



COMPARISON OF FRACTIONATED VERSUS BOLUS DOSE OF BUPIVACAINE IN SPINAL ANAESTHESIA FOR PATIENTS WITH PIH UNDERGOING ELECTIVE CAESAREAN SECTION.

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ABSTRACT **Introduction:** In this study we compared the effects of fractionated versus bolus dose of local anaesthetics in spinal anaesthesia for hemodynamic stability, characteristic of sensory and motor block and duration of analgesia in preeclamptic parturients.

Methods: 60 patients were divided into two groups (30 in each). Group B patients received bolus dose of local anaesthetics, while group F patients received fractionated dose of local anaesthetics. Characteristic of sensory and motor block, duration of analgesia and hemodynamic stability were compared.

Result: All the patients were haemodynamically stable in Group F as compared to Group B. Duration of sensory and motor block and duration of analgesia were longer in Group F as compared to Group B.

Conclusion: Fractionated dose of spinal anaesthesia provides dense block, greater haemodynamic stability, and longer duration of analgesia as compared to bolus dose.

KEYWORDS : spinal anaesthesia, preeclampsia, caesarean section, fractionated dose, Bupivacaine

INTRODUCTION

Hypertensive disorder of gestation, complicating 5% to 7% of all pregnancies to severe preeclampsia or eclampsia and increases morbidity to both mother and fetus. The administration of general anaesthesia (GA) in such high risk parturients may cause exaggerated cardiovascular response to laryngoscopy leading to intracranial haemorrhage and cerebral edema, cardiovascular decompensation causing pulmonary edema.[20] Similarly, an exaggerated pressor response to intubation may increase the maternal plasma catecholamine concentration, which in turn constricts the placental vessels and impairs the uteroplacental blood flow.[9,22] The administration of regional anaesthesia (RA) not only avoids the maternal complications with GA like difficult intubation, vasopressor response to intubation, but also maintain uteroplacental blood flow if hypotensive episodes are prevented and improve neonatal outcome.[12,13]

Spinal anaesthesia is the preferred technique for both elective and emergency caesarean section. SA using Bupivacaine has rapid onset of action, but it may precipitate hypotension. Patients with history of PIH (pregnancy induced hypertension) are more prone to severe maternal hypotension. Maternal hypotension may compromise uteroplacental perfusion can lead to fetal acid base abnormalities.[3]

Various measures like preloading with colloids and crystalloids, administration of vasopressor and left uterine displacement using wedge are taken to prevent hypotension. The incidence of hypotension is reported in approximately 90 % of cases, if no preventive measures are taken. [15,17]

Study done by Badhoka [2] et al showed that there are higher chances of hypotension with bolus dose of LA as compared to fractionated dose of LA. They observed that fractionated dose of the local anesthetic agent, in which two-third of the total calculated dose given initially followed by one-third dose after a time gap of 90 s, achieves adequate SA and provides a dense block with better haemodynamic stability.

In this study we compared the effect of fractionated versus bolus dose of LA in spinal anaesthesia for hemodynamic stability, characteristic of sensory and motor block and duration of analgesia in patients with history of mild to moderate PIH.

MATERIALS AND METHODS

After approval from institutional ethical committee and written informed consent, this study was conducted on 60 patients of American society of Anaesthesiologist Physical Status I to III, age from 18-40 yrs, height from 140-170 cm, singleton full term pregnancy with h/o mild to moderate PIH in our tertiary care centre. Patient with any cardiovascular or cerebrovascular disease, severe PIH, any contraindication to spinal anaesthesia, those weighing <45Kg or >100Kg, spinal deformity or h/o spinal surgery were excluded from study.

We calculated sample size using open EPI software based on pilot study, considering difference in MAP changes of 10mm Hg after 15 min of SA, with an error of 0.05 and power of the study 80% ,sample size was 60(30 in each group). Patients were randomly divided into two groups, using table of randomisation.

In anaesthesia pre check up room, 18G IV cannula was secured. After checking vitals, patients were premedicated with Inj. Glycopyrrolate 0.2 mg and Inj Ondansetron 0.1mg/kg IV, inj Ranitidine 150 mg . Preloading was done using Ringer lactate solution 10-15ml/kg over 15 min. Then patient were shifted to operation theatre. In OT, standard monitoring using non-invasive blood pressure (NIBP), pulse oximeter, ECG were applied and baseline pulse rate and BP were recorded.

Spinal anaesthesia was given in L2-L3 or L3-L4 intervertebral space with 25G spinal needle, after negative aspiration of clear and free CSF, inj Bupivacaine heavy (0.5%) was administered intrathecaly at the rate of 0.2ml/sec according to respective groups B and F. Total dose of LA was calculated as 0.07mg/cm of patients height in both the groups. Group B patients received bolus dose of LA while Group F received fractionated dose of Bupivacaine with one half of the total calculated dose given initially, then syringe was kept attach with spinal needle and patients were kept in sitting position for 90 secs, then remaining half dose was administered. Pt was kept in sitting position for 90 sec after bolus dose of Bupivacaine in group B to prevent observer's bias. Patients were turned to supine position and wedge was applied at right hip. We supplemented O₂ with ventimask at rate of 4 L/min.

Time of onset, peak level and regression of sensory and motor blockade were recorded and assessed. Sensory block was assessed by

pin prick method and motor block was assessed by modified Bromage scale. Assessment was done for every 2min till maximum sensory and motor blockade achieved and every 30 min postoperatively till sensory and motor block effect normalises. The time of onset for sensory and motor blockade were defined as interval between intrathecal administration and time to achieve T10 block height or modified Bromage scale 3 respectively. Surgery was started after achievement of T6 sensory level and Modified Bromage scale 3. Patients who required general anaesthesia or inadequate sensory blockade were excluded from study.

Intraoperatively HR, NIBP, Spo2 were continuously monitored. Hypotension was treated with inj Ephedrine 5mg iv when mean arterial pressure decreased $\geq 30\%$ of baseline and repeated as required. Bradycardia, HR <60 /min was treated with inj Atropine 0.6mg iv. Total number of hypotensive episodes were recorded. After delivery, we administered inj Carboprost 200ug IM and inj Oxytocine 20IU diluted in 500ml RL slowly. Attending paediatrician assessed APGAR at 1 and 5 min. Incidence of nausea, vomiting, pruritus, urinary retention were noted.

Duration of sensory block was defined as interval between intrathecal administration of LA to S2 segment regression. Duration of motor blockade was defined as intrathecal administration of LA to achievement of modified Bromage scale 0. We assessed post-operative pain by Visual analogue scale every 30 min for 2 hour and every hourly for 6 hrs. Patients were given inj Diclofenac sodium 75mg IM when VAS ≥ 4 . Duration of analgesia was defined as time from intrathecal injection to first requirement of rescue analgesia.

All observation were recorded and results were analysed using Open Epi software. Quantitative data were presented as mean \pm sd and analysed using unpaired t test while Qualitative data were assessed using Chi square test. $P < 0.05$ was considered statistically significant.

RESULTS

Demographic profile was comparable in both the groups (table 1) Onset of sensory and motor blockade was statistically significant among two groups - 1.44 \pm 0.12 (group B) and 1.27 \pm 0.19 (group F) and 5.36 \pm 0.79 (group B) and 4.55 \pm 0.52 (group F), respectively. Duration of sensory and motor regression was statistically significant among two groups- 176 \pm 14 (group B) and 216 \pm 18 (group F) and 130 \pm 11 (group B) and 155 \pm 15 (group F), respectively. (table 2)

Patients were haemodynamically more stable in Group F as compared to Group B [Figure 1]. Four patients (13.33%) in Group F and 11 patients (36.66%) in Group B required vasopressor [$P = 0.03$]. Duration of analgesia was longer in Group F (200 \pm 20) as compared to Group B (160 \pm 27) [$P < 0.000$].

Four patients in Group B and two patients in group F developed nausea and vomiting. One patient in each of the Group developed shivering. None of the patients developed dryness of mouth, pruritus, sedation, respiratory depression, bradycardia and headache in both the groups.

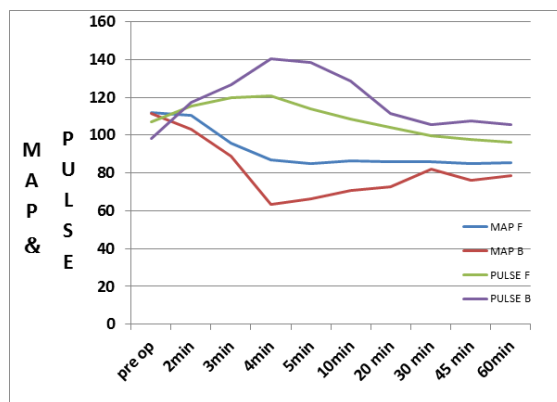
Table 1 (demographic profile)

DEMOGRAPHIC PROFILE	MEAN \pm SD		P value
	Group B	Group F	
Age (years)	24.63 \pm 3.65	25.33 \pm 3.07	0.42
Height (cm)	154 \pm 3.81	154.63 \pm 3.42	0.99
Weight (kg)	58.5 \pm 7.89	56.93 \pm 6.19	0.39
Duration of surgery (min)	55.16 \pm 3.35	54.9 \pm 4.24	0.79
Gestational age (weeks)	36.4 \pm 1.06	36.6 \pm 1.4	0.7
Dose (ml)	2.15 \pm 0.05	2.16 \pm 0.04	0.39
APGAR score	8.1 \pm 0.09	8.3 \pm 0.3	0.12

Table 2 (characteristics of sensory and motor block)

	MEAN \pm SD		P value
	Group B	Group F	
Sensory block			
Onset in minutes	1.44 \pm 0.12	1.27 \pm 0.19	0.000
Peak level of block in minutes	5.53 \pm 0.71	6.63 \pm 0.72	0.000
Regression in minutes	176 \pm 14	216 \pm 18	0.000
Motor block			
Onset in minutes	5.36 \pm 0.79	4.55 \pm 0.52	0.000
Regression in minutes	130 \pm 11	155 \pm 15	0.000

Figure 1 (intra operative hemodynamic changes)



DISCUSSION

In pregnancy induced hypertension, there is an abnormal trophoblastic invasion of the maternal spiral arteries, leads to impaired uteroplacental perfusion. Vasoconstriction and maternal hypertension occur due to release of vasoactive factors into the maternal circulation and endothelial dysfunction.[16,20] The sympathetic blockade that result from neuraxial anesthetic technique for LSCS, reduces serum catecholamine levels, decreases uteroplacental resistance and improves intervillous blood flow in pre-ecliptic parturients. These physiological effects of neuraxial blockade are potentially beneficial in hypertensive parturients. Spinal anaesthesia has no effect on APGAR score and umbilical artery pH in pre-eclampsia as long as the systolic blood pressure is maintained around 80% from baseline.

Risk-benefit profiles of spinal anaesthesia and general anaesthesia for pre-eclampsia strongly favour the use of spinal anaesthesia when feasible. Potential complications of general anaesthesia, such as hypertensive crisis, stroke, and difficult airway management, are leading causes of morbidity and mortality in the pre-ecliptic population. In addition, exaggerated pressure response to laryngoscopy may increase maternal catecholamines and compromise uteroplacental blood flow and increase fetal acid base abnormalities. [11]

In day to day practice, number of LSCS has been rising rapidly. For spinal anaesthesia most commonly inj Bupivacaine heavy (0.5%) is used with dosage between approximately 12 to 15 mg. It has rapid onset of action but maternal hypotension and high spinal blockade are common occurrence after unadjusted dosage of LA.[5,8] Results of various clinical studies confirm that height and weight are important patient factors for deciding final level of block height. [4,14]. Harten compared the effect of two dosage regimens, fixed dose versus adjusted dose considering height and weight, and concluded that adjusted dose is associated with lower incidence of hypotension and better fetal outcome.[10]

Schnider[21] et al concluded that onset time for adequate sensory block is proportional to height of patients while inversely proportional to weight. 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.[18] 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 pharmacokinetic and pharmacodynamic changes.[1,19]

Daneli[4] et al used 0.5% hyperbaric Bupivacaine in a dose of 0.06 mg/cm, which was adequate for providing effective spinal block in 95% of woman undergoing LSCS. Jigisha Badheka[2] used a dose of 0.07mg/cm, 0.5% Bupivacaine in her study to compare the effect of fractionated versus bolus dose of LA in spinal anaesthesia for LSCS. For fractionated dose, they administered initial two third dose then after 90 sec time gap, the remaining one third dose was administered. Similarly, in our study we used the dosage of 0.07 mg/cm of height, considering height is the only parameter. In fractionated group we administered one half of total calculated dose then after 90 sec time gap we administered remaining dose.

In our study, we compared the effect of fractionated versus bolus dose of LA in SA for hemodynamic stability, characteristics of blockade and duration of analgesia in mild to moderate PIH patient undergoing LSCS.

In our study, bolus group received a mean (range) dose of 2.15(2–2.4) ml whereas fractionated group received a mean (range) dose of 2.16 (2–2.5) ml which were comparable among the two groups. We did not observe any sensory blockade above T4 level in either group as shown in Table 2.

Fahmy and colleagues[6] compared the hemodynamic and anaesthetic effect of same dose of bolus versus fractionated Bupivacaine. He concluded that fractionated dose of Bupivacaine prolonged the duration of sensory and motor blockade with better hemodynamic stability. Favarel et al[7] studied a randomised trial in 60 patients undergoing hip fracture surgery and concluded that titrated dose of Bupivacaine was safer, more efficient and provide better cardiovascular stability than a single bolus dose. Jigisha et al[2] concluded that fractionated dose provide better hemodynamic stability, longer duration of analgesia than bolus dose of LA in patients undergoing LSCS. The results of above studies were comparable with ours.

For control of maternal hypotension, we used inj ephedrine. In our study, we found more hypotension with single bolus dose of LA in spinal anaesthesia as compared to fractionated dose. However, Apgar scores were almost similar in both groups in our study.

The limitations of our study were that we had assessed neonatal outcome by Apgar score only and not able to include umbilical cord pH or blood gas values or uteroplacental blood flow. Hence, we were unable to comment further on uteroplacental perfusion.

Further studies and research comparing bolus and fractionated dose in patients undergoing various surgeries and LSCS for severe PIH can be done to evaluate the effectiveness of fractionated dose in maintaining haemodynamic stability.

CONCLUSION

Fractionated dose of SA provides dense block, greater haemodynamic stability and longer duration of analgesia compared to bolus dose in patients undergoing elective caesarean section. To prevent sudden hypotension in PIH patients, fractionated dose of SA can be an acceptable and safe alternative in LSCS.

Conflict of interest- Nil

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REFERENCES

- Andreasen KR, Andersen ML, Schantz AL. Obesity and pregnancy. *Acta Obstet Gynecol Scand* 2004;83:1022-9.
- Badheka Jigisha, Vrinda Pravinbhai Oza, Ashutosh Vyas Comparison of fractionated dose versus bolus dose injection in spinal anaesthesia for patients undergoing elective caesarean section, *Indian journal of anaesthesia*, volume 61, page 55-60
- Ben-David B, Solomon E, Levin H, Admoni H, Goldik Z. Intrathecal fentanyl with small-dose dilute Bupivacaine: Better anesthesia without prolonging recovery. *Anesth Analg* 1997;85:560-5.
- Danelli G, Zangrillo A, Nucera D, Giorgi E, Fanelli G, Senatore R, et al. The minimum effective dose of 0.5% hyperbaric spinal Bupivacaine for caesarean section. *Minerva Anestesiologica* 2001;67:573-7.
- De Simone CA, Leighton BL, Norris MC. Spinal anesthesia for cesarean delivery. A comparison of two doses of hyperbaric Bupivacaine. *Reg Anesth* 1995;20:90-4.
- Fahmy NR. Circulatory and anesthetic effects of Bupivacaine for spinal anaesthesia fractionated vs. bolus administration. *Anesthesiology* 1996;3:85.
- Favarel GJ, Sztark F, Petitjean ME, Thicoipe M, Lassie P, Dasbadie P. Haemodynamic effects of spinal anaesthesia in the elderly: Single dose versus titration through a catheter. *Reg Anaesth Pain Med* 1999;24:417-42.
- Finucane BT. Spinal anesthesia for caesarean delivery. The dosage dilemma. *Reg Anesth* 1995;20:87-9.
- Gin T, O'Meara ME, Kan AF, Leung RK, Tan P, Yau G. Plasma catecholamines and neonatal condition after induction of anaesthesia with propofol or thiopentone at caesarean section. *Br J Anaesth*. 1993;70:311-6. [PubMed]
- Harten JM, Boyne I, Hannah P, Varveris D, Brown A. Effects of a height and weight adjusted dose of local anesthetic for Bolus versus fractionated spinal anaesthesia in LSCS 60 *Indian Journal of Anaesthesia* | Vol. 61 | Issue 1 | January 2017 spinal anaesthesia for elective caesarean section. *Anesthesia* 2005;60:348-53.
- Henke, Vanessa G. MD, spinal anesthesia in severe preeclampsia. *Anesthesia & Analgesia*; September 2013 - Volume 117 - Issue 3 - p 686-693
- Lawes EG, Downing JW, Duncan PW, Bland B, Lavies N, Gane GA. Fentanyl-droperidol supplementation of rapid sequence induction in the presence of severe pregnancy-induced and pregnancy-aggravated hypertension. *Br J Anaesth*. 1987;59:1381-91. [PubMed]
- Loughran PG, Moore J, Dundee JW. Maternal stress response associated with caesarean delivery under general and epidural anaesthesia. *Br J Obstet Gynaecol*. 1986;93:943-9. [PubMed]
- McCulloch WJ, Littlewood DG. Influence of obesity on spinal analgesia with isobaric 0.5% Bupivacaine. *Br J Anaesth* 1986;58:610-4.
- Moran DH, Perillo M, LaPorta RF, Bader AM, Datta S. Phenylephrine in the prevention of hypotension following spinal anesthesia for cesarean delivery. *J Clin Anesth* 1991;3:301-5.
- Poston L. Maternal vascular function in pregnancy. *J Hum Hypertens* 1996;10:391-4.
- Riley ET, Cohen SE, Rubenstein AJ, Flanagan B. Prevention of hypotension after spinal anesthesia for cesarean section: Six percent tetrastarch versus lactated Ringer's solution. *Anesth Analg* 1995;81:838-42.
- Rodrigues FR, Brandão MJ. Regional anesthesia for cesarean section in obese pregnant women: A retrospective study. *Rev Bras Anestesiologia* 2011;61:13-20.
- Saravanakumar K, Rao SG, Cooper GM. Obesity and obstetric anaesthesia. *Anaesthesia* 2006;61:36-48.
- Saravanan P Ankichetty, Ki Jinn Chin, Vincent W Chan, Regional anesthesia in patients with pregnancy induced hypertension. *J Anaesthesiol Clin Pharmacol*. 2013 Oct-Dec; 29(4): 435-444.
- Schnider TW, Minto CF, Bruckert H, Mandema JW. Population pharmacodynamic modeling and covariate detection for central neural blockade. *Anesthesiology* 1996;85:502-12.
- Shnider SM, Wright RG, Levinson G, Roizen MF, Wallis KL, Rolbin SH, et al. Uterine blood flow and plasma norepinephrine changes during maternal stress in the pregnant ewe. *Anesthesiology*. 1979;50:524-7. [PubMed]