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A Prospective Randomised Double-Blind Comparative Study of Bolus versus Fractionated Dose Injection in Spinal Anaesthesia for Pregnant Women undergoing elective Caesarean Section

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Abstract

Background: Elective or emergency caesarean sections are routinely done under spinal anaesthesia (SA) with bolus dose of local anaesthetic drugs. SA with bolus dose injection provides rapid onset of action but with profound hypotension and can compromise the uteroplacental blood flow which in turn may lead to foetal acid base abnormalities.In our study we hypothesised that by using low dose bupivacaine in fractionated manner to achieve the adequate anaesthesia and stable haemodynamics andcompared with bolus dose of local anaesthetic drug in SA. The following variables were observed: onset of sensory and motor blockade, Mean Arterial Pressure (MAP) Heart Rate (HR), and duration of analgesia in patients undergoing elective lower segment caesareansection (LSCS). *Methods*: This study was conducted in sixty pregnant women who are undergoing elective lower segment caesarean section (LSCS) after taking permission from the institutional ethical committee. The pregnant women were divided into two groups. Group A patients received single bolus dose of bupivacaine heavy (0.5%) and Group B received the same dose of drug Bupivacaine in fractionated dose with two third of it initially followed by remaining one third dose after 60 secs. The intraoperative haemodynamics (MAP, HR) and duration of analgesia, time of onset and regression of sensory and motor blockade were recorded and analysed with appropriate statistical analysis. *Results:* The haemodynamics were more stable in group B patients as compared to group A. The requirement of vasopressor was significantly less in group B in contrast to group A (2.40±3.1 vs 5.50±3.79). There was statistically significant ($p<0.05$) delay in the sensory and motor onset in group B. The duration of analgesia was significantly longer in group B than group A (188.97±18.80 vs 154±22.56).There was no significant difference in the Apgar scores between the two groups ($p>0.05$). *Conclusion:* Fractionated dose of local anaesthetic drug in SA provided more haemodynamic stability and longer duration of analgesia compared to the bolus dose of local anaesthetic drug.

Keywords: SA; LSCS; Dose Fractionation; Hypotension; Analgesia.

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Introduction

Spinal anaesthesia is the most preferred anaesthetic technique for both elective and emergency lower segment caesarean section (LSCS). The most common side effect observed in these cases is hypotension which has profound effect on maternal and neonatal morbidity [1]. The various measures like low dose bupivacaine, prophylactic use of vasopressors, left uterine displacement, preloading or co-loading of crystalloids or colloids are being used to prevent maternal hypotension but with little success [2,3,4].

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Several factors like height, weight, pregnancy and anatomical changes influence the dose of local anaesthetic drug for its intensity and duration of spinal block [5]. Bhadeka Jigisha et al. [6] compared the fractionated dose with bolus dose in SA for haemodynamic stability and duration of analgesia in patients undergoing elective LSCS. In the study of Bhadeka Jigisha et al. [6] two thirds of the total dose of injection bupivacaine heavy (0.5%) was given initially followed by one third dose after 90 secs, while Bina Patel et al. [7] administered one half of the total calculated dose after 90 secs in sitting position and both concluded that there was greater haemodynamic stability, dense block and longer duration of analgesia in the fractionated dose of injection of SA. In another study after spinal injection patient was made to sit for another 30 secs before making supine and observed a slow predicted and desired level of analgesia in elderly patients [8]. We have contemplated a prospective randomised double blind comparative study with bolus vs fractionated dose by giving two thirds of the dose initially and then one third dose after 60 secs by using Bupivacaine heavy 0.5% 2 cc to observe the onset of sensory and motor blockade, MAP, HR, Apgar score and duration of analgesia in pregnantwomen undergoing elective LSCS.

Materials and Methods

The present study was carried out in sixty pregnantwomen (thirty in each group) from April 2016 to December 2017 in MRMCW (Malla Reddy Medical College for Women) after the Institutional ethics committee approval and written informed consent.

Study Population

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, because the haemodynamic parameters were recorded repeatedly during our study at 12 levels. Total sample size was 54, however because of possibility of dropout cases we have taken total of 60 cases (30 in each group).

The women included were of American Society of Anaesthesiologists' (ASA) physical status I–II, age from 18 to 40 years, height from 145 to 170 cm, singleton pregnancies posted for elective LSCS under SA. The women with pre-existing diseases, pregnancy induced hypertension, cardiovascular, cerebrovascular disease, any contraindication to SA, weighing <50 kg or >110 kg, taller than 170 cm or shorter than 140 cm, severely altered mental status, unco-operative patients, spine deformities and history of laminectomy were excluded from the study.

Randomisation Procedure

The patients were randomly divided into two groups using computer generated sequential number placed in sealed envelopes and opened only before the commencement of 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.

Study Procedure

All the women were premedicated with pantoprazole 40 mgIV. Standard monitors such as electrocardiogram (ECG), pulse oximeter (SpO_2) and non-invasive blood pressure (NIBP) were attached to the patient, and baseline blood pressure and heart rate (HR) were recorded. Intravenous (IV) line was started with 18-gauge IV cannula and preloaded with 10–15 ml/kg Ringer's lactate (RL) solution over period of 10 min.

SA was given in sitting position with 25gauge Quincke spinal needle in L3–L4 or L4–L5 interspace. After free flow of cerebrospinal fluid, 2ml of bupivacaine 0.5% heavy was injected with 5 ml syringe in all our cases according to respective groups A and B. The group A patients received a single bolus dose of bupivacaine over 10 secs. The group B patients received fractionated dose of bupivacaine with two thirds of the total calculated dose given initially followed by onethirds dose after 60 secs, both doses given at a rate of 0.2 ml/sec. The drug was injected with 5 ml syringe. After the initial twothirds of the dose, the syringe was kept in situ attached to the spinal needle for remaining 60 secs to avoid the CSF leak and then the remaining onethirds of the dose was administered. The women were turned to the supine position with a wedge under the right hip in both the groups and were supplemented with oxygen by Hudson mask at 5 L/min.

Intraoperatively, following parameters were monitored: Continuous ECG, HR, NIBP and SpO_2. The MAP and HR 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 (TB, T0,

T2, T4, T6, T8, T10, T15, T20, T25, T30, T40, T50 and T60).

Hypotension was treated when mean arterial pressure (MAP) decreased ≤ 20% of baseline with injection mephentarmine 5 mg given IV and repeated whenever needed. Hypotensive episodes and mephentarmine used were recorded for each patient. HR of < 50 beats/min was considered as bradycardia and treated with IV atropine 0.6 mg.

We assessed and recorded time of onset, level and regression of motor and sensory block. The confirmation of sensory block was assessed by loss of sensation to pinprick. Motor blockage was assessed by a modified Bromage scale. These tests were performed every 5 min till the achievement of maximum sensory and motor block (Bromage scale 3) and every 30 min postoperatively until the sensory and motor variables were back to normal. 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 reached the T8 dermatome level bilaterally and when Bromage scale of three was achieved. Patients with inadequate sensory blockade and requiring conversion to general anaesthesia were excluded from the study.

After delivery, we administered IV oxytocin 5 IU IV slowly and 15 IU in 500 ml RL. The incidence of nausea, vomiting, respiratory distress, shivering, pruritus, urinary retention was noted for 24 h postoperatively and treated accordingly. The attending paediatrician assessed Apgar scores at 1 and 5 min.

The duration of sensory blockade was defined as the interval from intrathecal administration of local anaesthetic to S2 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 scale zero (0).

Modified Bromage scale was used to assess motor block:

1. Grade 0 – No motor block.
2. Grade 1 – Inability to raise an extended leg, able to move knees and feet
3. Grade 2 – Inability to raise an extended leg, able to move knees but able to move feet.
4. Grade 3 – Complete motor block of lower limb.

Pain was assessed with the linear visual analogue scale (VAS) every 30 min postoperatively for the first 2 hrs afterwards hourly up to 6 hrs. The duration of analgesia was defined as the time from intrathecal injection till the first demand for rescue analgesic when VAS was ≥ 4. The patient was given diclofenac sodium 75 mg intramuscular as rescue analgesic.

Visual Analog Score (VAS), (0 to 10 cm where 0= no pain and 10= worst pain ever felt).

Statistical analysis

The normality distribution of the data was confirmed by Kolmogorov-Smirnov test. The continuous data was displayed by mean and standard deviation and discretedata as Median and interquartile range (IQR).

As all the assumptions of T-test & ANOVA were accomplished, Student t test used to compare the continuous data of the two groups and ANOVA (repeated measures) was performed for haemodynamic parameters, followed by Tukey-Kramer multiple comparison analysis. The discrete data Apgar score was compared by using Mann-Whitney U test. The chi-square test was performed for categorical data. The p value of < 0.05 was considered as significant.

Results

Demographic variables age, height and weight were comparable between the two groups (Table 1).

Table 1: Demographic variables

Demographic variables	Mean±SD Group A	Mean±SD Group B	p values
Age (yrs)	24.10±3.61	24.60±3.44	0.5852
Height(cms)	156.73±4.88	155.87±5.77	0.5325
Weight(kg)	61.97±8.45	60.63±8.44	0.5474

HR was statistically significant at T6, T8, T10, 15, T20, T25 minutes between the two groups ($p< 0.05$) (Table 2), however there was no statistically significant difference in MAP between the two groups (Table 3). (Fig. 1,2).

When analysed within the groups the haemodynamic variables in both the groups were significantly ($p<0.05$) different at all time intervals in comparison to TB and T0 levels (Figure 1,2).

The onset of sensory,motor blockade and two segment sensory regression was delayed in the study group B and this difference was statistically significant ($p<0.05$). The duration of sensory and motor regression was also significantly ($p<0.05$)

Table 2: Heart Rate (HR) in both the groups

HR (Beats/min)	Group A (Mean±SD)	Group B (Mean±SD)	p value
TB (Basal)	99.17±15.59	97.77±13.62	0.712
T0	99.40±14.41	95.93±16.03	0.382
T2	100.07±19.11	95.97±18.81	0.405
T4	95.00±17.42	101.23±19.82	0.200
T6	87.80± 17.42	98.10±23.07	0.009*
T8	80.77±15.71	95.87±23.07	0.004*
T10	84.73±15.83	95.67±19.21	0.019 *
T15	86.83±18.54	98.87±16.35	0.009*
T20	90.37±13.31	98.67±14.50	0.025*
T25	92.17±13.56	101.00±15.18	0.021*
T30	92.87±16.73	100.03±13.40	0.072
T40	91.23±14.21	96.33±10.99	0.125
T50	88.50±11.96	93.97±10.59	0.065
T60	85.87±9.81	91.30±11.36	0.522

Note: * statistically significant.

Table 3: Mean Blood Pressure (MAP) in both the groups

MAP (mmHg)	Group A (Mean±SD)	Group B (Mean±SD)	p value
TB (Basal)	84.90±9.58	86.50±10.06	0.530
T0	83.53±12.65	85.80±12.31	0.485
T2	74.43±17.14	79.13±12.11	0.225
T4	68.63±16.34	71.30±14.07	0.501
T6	68.03±13.67	70.73±11.80	0.416
T8	71.50±13.24	70.97±11.96	0.871
T10	74.27±13.23	71.13±11.67	0.335
T15	71.83±12.55	68.61±10.24	0.276
T20	70.83±12.67	69.70±10.62	0.708
T25	71.37±12.38	67.37±11.58	0.201
T30	71.27±10.72	66.23±11.29	0.082
T40	71.70±9.87	71.13±9.67	0.823
T50	74.87±10.23	75.07±9.87	0.939
T60	75.93±9.22	73.80±8.10	0.347

Note: * statistically significant

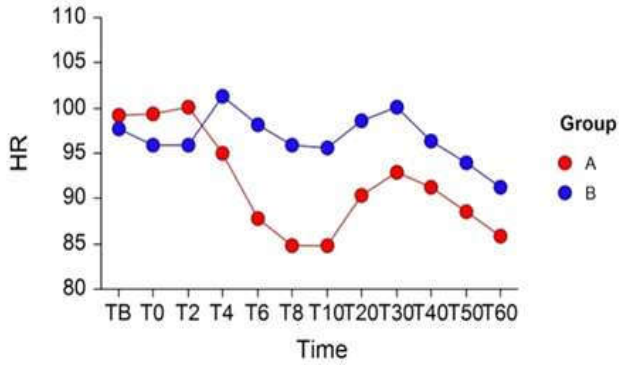

Fig. 1: Depicting the mean Heart Rate (HR) in both the groups

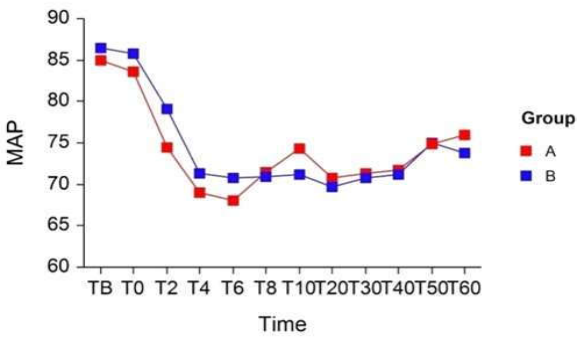

Fig. 2: Depicting the mean Arterial Pressure (MAP) in both the groups

Table 4: Showing different variables in both the groups

Variables in mins (Mean±SD)	Group A	Group B	P value
Onset of sensory block	2.50±0.68	4.00±1.41	0.0001*
Onset of motor blockade	4.97±1.59	7.23±2.50	0.0001*
Two segment sensory regression	97.13±24.85	74.43±19.68	0.0002*
Duration of motor block	180.oo±26.73	204.67±21.81	0.0002*
Duration of analgesia	154±22.56	188.97±18.80	0.0001*
Apgar Score(IQR)	8±1	8.5±10	0.199
Mephenteramine used(mg)	5.50±3.79	2.40±3.1	0.0010*

Note: * statistically significant.

prolonged in group B. There was no statistically significant difference in the Apgar scores between the two groups ($p>0.05$). The requirement of mephenteramine which was used as rescuedrug to control blood pressure was significantly ($p<0.05$) different in between the groups and more in group A (Table 3).

Quality of sensory and motor blockade were comparable in both the groups with no rescue analgesic requirement. The adverse effects like nausea, vomiting and shivering monitored intra and post operatively were comparable in both the groups.

Discussion

Even though spinal anaesthesia is the most preferred, safe and economical anaesthetic technique for both elective and emergency lower segment caesarean section (LSCS), the most common side effect like hypotension, maternal and neonatal morbidity [1] are not successfully reduced. The following measures were used to prevent maternal hypotension: low dose bupivacaine, prophylactic use of vasopressors, left uterine displacement, preloading or co-loading of crystalloids or colloids are but of little success [2,3,4]. The incidence of hypotension is reported to be approximately 90% of cases, if preventive measures are not taken [2,9].

Several factors like height, weight, pregnancy and anatomical changes influence the dose of local anaesthetic drug for its intensity and duration of the block.In the study conducted by Danelli et al. [5] dose of 0.5% hyperbaric bupivacaine in relation to patient's height was used; they concluded that a dose as low as 0.06 mg/cm height represents the dose of intrathecal bupivacaine providing effective spinal block in 95% of women undergoing elective caesarean section. Many studies were published to reduce the height of sensory block and hypotension using opioid as additives to the local anaesthetics for SA. Himabindu et al. [10] used fentanyl as additive to LA and concluded that there is faster onset of sensory blockade with haemodynamic stability and prolonged duration analgesia.

BadhekaJigisha et al. [6] compared fractionated dose with bolus dose in SA for patients undergoing elective LSCS. In their study, fractionated dose with twothirds of the total dose of injection bupivacaine heavy (0.5%) was given initially followed by onethird dose after 90 sec. Where as in the study by Bina Patel et al. [7] in PIH patients, one half of the total calculated dosewas given initially and the remaining half dose was administered after 90 secs in sitting position and both concluded that there was greater haemodynamic stability, dense block and longer duration of analgesia in the fractionated dose of injection of SA. In another study after spinal injection patient was made to sit for 30 seconds before making supine and observed that slow predicted and desired level of analgesia was obtained in elderly patients [8]. As the waiting times after SA are different in different studies [6,7] we have waited 60 seconds after giving the initial twothirds of the total calculated dose and then the remaining onethird dose was given. We observed onset of sensory and motor blockade, haemodynamics, Apgar score and duration of analgesia in patients undergoing elective LSCS.

Our study results are comparable to the study of Bhadeka Jigisha et al.[6] in providing stable HR in the fractionated dose group. However, there was no significant change in MAP in our study in both the groups, probably because the BP was maintained with the use of mephenteramine.

Fahmy et al. [11] compared the circulatory and anaesthetic effects of bolus versus fractionated administration of bupivacaine and concluded that when the same dose of bupivacaine is administered in a fractionated manner, it is associated with lesser degree of hypotension. Our study is inagreement with the study of Bina Patel et al. [7] who observed more stable haemodynamics and less vasopressors requirement with fractionated dose SA as compared to the single bolus use of SA in LSCS. Favarel et al. [12]

in his study on titrated dose of Bupivacaine studied a randomised trial in 60 patients undergoing hip fracture surgery and concluded that was safer, more efûcient and provide better cardiovascular stability than a single bolus dose.

Our study results are in concurrence with the study of Agrawal N et al. [8] who concluded that sitting position for 30 seconds after spinal anaesthesia helps to prevent high spinal and gives better haemodynamic stability.

In our study, there was delay in the onset of both sensory and motor block in the fractionated dose of SA and is same as the study of Agrawal N et al.[8] Essam E et al. [13] also observed faster onset of spinal anaesthesia in patients who were made supine immediately after subarachnoid block as compared to who were kept sitting for 30 secs. The above study results in concurrence with our study results. There was early onset of both sensory and motor blockade in the fractionated group as compared to bolus group in studies conducted by BhadekaJigisha et al[6] and Bina Patel et al. [8] which contradicts our study results. The fractionated dose of Bupivacaine prolonged the duration of sensory and motor blockade in the study of Fahmy and colleagues [10] and this is inagreement with our study. Similarly, our study results are in concurrence with the studies of Bhadeka Jigisha et al. [6] and Bina Patel et al. [9] with regard to prolonged duration of analgesia.

Apgar scores were slightly better in the group B in comparison to the conventional method group but not statistically significant and these results are similarto the study results of Bhadeka Jigisha et al.[6] and Bina Patel et al.[7].

Conclusion

Even slight alteration in the spinal anaesthetic technique, by giving the calculated dose in fractionated manner as compared to the bolus injection can give better outcome in patients undergoing elective LSCS. High spinal block and sudden hypotension can be prevented by using this method. This makes the fractionated dose method as an acceptable and safe alternative technique in LSCS.

Acknowledgement

Nil

Conflict of Interest

Nil

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