*Original Research Article*

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# Comparative Study of Intrathecal Bupivacaine 0.5% and Intrathecal Bupivacaine 0.5% with Fentanyl in Pre-Eclamptic Parturients Undergoing Elective Caesarean Section

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**Abstract**

*Aim*: To evaluate the time of onset, duration of sensory blockade & motor blockade, haemodynamic effects, time duration of post-operative analgesia as well as complications of intrathecal Bupivacaine 0.5% and intrathecal Bupivacaine 0.5% with Inj. Fentanyl 20 mcg in pre-eclamptic parturients opting for elective lower segment caesarean section. *Material & Methods:* A total number of 60 pre-eclamptic parturients with mild to moderate preeclampsia opting for elective lower segment caesarean section were included in a prospective randomized double-blinded control study. Parturients were assigned to receive spinal anaesthesia (SAB) randomly with hyperbaric Inj. Bupivacaine 0.5% 1.8 ml (Group B) or hyperbaric Inj. Bupivacaine 0.5% 1.4 ml along with Inj. Fentanyl 20mcg (0.4ml) (Group F), total of 1.8 ml. The onset, duration, and recovery from sensory blockade and motor blockade, time required to obtain maximum sensory blockade and duration of spinal anaesthesia were noted. The statistical analysis was done by Chi-square test and student's t-test. *Results*: The onset of both sensory and motor blockade was slower in group B. The durations of sensory block (150±20.24 min) and motor block (135±18.06 min) were significantly long enough in the group F. Haemodynamic parameters were significantly stable in Fentanyl group. *Conclusion*: The addition of Fentanyl 20 mcg to subarachnoid block in mild to moderate pre-eclamptic parturients opting for elective lower segment caesarean section, increased the duration of analgesia, with less side effects and without adverse neonatal outcome. Thus, intrathecal Fentanyl is advantageous in pre-eclamptic parturients with minimal side effects.

**Keywords:** Subarachnoid Block; Fentanyl; Bupivacaine; Analgesia; Pre-Eclampsia.

## Introduction

Lower segment caesarean section is commonly performed surgery in the women of childbearing age group. However, the choice of anaesthesia depends on the urgency and indication of surgery will of the patient, and judgement of anaesthesiologist. However, SAB is simpler to perform, less time consuming with very rapid onset and provides a dense motor blockade with accuracy and higher degree of success. The safety of regional anaesthesia for pre-eclamptic patients undergoing caesarean section is established [1-3]. Because of the small dosage of local anaesthetic used, there is less chance of local anaesthetic toxicity and minimal risk of transfer of the drug to the foetus. There are lesser chances of pulmonary aspiration, difficult airway management, less neonatal depression and mother is awake at the time of delivery. The limitation in pre-eclamptic subject is hypotension and short duration of post-op analgesia. With hyperbaric Bupivacaine the high level of block, short duration of action and hypotension are seen commonly. It is advantageous to add opioids to local anaesthetics for synergistic analgesic effect, improved haemodynamic stability and lesser incidence of side effects like nausea, vomiting, respiratory depression. Derivative of phenylpiperidine-fentanyl is synthetic *mu* opioid receptor agonist. As

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an adjuvant, onset of action is fast, effect is prolonged and there is haemodynamic stability with minimal side effects. Though there are such studies in normal parturients, less literature is available in pre-eclamptic females. Hence, we compare the effects of hyperbaric Bupivacaine with combination of hyperbaric Bupivacaine and Fentanyl in pre-eclamptic parturients.

## Materials & Methods

This prospective randomised double blinded control study was done at Department of Anaesthesiology. After approval from the Ethical Committee of the institution, informed written consent was taken from all 60 patients of ASA 1 and 2, having mild to moderate PIH, and posted for elective caesarean section randomly via simple randomization. Blood pressure was ranging between 140/90 mmHg to 160/110 mm Hg. Exclusion criteria was severe anaemia, severe pre-eclampsia, foetal distress, coagulopathies, placenta previa, cardiac diseases, endocrinal disorder, or receiving anticoagulants or other drugs were not included in the study. The study was conducted in two groups; Group B- hyperbaric Bupivacaine 0.5% 1.8ml and Group F- hyperbaric Bupivacaine 0.5% 1.4 ml plus Fentanyl 20 micrograms (0.4ml), total 1.8ml was used respectively. Pre-anaesthetic examination of patients included detailed general physical, systemic and spine examination followed by airway assessment. Investigations like Hemogram, Urine for Routine and Microbiology, Blood Urea, Serum Creatinine, Blood grouping, and Blood Sugar were done. Patients were premedicated with Tab. Ranitidine (150mg) on previous night.

Inj. Ranitidine and Inj. Ondansetron was given one hour before surgery. After shifting to the operation theatre, the patient was preloaded with 250-500 ml of Ringer Lactate with 18 gauge needle over 15- 30 minutes in the left lateral position. Crystalloid or colloid solutions can be used to preload in normal parturients opting Subarachnoid block (SAB) for elective lower segment caesarean sections. Though it is not effective always. Hence it is more significant in PIH patients due to hypovolemia and vasospasm. Monitors pulse oximeter, Non-invasive blood pressure, ECG were connected to the patient and base line readings were recorded. With patient in the left lateral position, as per aseptic precautions spinal anaesthesia was given with spinal needle 25 gauge at $L_3$- $L_4$ space after free flow of CSF, by anaesthesiologist not involved in this study. Blinding of study was done by sealed envelope method where group B received hyperbaric bupivacaine 0.5% 1.8ml and group F received hyperbaric bupivacaine 0.5% with Inj. Fentanyl 20 mcg (0.4ml), total 1.8 ml. Parturients were shifted to supine position with wedge under right buttock on horizontal table. Supplemental $O_2$ was given through face mask at the flow rate of 4 litres/minute. The parameters of monitors were recorded at 0, 2$^{nd}$, 4$^{th}$, 6$^{th}$, 8$^{th}$, 10$^{th}$ minutes followed by every 15$^{th}$ min till the surgery ended. Ephedrine was used safely for maintaining of blood pressure (when mean arterial BP was<20%). Inj. Atropine 0.6 mg was given when heart rate decreased less than 50 beats per minute. The onset and duration of sensory blockade was assessed by pinprick method. The time taken from intrathecal injection to the highest level of sensory block was recorded. The onset and duration for motor blockade were noted. Grading of motor block was done using *Bromage scale*.

Bromage Scale for motor block Grade

0 No motor block

1 Inability to raise the extended leg

2 Inability to flex the knee, able to flex the ankle

3 Inability to flex the ankle - complete motor block

Duration of motor blockade was calculated from zero time to recovery of motor block. The duration of analgesia that is from the time of intrathecal Injection to first dose of rescue analgesics were recorded. Neonatal outcome in study was assessed by APGAR score at 1$^{st}$ and 5$^{th}$ minutes.

### Statistical Analysis

The data was tabulated and quantitative variables were reported like mean and standard deviation. Student's t test was used and p value obtained. Categorical variables were compared using Chi-square test and p value was calculated. p value less than 0.05 was taken as statistically significant. With mean age in group F (25.70±5.6) and group B (24.60±5.5), with p value of 0.4458; weight in group F (72.32 ± 8.06) and group B (73.16±9.5), with p value of 0.7133; height in group F (159.1±4.4) and group B (158.1±10.1), with mean p value of 0.6209. The differences in demographic variables were not statically significant between two groups of study.

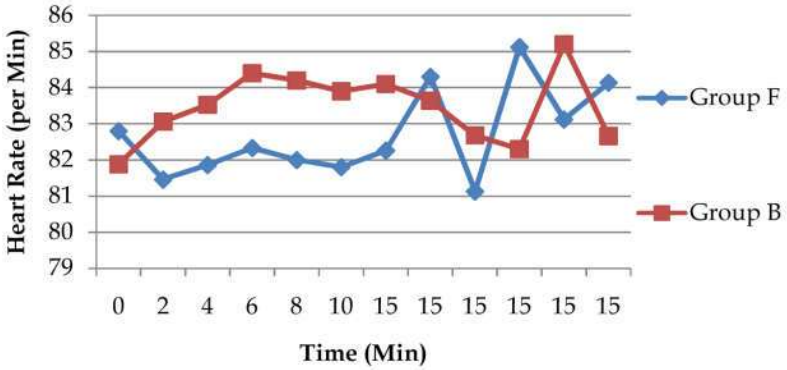
## Results

The mean time required to achieve peak sensory blockade and motor blockade was lesser in group F than group B. Duration of sensory blockade and

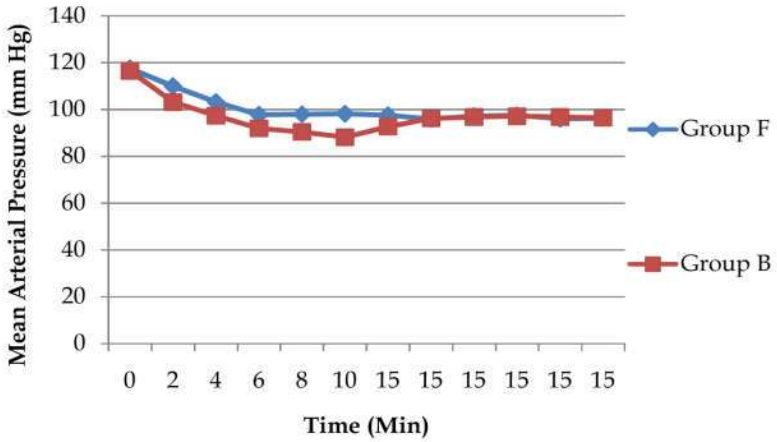
motor blockade were prolonged in Group F than Group B, and this was statistically significant with 'p' value<0.05 (Table 1). Changes in mean arterial blood pressures of Group F and Group B at 2nd, 4th, 6th, 8th, 10th, 15th minutes are significant statistically from the basal recordings. Neonatal APGAR scores were recorded for the prediction of neonatal outcome, which were influenced by anesthesia. APGAR score was recorded at 1st and 5th minute after delivery.

**Table 1:** Comparison of sensory and motor blockade between two groups

| | Group F (mean with SD) | Group B (mean with SD) | p value |
|---|---|---|---|
| Onset of sensory block (Min) | 1.2 ± 0.57 | 1.4 ± 0.52 | 0.1610 |
| Onset of motor block (Min) | 1.5 ± 0.38 | 1.7 ± 0.44 | 0.0645 |
| Effect of sensory level block [T4] (Min) | 3.91 ± 0.64 | 4.12 ± 0.42 | 0.1384 |
| Duration of sensory block [T10] (Min) | 150 ± 20.24 | 120 ± 18.42 | <0.0001 |
| Duration of motor block (Min) | 135 ± 18.06 | 104 ± 15.02 | <0.0001 |




**Graph 1:** Changes in Heart Rate in both groups
There were no statistically significant changes in heart rate of both the groups.




**Graph 2:** Changes in Mean Arterial Pressure between the two groups

## Discussion

Hypertensive disorder occurring during pregnancy is classified as per guidelines of International Society for the study of hypertension in different forms-

- Gestational hypertension - BP ≥ 140/90 mm Hg for the first time after 20 weeks, without proteinuria
- Pre-eclampsia – gestational hypertension with proteinuria (urinary excretion ≥ 300 mg /24 hours or 100mg/L).
- Eclampsia – Pre-eclampsia complicated with convulsions and/or coma.

Pre-eclampsia is defined as pregnancy induced hypertension associated with proteinuria, developing during the last trimester or during labour. It presents mostly between 33 weeks to 37 weeks of gestational age. The ultimate treatment being the delivery of the foetus as well as delivery of the placenta. The basic pathology in this syndrome is attributed to endothelial damage which causes

initiation of multiple organ disease and dysfunction. If not treated, associated with significant maternal morbidities like pulmonary oedema, intra-cerebral haemorrhage, acute renal failure, liver failure and coagulation abnormalities. Foetal complications include abruptio placenta, IUGR, premature delivery and IUD. Cardiovascular changes like labile blood pressure, intravascular volume depletion, decrease in colloid oncotic pressure, increase in resistance of systemic circulation and hypercoagulable state exist. Spinal anaesthesia is superior to epidural anaesthesia for lower segment Caesarean section due to more predictable distribution of block with denser block. However, a rapid onset with marked changes in cardiovascular system made it a critical choice. General anaesthesia being safe has its own limitations because of difficult intubation, hyperdynamic response during intubation, pulmonary aspiration etc. Dyer et al. found that pre-eclamptic patients have a less susceptibility to hypotension and less impairment of cardiac output than healthy patients after SAB for lower segment Ceasarean section [4].

Even though, recent studies conducted shown that fall in BP can be compared with either of two techniques besides maintaining comparable haemodynamics. A report of the National blood pressure Education Program Working group on High Blood Pressure in Pregnancy has stated that SAB can be used with safety in patient having severe preeclampsia undergoing lower segment caesarean delivery because the magnitude of declines in maternal blood pressure after spinal and epidural anaesthesia appears as same [5]. Use of SAB in severe preeclampsia demonstrating a lesser degree of hypotension when compared to healthy parturients for a caesarean section [6,7]. SP Ankichetty et al. study of 80 women having severe preeclampsia, who were randomly assigned to receive epidural, combined spinal-epidural or general anaesthesia, all three regimens appeared equally safe. General anaesthesia is associated with complications like significant hypertension during laryngoscopy procedure, at the time of tracheal intubation and again during emergence and extubation period, and spinal anaesthesia has got the addede advantage of simplicity, faster onset and reliability of the procedure. The haemodynamical chnages by spinal anaesthesia are comparable with General Anaesthesia in pre-eclampsia. The utero-placental blood flow is not changed in parturients receiving spinal anaesthesia.

Epidural anaesthesia with graded hypotension also has disadvantages like technical difficulty in PIH patient in labour, increased epidural vessel puncture, dural puncture chances, adequate analgesia not obtained and risk of high block. David Wilkinson in his studies showed the use of low dose of local anaesthetic in spinal anaesthesia in Caesarean section (7.5 mg of hyperbaric Bupivacaine) [8]. Then the patient lied supine in left lateral tilt and little head up tilt. The procedure was tolerated well enough and patient satisfaction was good.

Usage of a low dose of drug with opioid, over routine higher dose of drug for spinal anaesthesia, has increased these days. As it has benefits like decreased chances of hypotension and postoperative analgesia [10,11]. Administration of Fentanyl in intrathecal space is one of the methods for intraoperative anaesthesia and for post-operative analgesia [10,11,12]. As Fentanyl has higher affinity for non-specific binding sites on the lipid surface, little proportion of the administered drug enters to the cervical region [13]. Jaishribogra et al. found that mean time of onset of sensory blockade and peak level of analgesia were equivalent in both the groups and Fentanyl added Bupivacaine did not alter the onset [14]. Bupivacaine-Fentanyl combination was potent in abolishing visceral pain than Bupivacaine alone which was similar to our study in which mean onset of sensory blockade was (1.2±0.57min) in group F in comparison with to group B (1.4 ± 0.52min), even though the difference was not statistically significant ($p>0.05$).

Dahlgren G et al. concluded that time to obtain peak sensory level was shorter with Bupivacaine-Fentanyl combination than with Bupivacaine alone [15]. However onset and duration of motor blockade were comparable in both the groups, all patients had achieved grade 3 motor block. In study we did, time required for peak sensory level was faster in group F as compared to other group B. Thus, the difference was statistically significant ($p <0.05$). No significant drop in heart rate was noted any of the groups. Bendavid et al also highlightted that patients with plain Bupivacaine required treatment for hypotension more commonly than patients with Bupivacaine-Fentanyl combination [16], which was comparable with our study. This is because a low dose of Bupivacaine used in group F for the study. Seyedhejazi. M found that there was lesser number of patients who felt nausea and vomiting in group F which is mostly due to low dose of highly lipophobic opioids do not remain free in the cerebrospinal fluid for long time when injected in the subarachnoid space at the lumbar level of vertebrae to reach upto the chemoreceptor trigger zone in the concentration good enough to directly induce nausea [17]. The low dose,however,

sufficiently potentiate local anaesthesia mediated block to decrease nociceptive stimulation which occurs during manoeuvres like peritoneal pulling and uterine exteriorization with adequate sensory blockade, that's how it decreases nausea and vomiting. In or study, 5 patients from group F developed complaint like nausea and vomiting as compared to 12 patients of group B. Anchalee T et al. stated that there was a fall in shivering which was due to the addition of intrathecal Fentanyl that affected afferent thermal inputs of the spinal cord [18]. In our study, 3 patients from group F felt shivering in comparison to 7 patients of group B. Sergio DB stated that Sedation and pruritus were the main side effects [19]. But pruritus was not reported in any of the groups in our study. Sedation score was not studied in our study. Pitfalls of the study were inclusion of some patients taking anti hypertensives, and uterine artery pH studies were not done for neonatal outcome.

## Conclusion

Thus, low dose Fentanyl along with Bupivacaine provides better analgesia, good haemodynamic stability and lesser complications like vomiting, nausea, respiratory depression, shivering along with effective analgesia in post operative recovery time in pre-eclamptic parturients undergoing elective caesarean section. Fentanyl with its synergistic action with Bupivacaine, reduces the dose of Bupivacaine with fewer side effects and assures a better quality of anaesthesia with good neonatal outcome.

## References


1. Wallace DH, Leveno KJ, Cunningham FG, Giesecke A, Shearer H, Sidwai JE. Randomized comparison of general and regional anaesthesia for caesarean delivery in pregnancies complicated by severe preeclampsia. ObstetGynecol 1995;86;193-9.
2. Karinen J, Rosanen S, Alahuhuta S, Jouppilla R, Jouppilla P. Maternal and uteroplacental haemodynamic state in preeclamptic patients in during spinal anaesthesia for ceasareaan section. Br J anaesth 1996;76:616-20.
3. Norris MC. Height, weight and the spread of subarachnoid hyperbaric bupivacaine in the term Parturient. Aneasthanalg 1988;67;555.
4. Dyer RA, Piercy JL, Reed AR. The role of the anaesthetist in the management of the pre-eclamptic patient. Curr Opin Anaesthesiol. 2007;20:168–74.
5. Hood DD. Curry; spinal versus epidural anaesthesia for caesarean secton in several preeclamptic patients. A retrospective survey. Anaesthesiology 1999;90:1276-82.
6. Aya AG, Mangin R, Vialles N et al. Patients with severe preeclampsia experiences less hypotension during spinal anaesthesiafor elective caesarean deliverythan healthy parturients;A prospective cohort comparison. Anaesth Analg 2003;977:867-72.
7. Clark VA,Sherwood Smith GH. Stewart AV. Ephedrine requirements are reduced during spinal anaesthesia for the ceasarean section in preeclampsia. Int J Obstet Anesth. 2005;14:9–13.
8. Ngan Keewd, Khaw Ks, Ma KC et al. Maternal and neonatal effects of remifentanil at induction of general anaesthesia for caesarean delivery: A randomized, double-blind controlled trial. Anaesthasiolgy 2006; 104;14-20.
9. Wilkinson D. Low Spinal Anaesthesia for Caesarian Section S. Afr. Fam Pract., 1993.pp.7-10.
10. Report of the National Blood Pressure Education Programme Working on High Blood Pressure in Pregnancy, Am J Obstet Gynecol. 2000 Jul;183(1):S1-S22.
11. Akerman B, Arwestorm E., Post C. local anaesthetics potentiate spinal morphine antinociception. AnesthAnalg; 1988;67;943-948.
12. Chu C.C, Shu S.S., Lin S.M., Chu N.W., Leu Y.K., Tsai S.K., Lee T.Y. The effect of intrathecal bupivacaine with combined fentanyl in cesarean section. Acta Anaesthesiol Sin; 1995;33:149–I54.
13. McQuay H J., Sullvan A.I., Smallman et al. Intrathecal opiodspotency, and lipophilicity. Pain 1989;36;111-5.
14. Gourlay GK., Murphy T.M., Plummer J.L., et al. Pharmacokinetics of fentanyl in lumbar and cervical CSF following lumbar epidural and intravenous administration. Pain 1989:36:111-5.
15. Jaishri Bogra. Namitha Arora., Pratima Srivastava. Synergistic effect of intrathecal fentanyl and bupivacaine in spinal anesthesia for cesarean section, BMC Anesthesiology 2005;5:5.
16. Dahlgren G., Hultstrand G.C., Jakobsson J ., Norman M., AnaeshAnalg 1997;85:1288-93.
17. Ben-David B., Miller G, Gavriel R., Low-dose bupivacaine-fentanyl spinal anesthesia for cesarean delivery. Reg Anesth Pain Med. 2000 May-Jun;25(3):235-9.
18. Seyedhejazi M, Madarek E. The effect of small dose bupivacaine-fentanyl in spinal anesthesia on hemodynamic nausea and vomiting in cesarean section. Pak J Med Sci 2007 Oct - Dec;23(5):747-50.
19. Techanivate A, Rodanant O, Tachawattanawisal W, Somsiri T: Intrathecal fentanyl for prevention of shivering in cesarean section. J Med Assoc Thai 2005;88:1214-21.
20. Belzarena S.D. Clinical effects of intrathecally administered fenta- nyl in patients undergoing cesarean section. Anesth Analg; 1992;74:653–657.