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COMPARISON OF BOLUS DOSE VERSUS FRACTIONATED DOSE OF INJECTION BUPIVACAINE HEAVY (0.5%) IN SPINAL ANAESTHESIA FOR PATIENTS UNDERGOING EMERGENCY CAESAREAN SECTION: A RANDOMISED STUDY

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ABSTRACT

Background and Aims: Bolus dose of spinal anaesthesia (SA) has rapid onset but precipitate hypotension, whereas fractionated dose of local anaesthetic with a time gap provides a dense block, maintains hemodynamic stability with prolonged prolonged duration of analgesia. We compared fractionated dose with bolus dose in SA for haemodynamic stability and duration of analgesia in patients undergoing emergency lower segment caesarean section (LSCS).

Methods: After clearance from the Institutional Ethics Committee, study was carried out in sixty patients undergoing emergency LSCS and patients were divided into two groups, GROUP B and GROUP F. Group B received single bolus dose of bupivacaine heavy (0.5%) and Group F fractionated dose of bupivacaine heavy (0.5%) with two-third of the total dose given initially followed by one-third dose after 90 sec. Student's unpaired t-test was used to analyse Time of onset and regression of sensory and motor blockage, intraoperative haemodynamics and duration of analgesia.

Result: All the patients were haemodynamically stable in Group F as compared to Group B. Four patients in Group F and thirteen patients in Group B required vasopressor. Duration of sensory and motor block and duration of analgesia were longer in Group F (278.83 ± 20.67 min) compared to Group B (236.5 ± 31.92 min) $P < 0.05$.

Conclusion: Fractionated dose of bupivacaine in spinal anaesthesia provides greater hemodynamic stability and longer duration of analgesia compared to bolus dose.

KEYWORDS : Spinal anaesthesia, dose fractionation, bolus dose, hypotension.

INTRODUCTION

Bupivacaine is routinely used in spinal anaesthesia for both elective and emergency caesarean section. Though SA has a rapid onset but it precipitates hypotension at the same time. Maternal hypotension may decrease uteroplacental perfusion resulting in foetal acid-base abnormalities.[1]

There are various measures to prevent maternal hypotension such as preloading with fluids either colloids or crystalloids before SA, prophylactic administration of vasopressor and left uterine displacement.

When no preventive measures are taken to reduce hypotension, the incidence of hypotension is reported to be 92%–94%. [2, 3]Dose of hyperbaric bupivacaine is decided depending on factors such as weight, height, anatomy of spine and pregnancy for its intensity and duration of the spinal block. The study done by Danelli *et al*.[4] showed that 0.06 mg/cm height is the minimum effective dose of intrathecal bupivacaine which provides effective spinal block in 95% of the women undergoing caesarean section.

Bolus dose of local anaesthetic agent in SA causes more hypotension whereas fractionated dose in which two-third of the total calculated dose given initially followed by one-third dose after a time gap of 90 sec, achieves adequate SA and provides a dense block with haemodynamic stability. There are no studies available which compared these two techniques in pregnant patients for emergency LSCS. Through this prospective, randomised, double-blind study we aimed to compare fractionated dose versus bolus dose of bupivacaine heavy (0.5%) in SA for haemodynamic stability and duration of analgesia in patients undergoing emergency lower segment caesarean section (LSCS). We also compared the characteristics of sensory and motor block.

METHODS

After the approval from Institutional Ethics Committee and written informed consent, this study was carried out on sixty female patients (thirty in each group) of the American Society of Anaesthesiologists physical status I–III, age from 20 to 40 years, height from 140 to 170 cm, singleton pregnancies scheduled for emergency LSCS under SA. Patients with pre-existing diseases or pregnancy induced hypertension, cardiovascular or cerebrovascular disease, any contraindication to SA, those weighing <50 kg or >110 kg and those taller than 170 cm or shorter than 140 cm and severely altered mental status, spine deformities or history of laminectomy were excluded from the study.

Standard monitors including non-invasive blood pressure (NIBP), electrocardiogram (ECG) and pulse oximeter (SpO2) were attached to the patient; baseline blood pressure and heart rate (HR) were recorded. Intravenous (IV) line was taken with 18-gauge IV cannula and patients were premedicated with ranitidine 1 mg/kg and ondansetron 0.1 mg/kg IV. The patients were preloaded with Ringer's lactate (RL) solution 10–15 ml/kg over 10 min.

SA was administered in sitting position with 23-gauge Quincke spinal needle in L3–L4 or L4–L5 interspace after infiltrating skin with 2% lignocaine (2 ml). After aspiration of CSF, injection bupivacaine heavy 0.5% was injected according to respective groups, B and F. Total dose of SA was calculated as 0.07 mg/cm of the height of the patient. The patients were randomly divided into two groups. Group B patients received a single bolus dose of bupivacaine over 10 sec at a rate of 0.2 ml/sec. Group F patients received fractionated dose of bupivacaine with two-third of the total calculated dose given initially followed by one-third dose after 90 s, both doses given at a rate of 0.2 ml/s. Syringe was kept attached to the spinal needle for remaining 90 s after injection of initial two-third dose, after which remaining one-third dose was administered.

Group B patients were kept sitting for 90 s after completion of the subarachnoid injection, to prevent observer's bias. With a wedge under the right hip, patients were turned into the supine position in both groups. Oxygen supplemented with Hudson's mask at 3 L/min.

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 conducted in a double-blind fashion such that the patient and the assessor were unaware of the group. The assessor was kept blinded during the administration of the drug. Only the attending consultant administering the SA knew the group allocation.

Time of onset, level and regression of motor and sensory block were assessed and recorded. Sensory block was assessed and confirmed by loss of sensation to pinprick. Modified Bromage scale was used to assess motor blockage. These tests were performed every 5 min till the achievement of maximum sensory and motor block (Bromage scale 3) and every 30 min post operatively 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.

When loss of pinprick sensation reached the T6 dermatome level bilaterally and when Bromage scale of three was achieved, surgical incision was allowed. Patients with inadequate sensory blockade and requiring conversion to general anaesthesia were excluded from the study.Intra operatively, patients were continuously monitored with ECG, HR, NIBP and SpO2. Hypotension was treated when mean arterial pressure (MAP) decreased ≤ 20% of baseline with injection mephentermine 5 mg given IV and repeated when needed. The number of hypotensive episodes and mephentermine used were recorded for each patient. Bradycardia (HR of < 60 beats/min), if present was treated with IV atropine 0.6 mg.

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 scales zero (0)*. Pain assessed using linear visual analogue scale (VAS) every 30 min post operatively for the first 2 h then hourly up to 6 h. 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.

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

All the observations were recorded and results were analysed statistically using Microsoft Excel 2007. Qualitative data like age and maximum dermatome achieved were analysed statistically using Chi-square test. Quantitative data were presented as mean ± standard deviation (SD) and analysed using the unpaired *t*-test. $P < 0.05$ was considered statistically significant.Sample size calculation was based on the pilot study, considering the difference in MAP changes of 6 mmHg after 15 min of SA. With an α-error of 0.05 and power of study 90%, the sample size came to 28. We enrolled thirty patients in each group considering the drop outs.

RESULTS

Both groups were comparable in their demographic profiles [Table 1].

Table 1: Demographic variable and operative data

Demographic Profile	Mean ± SD		*P* value
	Group B	Group F	
Age (years)	27.63 ± 3.2	26.26 ± 3.1	> 0.05
Height (cms)	153.87 ± 4.31	152.9 ± 5.31	0.2
Weight (kg)	66.63 ± 7.79	65.13 ± 7.37	0.3
Duration of surgery (min)	50.5 ± 12.12	51 ± 11.57	0.1
Gestational age (weeks)	34.9 ± 1.44	35.1 ± 1.29	0.6
Apgar score	8.5 ± 0.5	8.37 ± 0.4	0.1
Dose (ml)	2.14 (2-2.4)	2.2 (2-2.6)	0.7
Intervertebral space chosen for sub arachnoid block (%)			
L3-L4	55.33	50	
L4-L5	45.67	50	

SD- Standard Deviation

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- 160 ± 29 and 235 ± 42 min in Group F and 144 ± 25 and 203 ± 42 min in Group B, respectively, $P < 0.05$ [Table 2].

Table 2: Characteristics of sensory and motor block

Characteristics of block	Mean ± SD		*P* value
	Group B	Group F	
Sensory Block			
Onset in mins	1.4 ± 0.509	1.29 ± 0.5	0.076
Peak level of block in mins	5.57 ± 1.72	6.16 ± 1.25	0.08
Regression in mins	160 ± 29	235 ± 42	0.000014
Motor Block			
Onset in mins	5.767 ± 1.13	4.666 ± 1.074	0.000031*
Regression in mins	144 ± 25	203 ± 42	0.00006*

*$P \leq 0.05$ is significant
SD- Standard Deviation

Patients were haemodynamically more stable in Group F as compared to Group B [Figure 1].

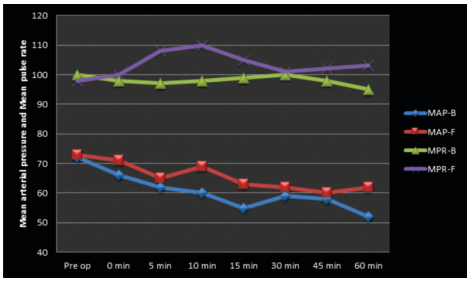

Figure 1: Intraoperative haemodynamic changes

4 patients (13.33%) in Group F and 13 patients (43.33%) in Group B required vasopressor [$P = 0.013$, Figure 2].

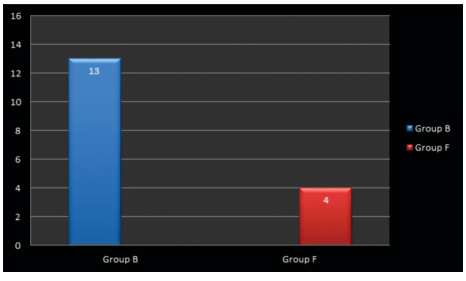

Figure 2: No. of patients requiring intraoperative vasopressor [$P = 0.013$]

Figure 3 shows a longer duration of analgesia with Group F as compared to Group B [$P < 0.001$].

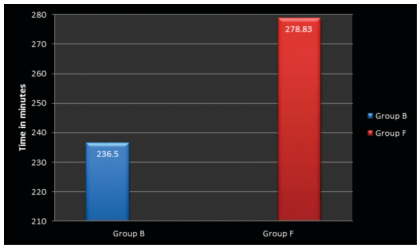

Figure 3: Duration of analgesia in minutes [$P < 0.001$]

In Group B, one patient developed nausea and vomiting and one developed hypotension. One patient in each of the Groups B and F complained of shivering. Dryness of mouth, pruritus, sedation, respiratory depression, bradycardia and headache were not seen in any of the patients in both groups.

DISCUSSION

There has been a rapid rise in the incidence of caesarean section deliveries.With unadjusted doses of local anaesthetic agents in SA, maternal hypotension and high spinal blockade are a common occurrence. Most common complication of 0.5% hyperbaric bupivacaine between dosage of 12 and 15 mg is maternal hypotension. High SA has been reported with doses larger than 12 mg of bupivacaine in patients undergoing caesarean section. [5, 6] Neonatal outcome depends on the maintenance of normal maternal blood pressure. A national survey done in United Kingdom revealed that various dosage regimens have been used for caesarean section. [7]

In our study, we compared bolus dose versus fractionated dose of hyperbaric bupivacaine 0.5% in SA for haemodynamic stability and duration of analgesia in patients undergoing emergency LSCS. Clinical studies have shown that weight [8] and height [4] are significant variables in predicting the final level of the block. Some studies used a fixed dosage regimen while others used the dose of bupivacaine as per patient's characteristics. *Harten* compared the effects of fixed as well as adjusted dose and concluded that successful SA for caesarean section has been associated with a low incidence of hypotension with dosage regimen adjusted for height and weight. [9]

Schnider et al. [10] 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. [11] When same dose of local anaesthetic is used in both obese and a non-obese pregnant woman then it is more difficult to predict the extension of the blockade. A retrospective study done on pregnant women with obesity class 3, shows a higher percentage of hypotension, 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. [12] The need of local anaesthetic in SA is lower in pregnant patients. Mechanisms suggested for this include pregnancy- specific hormonal changes, which affect the action of neurotransmitters in the spinal column, increased permeability of neural membranes and other pharmac okinetic and pharmacodynamic changes. [13,14]

Danelli *et al.* [4] conducted a study with dose of 0.5% hyperbaric bupivacaine in relation to patients height was used; which 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. Similarly, we considered only height as a predictor for calculating the dose of bupivacaine. We conducted pilot studies of five cases with bupivacaine 0.06 mg/cm of height, but the adequate sensory level was not achieved. Hence, we used the dosage of 0.07 mg/cm height in our study.

In our study, Group B received a mean (range) dose of 2.14 (2–2.4) ml whereas Group F received a mean (range) dose of 2.2 (2–2.6) ml which were comparable among the two groups. These doses are comparable to the fixed dose used in the study done by Harten *et al.* [9] Furthermore, a survey in the United Kingdom showed that the mean (SD) volume of bupivacaine 0.5% with a fixed dosage scheme is 2.57 ml, whereas a mean volume of 2.34 ml with minimum volume ranges of 1.2–3.0 ml is given with a variable dose scheme. [7]

As shown in Table 2, we did not observe sensory blockade above T4 level in either groups. Russell and Holmqvist [15] found that of all the patients undergoing LSCS, 25% 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. [9] The study suggested that adjusting the dose to height and weight increases the safety margin of SA.

Fahmy [16] compared the circulatory and anaesthetic effects of bolus versus fractionated administration of bupivacaine and found that fractionated dose prolonged the duration of action with more circulatory stability. He also observed prolonged duration of sensory and motor blockade and lesser degree of hypotension when the same dose of bupivacaine is administered in a fractionated manner. Favarel *et al.* studied sixty elderly patients undergoing surgery for hip fracture for haemodynamic tolerance of titrated doses of bupivacaine versus single dose SA and concluded that titrated doses of bupivacaine was safe, efficient and provided better haemodynamic stability than single dose SA. [17] The results of above studies were comparable with ours.We used injection mephentermine to control maternal blood pressure during caesarean section. Bhardwaj *et al.* [18] compared the ephedrine, phenylephrine and mephentermine for control of maternal blood pressure during caesarean section and concluded that all three were equally effective in maintaining maternal blood pressure as well as umbilical pH during SA for caesarean section.

In our study, when single bolus dose of 0.5% bupivacaine heavy was used, degree of hypotension was more. However, fractionated dose produced a longer duration of surgical analgesia with a minimal requirement of vasopressors and no undesired side effects such as hypotension. Apgar scores were almost similar in both groups in our study.The limitations of our study was that we had assessed neonatal outcome by Apgar score only and not umbilical cord blood gas values and pH or uteroplacental blood flow. Hence, no comments could be added further on uteroplacental perfusion.
To evaluate the effectiveness of fractionated dose in maintaining hemodynamic stability further studies and research can be done for comparing bolus and fractionated dose in pregnancy induced hypertension and gestational hypertension patients undergoing LSCS.

CONCLUSION

Fractionated dose of hyperbaric bupivacaine 0.5% provides greater hemodynamic stability and prolonged duration of analgesia compared to bolus dose in patients undergoing emergency caesarean section. To prevent sudden hypotension, fractionated dose of hyperbaric bupivacaine 0.5% is an acceptable and safe alternative in LSCS.

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CONFLICTS OF INTEREST

There are no conflicts of interest.

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