (years)	Group B(n=40)		Group F(n=40)		P value
	n	%	n	%	
d"20	4	10.0	3	7.5	
21-25	28	70.0	26	65.0	
26-30	7	17.5	8	20.0	
>30	1	2.5	3	7.5	
Mean±SD	25.6	±4.3	26.0	±3.9	0.664^{ns}
Range (min-max)	19	-32	18	-35	

ns= not significant, P value reached from unpaired t-test

Table I shows that 28(70.0%) patients were belonged to age 21-25 years in group B and 26(65.0%) in group F. The mean age was found 25.6±4.6 years in group B and 26.0±3.9 years in group F. The mean age difference was not statistically significant (p>0.05) between two groups.

Table II

Distribution of the study patients according to BMI (n=80)

BMI (kg/m^2)	Group B(n=40)		Group F(n=40)		P value
	n	%	n	%	
Normal (18.5-22.9)	29	72.5	27	67.5	0.626^{ns}
Over weight (23.0-26.9)	11	27.5	13	32.5	

ns= not significant, P value reached from chi square test

Table II shows that 29(72.5%) patients were found BMI 18.5-22.9 kg/m^2 in group B and 27(67.5%) in group F. The difference was not statistically significant (p>0.05) between two groups.

Table-III

Distribution of the study patients according to duration of surgery (n=80)

Duration of surgery (min)	Group B(n=40)		Group F(n=40)		P value
	n	%	n	%	
d"60	35	87.5	37	92.5	
>60	5	12.5	3	7.5	
Mean±SD	50.7	±9.4	51.9	±9.3	0.568^{ns}
Range (min-max)	40	-65	40	-60	

ns= not significant, P value reached from unpaired t-test

Table 3.3 shows that 35(87.5%) patients were found duration of surgery d"60 minute in group B and 37(92.5%) in group F. The mean duration of surgery was found 50.7±9.4 minute in group B and 51.9±9.3 minute in group F. The mean duration of surgery was not statistically significant (p>0.05) between two groups.

Table IV

Distribution of the study patients according to gestational age (n=80)

Gestational age (weeks)	Group B(n=40)		Group F(n=40)		P value
	n	%	n	%	
Preterm (<37 weeks)	38	95.0	39	97.5	
Term (≥37 weeks)	2	5.0	1	2.5	
Mean±SD	36.2 ±1.1		35.8 ±0.9		0.079^{ns}
Range (min-max)	35	-38	36	-37	

ns= not significant, P value reached from unpaired t-test

Table 4 shows that 38(95.0%) patients were found gestational age <37 weeks in group B and 39(97.5%) in group F. The mean gestational age was found 36.2±1.1 weeks in group B and 35.8±0.9 weeks in group F. The mean gestational age was not statistically significant (p>0.05) between two groups.

Table V

Distribution of the study patients according to APGAR score (n=80)

APGAR score	Group B(n=40)		Group F(n=40)		P value
	n	%	n	%	
At 1 min					
<7	39	97.5	40	100.0	0.500^{ns}
≥7	1	2.5	0	0.0	
At 5 min					
<7	40	100.0	40	100.0	-
≥7	0	0.0	0	0.0	

ns= not significant, P value reached from chi square test

Table V shows that APGAR score ≥7 at 1 minute was found 39(97.5%) in group B and not found in group F. The difference was not statistically significant (p>0.05) between two groups.

Table VI

Distribution of the study patients according to intervertebral space chosen (n=80)

Intervertebral space chosen	Group B(n=40)		Group F(n=40)		P value
	n	%	n	%	
L3-L4	40	100	40	100	

ns= not significant, P value reached from chi square test

Table VI shows that 40(100%) patients were found intervertebral space chosen L3-L4 in group B and 40(100%) in group F.

Table VII

Distribution of the study patients according to ASA grade (n=80)

ASA grade	Group B(n=40)		Group F(n=40)		P
	n	%	n	%	value
I	28	70.0	25	62.5	0.478^{ns}
II	12	30.0	15	37.5	

ns= not significant, P value reached from chi square test

Table VII shows that 28(70.0%) patients were found ASA grade I in group B and 25(62.5%) in group F The difference was not statistically significant (p>0.05) between two groups.

Table VIII

Heart rate in different follow up (n=80)

Heart rate (beat/min)	Group B(n=40)		Group F(n=40)		P value
	Mean	±SD	Mean	±SD	
Baseline spinal anesthesia	98.8	±7.6	95.9	±7.9	0.098[ns]
At 1 min	97.1	±8.0	96.3	±8.1	0.658[ns]
At 3 min	93.9	±7.9	98.7	±8.0	0.008[s]
At 5 min	94.2	±8.0	100.5	±8.3	0.0009[s]
At 10 min	94.1	±7.3	101.8	±8.6	<0.001[s]
At 15 min	95.3	±6.5	99.1	±7.4	<0.001[s]
At 30 min	95.1	±3.8	99.5	±6.9	0.01[s]
At 45 min	95.9	±7.0	100.4	±7.1	0.005[s]
At 60 min	96.6	±7.2	99.7	±7.0	0.055[ns]

ns= not significant, P value reached from unpaired t-test

Table VIII shows that mean heart rate- before spinal anesthesia, at 3 min, at 5 min, at 10 min, at 15 min, at 30 min and at 45 min were statistically significant ($p<0.05$) between two groups.

Table IX

Systolic arterial pressure in different follow up (n=80)

Systolic arterial pressure (mmHg)	Group B(n=40)		Group F(n=40)		P value
	Mean	±SD	Mean	±SD	
Before spinal anesthesia	110.1	±10.9	112.0	±12.1	0.728[ns]
At 1 min	108.2	±10.7	110.4	±11.8	0.635[ns]
At 3 min	99.8	±10.8	108.3	±11.5	0.005[s]
At 5 min	98.5	±11.0	105.8	±11.3	0.001[s]
At 10 min	98.7	±10.9	105.6	±11.2	0.01[s]
At 15 min	97.6	±10.7	104.5	±10.8	0.005[s]
At 30 min	95.0	±10.6	104.5	±11.0	0.004[s]
At 45 min	95.4	±10.5	102.9	±10.7	0.003[s]
At 60 min	99.1	±10.6	99.7	±10.6	0.800[ns]

ns= not significant, P value reached from unpaired t-test

Table IX shows that mean systolic arterial pressure - before spinal anesthesia, at 3 min, at 5 min, at 10 min, at 15 min, at 30 min and at 45 min were statistically significant ($p<0.05$) between two groups.

Table X

Diastolic arterial pressure in different follow up (n=80)

Diastolic arterial pressure (mmHg)	Group B(n=40)		Group F(n=40)		P value
	Mean	±SD	Mean	±SD	
Before spinal anesthesia	79.2	±6.9	82.4	±7.1	0.611[ns]
At 1 min	75.5	±6.4	76.8	±6.9	0.639[ns]
At 3 min	73.4	±6.0	77.5	±7.2	0.007[s]
At 5 min	73.1	±6.3	76.3	±6.8	0.03[s]
At 10 min	75.9	±6.5	80.0	±6.7	0.006[s]
At 15 min	75.2	±6.4	79.2	±6.8	<0.001[s]
At 30 min	70.7	±6.8	74.1	±6.9	0.02[s]
At 45 min	71.8	±6.7	75.4	±6.7	0.01[s]
At 60 min	76.4	±6.6	78.5	±6.7	0.16[ns]

ns= not significant, P value reached from unpaired t-test

Table X shows that mean diastolic arterial pressure - before spinal anesthesia, at 3 min, at 5 min, at 10 min, at 15 min, at 30 min and at 45 min were statistically significant ($p<0.05$) between two groups.

Table XI

Mean arterial pressure in different follow up (n=80)

Mean arterial pressure (mmHg)	Group B(n=40)		Group F(n=40)		P value
	Mean	±SD	Mean	±SD	
Before spinal anesthesia	89.50	±8.9	92.27	±9.6	0.16^{ns}
At 1 min	86.40	±8.6	88.00	±9.4	0.42^{ns}
At 3 min	82.20	±8.4	87.77	±9.3	0.006^{s}
At 5 min	81.57	±8.7	86.13	±9.1	0.02^{s}
At 10 min	83.50	±8.7	88.53	±9.0	0.01^{s}
At 15 min	82.67	±8.6	87.63	±8.8	0.01^{s}
At 30 min	78.80	±8.7	84.23	±9.0	0.007^{s}
At 45 min	79.67	±8.6	84.57	±8.7	0.01^{s}
At 60 min	83.97	±8.6	85.57	±8.7	0.41^{ns}

ns= not significant, P value reached from unpaired t-test

Table XI shows that mean arterial pressure - before spinal anesthesia, at 3 min, at 5 min, at 10 min, at 15 min, at 30 min and at 45 min were statistically significant ($p<0.05$) between two groups.

Discussion

In our study shows that 28(70.0%) patients were belonged to age 21-25 years in group B and 26(65.0%) in group F. The mean age was found 25.6±4.6 years in group B and 26.0±3.9 years in group F. The mean age difference was not statistically significant ($p>0.05$) between two groups. Badheka et al.[7] study reported similar observation they showed that the mean age was found 26.63±3.2 years in group B and 25.26±3.1 years in group F. The difference was not statistically significant ($p>0.05$) between two groups. Sridhar[9] study observed the mean age was found 25.73±2.6 years in group C (received 10 mg (2mL) of 0.5% hyperbaric bupivacaine along with 25 mcg of fentanyl intrathecally) and 24.8±3.1 years in group E (received 5 mg (1mL) of 0.5% hyperbaric bupivacaine along with 25 mcg of fentanyl intrathecally, followed by 6 mL of normal saline injected into the epidural space via epidural catheter). Patel et al. reported that the mean age was found 26.63±3.65 years in group B and 25.33±3.07 years in group F. The difference was not statistically significant ($p>0.05$) between two groups.[8]

In this current present study shows that 29(72.5%) patients were found BMI 18.5-22.9 kg/m^2 in group B and 27(67.5%) in group F. The difference was not statistically significant ($p>0.05$) between two groups. Schnider et al.[14] suggested that the onset time for achieving an adequate sensory level for surgery increases linearly with height and decreases with increasing weight while another clinical study demonstrated that the dose of intrathecal bupivacaine for caesarean delivery is similar in obese and normal weight women.[15] A retrospective study observed a higher percentage of hypotension in pregnant women with obesity class three, which might be due to the greater extension of a higher sympathetic blockade caused by compression of the subarachnoid space by the pregnant abdomen associated with obesity.[16]

In this series shows that 35(87.5%) patients were found duration of surgery d"60 minute in group B and 37(92.5%) in group F. The mean duration of surgery was found 50.7±9.4 minute in group B and 51.9±9.3 minute in group F. The mean duration of surgery was not statistically significant ($p>0.05$) between two groups. Badheka et al.[7] reported the mean duration of surgery was found 51.5±12.12 minute in group B and 52.0±11.57 minute in group F. The difference was not statistically significant ($p>0.05$) between two groups. Sridhar[9] study the mean duration of surgery was found 60.67±4.49 minute in group C and 58.17±7.13 minute in group E. The mean duration of surgery was not statistically significant ($p>0.05$) between two groups. Patel et al.[8] reported that the mean duration of surgery was found 55.16±3.35 minute in group B and 54.9±6.19 minute in group F. The difference was not statistically significant ($p>0.05$) between two groups.

In this study shows that 38(95.0%) patients were found gestational age <37 weeks in group B and 39(97.5%) in group F. The mean gestational age was found 36.2±1.1 weeks in group B and 35.8±0.9 weeks in group F. The mean gestational age was not statistically significant ($p>0.05$) between two groups. Similar observation was found Badheka et al.[7] study they showed that the mean gestational age was found 35.9±1.44 weeks in group B and 36.1±1.29 weeks in group F. The difference was not statistically significant ($p>0.05$) between two groups. Patel et al.[8] the mean gestational age was found 36.4±1.06 weeks

in group B and 36.6±1.4 weeks in group F. the difference was not statistically significant (p>0.05) between two groups.

In this present study shows that APGAR score e"7 at 1 minute was found 39(97.5%) in group B and not found in group F. The difference was not statistically significant (p>0.05) between two groups. Badheka et al.[7] the mean APGAR score was found 8.5±0.5 in group B and 8.37±0.4 in group F. The difference was not statistically significant (p>0.05) between two groups. Patel et al.[8] the mean APGAR score was found 8.1±0.09 in group B and 8.3±0.3 in group F. The difference was not statistically significant (p>0.05) between two groups.

In this present study shows that in sensory block, mean onset was found 1.5±0.5 minute in group B and 1.2±0.5 minute in group F. Mean regression was found 162.1±29.0 minute in group B and 236.2±42.8 minute in group F. The difference was statistically significant (p<0.05) between two groups. In motor block, mean onset was found 5.9±1.1 minute in group B and 4.8±1.0 minute in group F. Mean regression was found 146.5±26.3 minute in group B and 204.6±41.6 minute in group F. The difference was statistically significant (p<0.05) between two groups. Badheka et al.[7] onset of sensory and motor blockade was comparable between two groups while duration of sensory and motor regression was statistically significant among the two groups-161±29 and 236±42 min in Group F and 145±25 and 204±42 min in Group B, respectively, *P* <0.05. Russell and Holmqvist[18] found 25% of patients undergoing LSCS developed sensory blocks to the cervical dermatomal region, of which 10% extended to C1 or C2 when they used fixed dose of hyperbaric bupivacaine 0.5% 2.5 ml. Harten's study results showed that 17% of the patients presented with cervical dermatomal block levels in the fixed dose group and only 4.5% of the patients in the adjusted dose group reported cervical dermatomal block levels.[17] Karinen et al.[10] observed sensory block was adequate for surgery in both groups.

In this study shows that mean heart rate- before spinal anesthesia, at 3 min, at 5 min, at 10 min, at 15 min, at 30 min and at 45 min were statistically significant (p<0.05) between two groups. Karinen et al.[10] observed that changes in mean maternal HR did not differ between (*P* = 0.12) or within (*P*= 0.45) groups during the study

In this study we found mean arterial pressure - before spinal anesthesia, at 3 min, at 5 min, at 10 min, at 15 min, at 30 min and at 45 min were statistically significant (p<0.05) between two groups. Badheka et al.[7] study observed that patients were hemodynamically more stable in Group F as compared to Group B. Karinen et al.[10] changes in mean maternal SAP did not differ between groups (*P*= 0.39). Mean SAP decreased to a minimum of 86 (95% CI 78–93%) of baseline, that is from 127 (122–132) to 109 (98–119) mmHg (*P*= 0.002) in the fractionated-dose group and to 85 (79–92%), that is from 128 (123–134) to 106 (98–114) mmHg (*P*= 0.001) in the single-dose group.

Limitations of the study

The study population was selected from one selected hospital in Dhaka city, so that the results of the study may not reflect the exact picture of the country. Small sample size was also a limitation of the present study. Therefore, in future further study may be under taken with large sample size.

Conclusion

In conclusion heart rate, systolic arterial pressure, diastolic arterial pressure and mean arterial pressure were significantly difference at 3 min, at 5 min, at 10 min, at 15 min, at 30 min and at 45 min between two groups.

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