

Comparative Evaluation Of Low Dose Hyperbaric Bupivacaine With Or Without Fentanyl In Spinal Anaesthesia For Caesarean Section In Patients With Pregnancy Induced Hypertension

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Citation

F Sheikh, M Ahmed, M Ommid, S Gurcoo, N Shakoor, S Nazir, G Nisa. *Comparative Evaluation Of Low Dose Hyperbaric Bupivacaine With Or Without Fentanyl In Spinal Anaesthesia For Caesarean Section In Patients With Pregnancy Induced Hypertension*. The Internet Journal of Anesthesiology. 2013 Volume 31 Number 1.

Abstract

Neuraxial administration of opioid's along with local anesthetics improve the quality of intraoperative analgesia and also provides postoperative pain relief for longer duration. The present study was conducted to study and compare the effects of bupivacaine alone and its combination with fentanyl used intrathecally in parturients with PIH. 50 ASA grade II patients with PIH defined as blood pressure between 140-160/ 90-110 mmHg without proteinuria were selected and divided into 2 groups as Group (I)-Bupivacaine and Group (II)- Bupivacaine- Fentanyl group. Haemodynamic variables like systolic and diastolic blood pressure, heart rate were recorded every 2 minutes upto delivery of baby and then every 5 minutes until end of surgery. Sensory block and motor block alongwith side effects were recorded. Pain was evaluated using visual analogue scale and neonatal outcome assessed using APGAR scoring. The highest sensory level achieved in bupivacaine-fentanyl group was higher than in the group receiving plain bupivacaine. The time taken for sensory regression to T12 and duration of analgesia was longer in the Bupivacaine-Fentanyl group. We conclude the combination group prolongs the duration of sensory spinal block, increases the duration of analgesia without increasing the duration of motor block, does not cause any significant side effects and provides stable haemodynamic conditions without fetal or maternal compromise.

INTRODUCTION

Spinal anaesthesia has been widely used for caesarean section in normal as well as preeclamptic parturients and has been found to be efficacious and safe.^{1,2,3,4} After the discovery of opioid receptors in spinal cord and direct opioid action at this level, possibility of synergism between opioids and local anaesthetics, co administered intrathecally has been explored extensively in obstetric population undergoing caesarean delivery⁵. Although hypotension due to decrease in systemic vascular resistance resulting from the blockade of preganglionic sympathetic fibres⁶ remains a problem with all central neuraxial blocks; the synergistic action of local anaesthetics with opioid can be of great benefit in achieving adequate anaesthesia with lesser dose of local anaesthetics, thereby reducing chances and severity of hypotension. Neuraxial administration of opioids along with local anaesthetics improves the quality of intra-operative analgesia and also provides postoperative pain relief for longer duration⁷ Opioids and local anaesthetics administered

together intrathecally have a potent synergistic analgesic effect Improving the quality of intraoperative analgesia and also provides postoperative pain relief for longer duration^{8,9} Bupivacaine was the first local anaesthetic that produced adequate pain relief, without a major effect on motor fibers¹⁰ Fentanyl is one of the most extensively used opioids for this purpose and has been found to be safe and effective both in terms of neonatal and maternal outcome not only in normal parturients but also in severely preeclamptic patients for labour analgesia and elective caesarean section^{11,12}

Considering the above facts, we designed the present study using low dose bupivacaine with low dose fentanyl to assess the hemodynamic stability, perioperative analgesia and neonatal outcome in pregnancy induced hypertensive patients.

MATERIAL AND METHODS

50 ASA Grade II patients with pregnancy induced hypertension scheduled for elective lower segment caesarean

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section under spinal anaesthesia were included in the study. Patients were thoroughly explained regarding nature of the study. Pregnancy induced hypertension was defined as blood pressure between 140 –160 / 90 – 110 mm Hg without proteinuria. Patients with singleton uncomplicated pregnancy were included.

Patients with eclampsia, coagulation abnormalities, thrombocytopenia, patients in labour and those with foetal distress requiring emergency caesarean section, any drug allergy, spinal deformity or any other standard contraindication to spinal anaesthesia were excluded from the study. Patients were randomly allocated to 2 groups of 25 each.

Group I received 2.0 ml (10mg) of 0.5 % hyperbaric bupivacaine and 0.5 ml of normal saline to make a total volume of 2.5ml.

Group II received 2.0 ml (10mg) of 0.5 % hyperbaric bupivacaine and 12.5 µg of fentanyl in normal saline to make a total volume of 2.5ml.

All the patients received oral metaclopramide 10 mg and ranitidine 150 mg, 45 minutes prior to scheduled surgery. Baseline systolic blood pressure, diastolic blood pressure, heart rate and oxygen saturation was recorded with the patient in semi recumbent position.

Patients were placed in sitting position and under all aseptic precautions, lumbar puncture was performed with 25 gauge Quincke spinal needle at L₃-L₄ intervertebral space. Free flow of CSF was confirmed. Patients were randomly allocated to either of the two groups and received either 2 ml of 0.5% hyperbaric bupivacaine with 0.5 ml of normal saline or 2 ml of 0.5% hyperbaric bupivacaine with 12.5 µg of fentanyl in normal saline intrathecally so as to make a total volume of 2.5 ml in both the groups. Hemodynamic variables like systolic blood pressure, diastolic blood pressure and heart rate were recorded every 2 minutes upto delivery of baby and then every 5 minutes until the end of surgery. Hypotension (MAP decrease of ≥ 20%) was recorded and treated by mephentermine 3mg and Bradycardia (HR<50bpm) with atropine 0.3mg boluses. Sensory testing was performed using a 21 gauge needle in a cephalad to caudal fashion. Dermatome level was tested every 2 minutes until the level stabilized for 3 consecutive tests. A sensory blockade upto T₅ was considered adequate to allow surgery to proceed. The time taken from intrathecal injection to attainment of the highest level of sensory block

was recorded. The time for sensory regression to T₁₂ from highest sensory level was also noted. Motor block was assessed as per Bromage scale. Duration of motor block was recorded from onset upto cessation of grade I block.

Side effects such as pruritis, nausea and vomiting, shivering, respiratory depression and urinary retention were recorded every 5 min for first 30 min, then at 10 min interval for remainder of the operation. Thereafter, patient was followed in post-operative ward for assessment of motor block, sensory regression and duration of complete analgesia. Rescue analgesia was given at a VAS score of 3 or more. Pain was evaluated using a standard 10 cm linear visual analog scale with 0 corresponding to no pain and 10 to the worst pain possible. Neonatal outcome was assessed using APGAR score at 1 minute and 5 minutes. Incidence of APGAR score <7 was recorded. The data was collected, assessed and statistically analyzed; a p value of < 0.05 was considered statistically significant.

RESULTS

All the patients in the 2 groups were comparable with respect to age, weight, baseline SpO₂ in the two groups. (Table 1)

Figure 1

Table 1: Comparison of Age and Weight and SpO₂ of the Studied Parturients in Group I and Group II

| | Control (Group I) | | | | Study (Group II) | | | | p value |
|----------------------|-------------------|-----|------|-----|------------------|------|------|-----|------------|
| | Min | max | Mean | SD | min | Max | Mean | SD | |
| Age (Years) | 22 | 31 | 26.8 | 2.8 | 21 | 31.0 | 26.3 | 2.7 | 0.538 (NS) |
| Weight (Kg) | 57 | 82 | 68.6 | 6.2 | 61 | 80.0 | 69.8 | 6.3 | 0.485 (NS) |
| SpO ₂ (%) | 94 | 98 | 96.6 | 1.2 | 94 | 98 | 96.5 | 1.1 | 0.771 (NS) |

NS: Not-significant

An adequate surgical block was documented before start of surgery and the time taken to reach this level was comparable between the two groups. Although there was no significant difference in the onset of sensory block and height of maximum sensory blockage between the two groups.

There was a significant difference (p value 0-000) in the time to regression of sensory anaesthesia below T₁₂ dermatome. It was 162.6 ±10.5 min in group I and 209.9 ±11.6 min. in group 2. Time to achieve maximum motor block and the degree of motor block was comparable. And

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all patients achieved motor block within 10 min. Time to complete resolution of motor block did not differ between the two groups (Table 2)

Figure 2

Table 2 : Spinal Block Characteristics

| | Control Group | Study Group |
|---|---------------|--------------|
| Time to sensory block to T4 (min) | 6.5 ± 1.5 | 6.3 ± 1.5 |
| Time to complete motor block (min) | 7.3 ± 3 | 7.7 ± 2.2 |
| Time taken for sensory regression to T12 (min) | 162.6 ± 10.5 | 209.9 ± 11.6 |
| Time to complete regression of motor block (Bromage 0) | 170.0 ± 19.7 | 170.0 ± 13.9 |
| Time from injection to 1 st dose of supplemental analgesia | 234.7 ± 32.9 | 326.1 ± 50.0 |

There was no significant changes in BP in the two groups till 4 min. after giving spinal block. Thereafter there was a fall in BP in both the groups at 4 and 6.min. However this was not < 20% of baseline in all patients. The fall was comparable between the two groups and did not vary significantly between the two groups. (Table 3)

The total requirements of mephentermine and i.v. fluids were similar in the two groups. One patient in the study group and three in the control group required mephentermine.

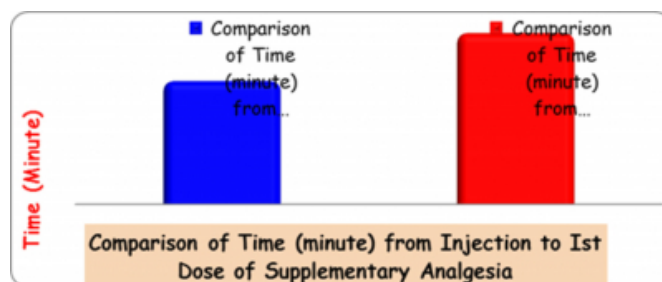
Figure 3

Table 3: Haemodynamic data

| Blood Pressure (mmHg) | Control Group | Study Group |
|---|---------------|--------------|
| Highest Systolic (Pre- operative) | | |
| Mean Systolic | 138.9 ± 9.7 | 136.4 ± 10.1 |
| Absolute Systolic | 156 | 154.0 |
| Highest Diastolic (Pre- operative) | | |
| Mean Diastolic | 91.3 ± 4.9 | 88.4 ± 6.9 |
| Absolute Diastolic | 100 | 100 |
| Lowest Systolic (Intra operative) | | |
| Mean Systolic | 119.7 ± 12.4 | 123.8 ± 5.7 |
| Absolute Systolic | 90 | 88 |
| Lowest Diastolic (Intra operative) | | |
| Mean Diastolic | 77.1 ± 5.6 | 79.0 ± 3.2 |
| Absolute Diastolic | 50 | 60 |

Duration of postoperative analgesia measured by the time to first dose of diclofenac was significantly longer in study group (326.1min.) compared to control group (234.7 32.9min.)[p=0-000].

Figure 4



Two patients in the control group and one in the study group had bradycardia, the statistical difference being insignificant. None of the patients complained of pruritis, respiratory (maternal / neonatal) or urinary retention. Incidence of nausea and vomiting in the control group was 3 times more than the fentanyl group but on application of students t-test the p value >0.05 showed insignificant statistical difference.

Figure 5

Table 4: Comparison of Side Effects in Group I and Group II.

| | Control (Group I) | | Study (Group II) | | p value |
|-----------------------------------|-------------------|------|------------------|-----|------------|
| | N | % | N | % | |
| Hypotension | 3 | 12.0 | 1 | 4.0 | 0.302 (NS) |
| Bradycardia | 2 | 8.0 | 1 | 4.0 | 0.556 (NS) |
| Pruritis | 0 | 0.0 | 0 | 0.0 | 1.000 (NS) |
| Nausea/ Vomiting | 3 | 12.0 | 1 | 4.0 | 0.297 (NS) |
| Shivering | 1 | 4.0 | 0 | 0.0 | 0.312 (NS) |
| Respiratory Depression (Maternal) | 0 | 0.0 | 0 | 0.0 | 1.000 (NS) |
| Urinary Retention | 0 | 0.0 | 0 | 0.0 | 1.000 (NS) |
| Respiratory Depression (Neonatal) | 0 | 0.0 | 0 | 0.0 | 1.000 (NS) |

NS: Not-significant

Similarly when fetomaternal characteristics were compared a nonsignificant difference was observed in neonatal birth weight between the two groups. 9 neonates in control and 8 in the study group had a 1minute Apgar score of ≤ 7. However both the neonatal groups achieved Apgar score of > 7 at 5 minutes.

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Figure 6

Table 5: Neonatal outcome

| | Control Group | Study Group |
|------------------------|---------------|--------------|
| Birth Weight (gms) | 3218 ± 393 | 3282 ± 408 |
| 1 min Apgar Score ≤ 7 | 9/25 (36%) | 8/25(32%) |
| 5 min. Apgar Score > 7 | 25/25 (100%) | 25/25 (100%) |

Figure 7

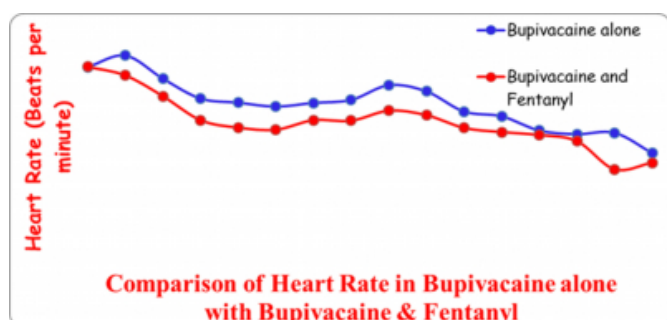
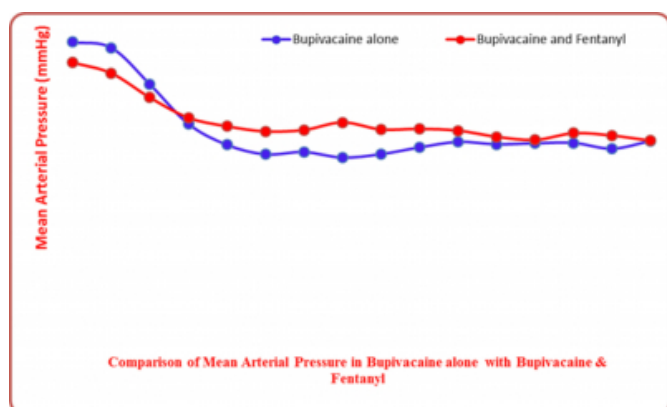


Figure 8



DISCUSSION

Pre-eclamptic parturient patients present a challenge to the anaesthetist because of problems that pre-eclampsia poses to the fetus and mother. The mother may develop cardiopulmonary and cardiorespiratory emergencies in addition to acute renal failure, severe thrombocytopenia and activation of the coagulation cascade¹³ Efficacy and safety of spinal anaesthesia with Bupivacaine has been studied by various investigators in preeclamptic patients^{2,13} Intrathecal opioids have been used for labour analgesia and for caesarean section in combination with varying doses of bupivacaine^{2,14} Opioids and local anaesthetics administered together intrathecally have a potent synergistic analgesic effect^{11,15,16} Improving the quality of intraoperative analgesia

and also provides postoperative pain relief for longer duration^{8,9}.

An increased dose of fentanyl 0.5-0.75 µg/kg intrathecally was associated with increased incidence of adverse effects in patients undergoing cesarean delivery¹⁷ In our study, the dose of 12.5 µg fentanyl has been chosen because it is in mid range for doses quoted in the literature^{18,19}

1 patient in the study group and 2 in the control developed bradycardia (HR < 50bpm), the incidence on comparison being insignificant. the findings being in accordance with similar studies^{7,20,21}

Parturients in both our groups showed a significant fall in MAP by 4-6 minutes, this fall was less than 20% of the baseline and was comparable in both the groups. Hypotension was defined as a decrease in mean arterial blood pressure by ≥ 20% and treated with mephenteramine 3mg boluses. One patient in study and 3 in control group developed hypotension, the incidence was insignificant as found by study by B.N. Biswas⁷. Similarly when diastolic blood pressure and mean arterial blood pressure were compared at all time intervals the results were statistically insignificant p value . >.05.

Wallace et al² used higher dosage of Bupivacaine (11.25mg) as compared to our study but their patients had a greater fall in MAP (25%). This may be due to the inclusion of laboring patients, who have pain and a relatively elevated MAP which produce exaggerated apparent decrease in BP after spinal anaesthesia²². We excluded laboring patients from our study. It has been observed that haemodynamic stability is unaffected by the addition of fentanyl to intrathecal bupivacaine. Experimental work and clinical activity after spinal anaesthesia is dose related to the bupivacaine, and that intrathecal fentanyl by itself nor in combination with bupivacaine causes further depression of sympathetic efferent activity²³.

The highest sensory level achieved was compared between the two groups and found to be statistically significant with a p value of 0.011. In the study group 16 patients while in the control group 7 patients achieved T₄ sensory level. Similar observations were recorded by B.N. Biswas⁷ S. Goel et al²¹ Time taken to reach the highest sensory level was comparable between the two groups and correlate well with other studies^{14,18,20} who showed no statistically significant difference regarding the latency of sensory block.

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The time taken for sensory regression to, T_{12} in study group was 209.9 ± 11.6 min while in control group it was 162.6 ± 10.5 min. This significant difference p value < 0.000 (S) was consistent with studies by Harbhej Singh et al¹⁴ Liu et al in²⁴. Ben-David, et al in.²³ Onset of motor block and regression of motor blockade were comparable in both the groups.

Various studies have found median effective dose of intrathecal fentanyl for labour analgesia to be approximately $14 \mu\text{g}$ ³. This preemptive and synergistic action of fentanyl may be responsible for lower analgesic requirement in study group as compared to control group. Time to first analgesic requirement was longer in the study group as compared to control group.

The side effect profile of this study revealed nausea and vomiting in 3 patients of control and 1 in study group. Many studies on the use of intrathecal fentanyl have demonstrated decreased incidence of intraoperative nausea and vomiting^{33,34}. No incidence of pruritis, maternal and fetal respiratory depression or urinary retention was reported in our study. Other studies using higher doses of fentanyl ($> 25\text{mcg}$) have demonstrated increasing side effects on administration of intrathecal opioids^{14,25,26,27}

Abbound et al have found that PET patients have higher catecholamine concentrations than patients with an uncomplicated gestation. PET parturients have decreased uterine blood flow²⁸. which puts them at increased risk of further undesirable fetal effects of elevated catecholamines. Fentanyl has been found to decrease circulating catecholamine levels in parturients due to pain relief and thus a reduction in maternal stress.²⁹

Foetus as such is at a greater jeopardy in PET in view of hazards like IUD, dysmaturity, asphyxia and prematurity³⁰. However regional anaesthesia has not shown to increase further risk³¹ None of the neonates in the study group had a 1min or 5min. Apgar score less than 7.

Although studies have shown poor correlation between the degree of hypotension during regional anaesthesia and neonatal umbilical acid-base status and uteroplacental perfusion³², one of the limitations of this study was that umbilical pH and blood gas status could not be done for evaluation of fetal outcome.

CONCLUSION

The spinal fentanyl- bupivacaine mixture produces a significant prolongation of sensory block, prolongs the duration of analgesia and achieves a higher quality of sensory block as compared to bupivacaine alone. This combination does not hasten the onset of sensory or motor block and does not prolong the duration of motor block. Fentanyl –bupivacaine combination does not produce haemodynamic instability, or adversely effect foetal outcome and may even have an additional advantage by preventing nausea and vomiting.

Figure 9

Table 6: Comparison of Observed Parameters between the following studies

| | Our study | B N Biswas et al | Mahajan R et al | Harbhej Singh et al |
|---|--|---------------------------------------|------------------------------------|-------------------------------------|
| Highest sensory level achieved | T ₄ | T ₅ | T ₄ | T ₇ |
| Time to highest sensory level (min) | 6.3 ± 1.5 | 7 ± 2.4 | 3.8 ± 2.1 | 7.5 ± 3.2 |
| Time for sensory regression (min) | To T ₁₂ : 209.9 ± 11.6 | To L ₁ : 151 ± 7.33 | To T ₁₂ : 240 (mean) | To L ₁ : 141 ± 37 |
| Onset of Grade III motor Block (min) | 7.7 ± 2.2 | 5.4 ± 1.1 | 9.1 ± 7.6 | 8.6 ± 4.1 |
| Recovery time to Bromage grade 0 (min) | 170 ± 13.9 | 127 ± 7.1 | 128 ± 19.26 | 169 ± 37 |
| Time taken from injection to 1st dose of supplemental analgesia (min) | 326.1 ± 50 | 248 ± 11.76 | 358.8 ± 114 | - |
| Hypotension | 4% | 30% | - | 43% |
| Bradycardia | 4% | 20% | - | 14% |
| Pruritis | 0% | 0% | - | 2% |
| Nausea/ Vomiting | 4% | 5% | - | 0% |
| Shivering | 0% | 5% | - | 0% |
| Respiratory Depression (Maternal) | 0% | 0% | - | 0% |
| APGAR Score 1 Min | 7 – 9 | 7 – 9 | <7 (2 out of 14 patients) | - |
| 5 Min | 9 – 10 | 9 – 10 | <7 (1 out of 14 patients) | - |

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