Original Research Article

Efficacy of intrathecal fentanyl along with bupivacaine and bupivacaine alone in lower segment caesarean section

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Abstract

Background: Spinal anesthesia is oldest and all over the world till date one of the most frequently employed methods of regional anesthesia. The addition of opiates like the lipophilic opioid Fentanyl to local anaesthetics produces many of its clinical effects very early after intrathecal administration.
Aim: The study was designed to compare the efficacy of intrathecal Fentanyl along with Bupivacaine and Bupivacaine alone and their effect on prolonging the duration of postoperative analgesia in lower segment caesarean section without any adverse effects.
Materials and methods: Fifty ASA physical status I and II patients scheduled for elective lower segment caesarean section surgery were studied. Patients were randomly divided into two groups i.e., group FB and group B consisting of 25 patients each. Patients in group FB were given 8.5 mg of 0.5% hyperbaric Bupivacaine plus 25 µg of Fentanyl (0.5 cc) and group B received 8.5 mg of 0.5% hyperbaric Bupivacaine plus 0.5 cc of normal saline to adjust the final volume to 2.2 cc.
Results: It was found that addition of 25 µg of Fentanyl to 8.5 mg of 0.5% hyperbaric intrathecal Bupivacaine had no effect on the onset of analgesia to pin prick, maximum level of analgesia and time to achieve maximum level. Fentanyl did not prolong the Bupivacaine sensory block but there was a significant prolongation of postoperative analgesia with addition of Fentanyl. Fentanyl 25 µg did not enhance the onset and duration of sensory block produced by 8.5 mg of 0.5% hyperbaric intrathecal Bupivacaine. Fentanyl however, prolonged post-operative analgesia and lowered the incidence of shivering. The incidence of pruritus was high, but it was usually mild in Fentanyl 25 µg along with 8.5 mg of 0.5% hyperbaric Bupivacaine.

Conclusions: Intrathecal Fentanyl with Bupivacaine is very much safer than other opioids like morphine which has more postoperative complications like intense, intermittent respiratory depression.

Key words

Intrathecal, Fentanyl, Bupivacaine.

Introduction

Spinal anesthesia is oldest and all over the world till date one of the most frequently employed methods of regional anesthesia. Spinal anesthesia is the regional anesthesia obtained by blocking the spinal nerves in the subarachnoid space. The anaesthetic agents are deposited in the subarachnoid space and act on the spinal nerve roots, ensuing anesthesia is predictable, occurs rapidly and is associated with profound muscle relaxation and contraction of the gastrointestinal tract. The technique is particularly useful for surgery involving the lower extremities, pelvis, perineum and lower abdomen [1, 2].

Lidocaine has been a popular anesthetic for various short surgical procedures. When hyperbaric 2% or 5% lidocaine is used for spinal anesthesia patients recover rapidly. With hyperbaric spinal lidocaine several studies reported transient neurological symptoms. These observations have generated interest in an alternative local anaesthetic solution. Some investigators have examined small doses of spinal Bupivacaine to be used in surgical procedures lasting for less than one to two hours [3].

The addition of opiates like the lipophilic opioid Fentanyl to local anaesthetics produces many of its clinical effects very early after intrathecal administration. In the intra-operative period it enhances surgical anaesthesia and prolongs the duration of analgesia in the postoperative period. The study was designed to compare the efficacy of intrathecal Fentanyl along with Bupivacaine and Bupivacaine alone and their effect on prolonging the duration of postoperative analgesia in lower segment caesarean section without any adverse effects .

Materials and methods

The study protocol was approved by the ethical committee of Gandhi Medical College of NTR University of Health Sciences. A written, informed consent was obtained from all the patients. A total 50 patients were included in study. A clinical study was undertaken using spinal anaesthesia as an anaesthetic technique, to study the clinical effects of intrathecally administered preservative free Fentanyl along with hyperbaric Bupivacaine.

Inclusion criteria

- ASA physical status I and II patients scheduled for elective lower segment caesarean section surgery
- Age group of 18 –40 years
- Patients giving valid informed consent
- Those patients scheduled to undergo elective scheduled for lower segment caesarean section

Exclusion criteria

- Patient refusal
- Patients belonging to ASA physical status III and IV
- Patients physically dependent on narcotics
- Patients with history of drug allergy
- Patients with gross spinal abnormality, localized skin sepsis, hemorrhagic diathesis or neurological involvement / diseases
- Patients with cardiac, pulmonary, hepatic or renal disorders
- Patients with peripheral neuropathy

Visual analogue scale (VAS) constituting of 100mm line (with 0=no pain, 100=severe

possible pain) was explained to all patients in their preoperative check up.

Detailed history and a complete preoperative examination was made so as to exclude patients with any systemic disorders especially neurological disease and bleeding diathesis. All patients were subjected to routine investigations such as urine analysis, complete blood picture, blood sugar, blood urea and blood grouping and typing was obtained. Patients were randomly divided into two groups i.e., group FB and group B consisting of 25 patients each. Patients in group FB were given 8.5 mg of 0.5% hyperbaric Bupivacaine plus 25 µg (0.5 cc) of Fentanyl and group B received 8.5 mg of 0.5% hyperbaric Bupivacaine plus 0.5 cc of normal saline to adjust the final volume to 2.20 cc. The demographic and pre-anesthetic hemodynamic data were comparable in both the groups.

Technical Aspects

Premedication, especially with analgesics was avoided as this might influence and modify the hemodynamic changes produced. Preoperatively, heart rate and blood pressure of the patients were recorded and an intravenous line established with a large bore intravenous cannula in a large peripheral vein. Pre-loading with intravenous fluids with a dose of 15ml/kg of crystalloid solution (ringer lactate) infused over 20-30 minutes.

Intraoperatively heart rate, blood pressure, respiration and oxygen saturation levels of the patients were monitored at frequent intervals. Sterility was given vital importance since infection introduced from outside is a dangerous avoidable complication. After thorough scrubbing a sterile gown and gloves are worn. The necessary equipment, which includes towels, cotton swabs, swab holding forceps, a gallipot for skin cleaning solutions and glass syringes that were sterile packed were used. The patient's back was cleaned widely using surgical spirit and draped with sterile towels. The operating table was adjusted to a horizontal position. The patient was placed in the lateral decubitus position with the shoulders and anterior superior iliac spine in straight line with back of the patient parallel to the edge of the operating table nearest to the anaesthesiologist, with thighs flexed on the abdomen and neck flexed. Lumbar puncture was done using midline approach at L_3-L_4 space using a 23 gauge disposable quinckie needle which tends to split the dural fibres rather than cut them, when introduced with the bevel parallel to dural fibres. This was done to decrease the incidence of postspinal headache due to cerebrospinal fluid leak. After lumbar puncture was performed and subarachnoid space entered a free flow of cerebrospinal fluid was obtained and the drug, either 8.5 mg of 0.5% hyperbaric Bupivacaine with 25 µg of Fentanyl or 8.5 mg of 0.5% hyperbaric Bupivacaine with 0.5 cc normal saline was instilled and the time recorded. The patient was immediately turned into supine position for the rest of the study. Then crystalloids (ringer lactate) were infused 8 ml/kg for over 30 minutes. Later fluids were administered on the basis of changes in arterial pressure. All the patients received 100 percent oxygen via face mask till the baby is delivered.

The following parameters were recorded

- For the first 45 minutes during and after the spinal injection systolic, diastolic arterial pressures, heart rate, SpO_2 and respiratory rate were recorded every 5 minutes.
- Level of sensory block defined as loss of sharp sensation to pinprick, was recorded bilaterally at the midclavicular line for every 30 sec. until sensory analgesia established at T_{10} level, then every one minute until maximum level had stabilized for 3 consecutive tests, then testing was conducted every 15 minutes until 2 segmental regression occurred.
- Duration of 2 segment regression.
- Duration of Post-Operative analgesia was measured as the time between the administration of local anaesthetic with opioid intrathecally and first request for supplemental analgesic. 100mm visual

analogue scale was made use of. A score of 40 on the scale was taken as the end point of analgesia provided by the intrathecal administration of local anaesthetic with opioid.

- Any complications were noted – A decrease in systolic arterial pressure of more than 30 percent or more below preoperative levels as well as decrease in heart rate of more than 20 percent were considered significant and treated with 3mg ephedrine and 0.6mg atropine sulphate respectively. A respiratory rate less than 10 per minute and SpO_2 less than 90 percent were considered respiratory depression and was noted.

Patients were followed throughout their hospital stay and complications were recorded. The results were expressed as the arithmetic mean and standard deviation. A P value of less than 0.05 was considered as statistically significant.

Results

This study of the clinical effects of intrathecally administered Fentanyl (preservative free) along with 0.5% hyperbaric Bupivacaine was conducted in ASA-I and II patients undergoing elective lower segment caesarean section. There were 25 patients in each group. Preloading with intravenous fluids with a dose of 15 ml/kg of crystalloid solution (ringer lactate) infused over 20-30 minutes. 25 patients in the control group received 8.5 mg of 0.5% hyperbaric Bupivacaine with 0.5 ml of normal saline intrathecally. 25 patients in the study group received 8.5 mg of 0.5% hyperbaric Bupivacaine with 25 µg of Fentanyl intrathecally. The time of onset of analgesia, level of analgesia, adverse effects, treatment given, 2 segment regression time and the duration of analgesia were recorded. Pulse rate, blood pressure, peripheral arterial oxygen saturation and respiratory rate were recorded every 5 minutes. Duration of post-operative analgesia was measured as the time between the administration of local anaesthetic with opioid intrathecally and first request for supplemental analgesic. 100mm visual analogue scale was made use of. A score of 40 on the scale was taken as the end point of analgesia provided by the intrathecal administration of local anaesthetic with opioid. Time was noted, which indicated the duration of post-operative analgesia and supplemental analgesic by injection form was administered. The groups were demographically and hemodynamically similar in all respects as per **Table - 1**.

Table – 1: Patients characteristics and pre-operative hemodynamic variables.

Patient Characteristics	**Study Group (Group FB) n=25**	**Control Group (Group B) n=25**
Age (years)	23 + 3.65	23.5 + 3.61
Weight	62.6 + 7.43	60.9 + 5.58
Pulse Rate (/mt)	86 + 7.32	87 + 8.60
Systolic blood pressure (mm Hg)	120 + 9.35	119 + 10.9
Diastolic blood pressure (mm Hg)	79.2 + 6.40	78 + 8.16
Respiratory Rate (BPM)	17.6 + 2.02	16.9 + 2.14

FB group mean onset of analgesia 2 min 34 sec, B group mean onset of analgesia 2 min 44 sec. This showed that there was not much difference in the onset of analgesia between FB and B Groups. The values were statistically not significant (P >0.05).

Time to reach highest sensory level in group FB - 6.10 + 1.66 Minutes, group B - 6.20 + 1.01 Minutes.

The values were shown in mean and standard deviation. There was no significant difference

between the time to reach highest sensory level in both the groups (**Table – 2**). Majority of the patients in both the groups had highest sensory levels of T_4 as per **Table - 3**. There was no significant difference between the two groups in 2 segment regression.

In the Study Group i.e., Group FB duration of postoperative analgesia varies between 3.15 Hrs. to 4.30 Hrs.In the Control Group i.e., Group B the duration of postoperative analgesia is between 2.00 Hrs. to 4.00 Hrs.
Group FB mean duration 3 Hrs. 58 Mins.
Group B mean duration 3 Hrs.
Postoperative analgesia lasted longer in the Group FB than in Group B. There was a significant difference of duration of postoperative analgesia between the two groups (**Table – 4**).

Table – 2: Onset of Sensory Blockade and time to reach highest sensory level.

Onset of Sensory Blockade	**(Group FB) n=25**	**(Group B) n=25**
1 min	0	0
1 min 30 sec	2	1
2 min	7	9
2 min 30 sec	6	5
3 min	6	5
3 min 30 sec	3	1
4 min	1	2
4 min 30 sec	0	0
5 min	0	2
Time to reach highest sensory level		
4 min	2	1
4 min 30 sec	0	0
5 min	5	3
5 min 30 sec	0	2
6 min	7	9
6 min 30 sec	2	4
7 min	5	4
7 min 30 sec	1	0
8 min	1	1
8 min 30 sec	0	0
9 min	2	1

Table – 3: Highest Level of Sensory Block.

Level of sensory block	**(Group FB) n=25**	**(Group B) n=25**
T_6	7(28)	7(28)
T_5	4(16)	5(20)
T_4	14(56)	13(52)

Pruritus (20%) is the most common adverse effect followed by nausea, bradycardia and hypotension in Group FB. None of the patients had vomiting, shivering and respiratory depression. Only 6 patients (24%) had adverse effects in Group B out of which 3 patients (12%) had shivering, 2 patients (8%) had hypotension and 1 patient (4%) bradycardia (**Table – 5**).

Table – 4: Duration of postoperative analgesia.

Time	**(Group FB) n=25**	**(Group B) n=25**
2.00 Hrs.	0	1
2.15 Hrs.	0	1
2.30 Hrs.	0	3
2.45 Hrs.	0	3
3.00 Hrs.	0	9
3.15 Hrs.	2	5
3.30 Hrs.	6	0
3.45 Hrs.	5	0
4.00 Hrs.	5	3
4.15 Hrs.	2	0
4.30 Hrs.	5	0
4.45 Hrs.	0	0
5.00 Hrs.	0	0

* P Value < 0.05 is significant.

Table – 5: Complications in study.

Adverse Effects	**(Group FB) n=25**	**(Group B) n=25**
Nausea	3(12%)	0
Vomiting	0	0
Pruritus	5(20%)	0
Bradycardia	3(12%)	1(4%)
Hypotension	2(8%)	2(8%)
Shivering	0	3(12%)
Respiratory depression	0	0

Discussion

In recent years, neuraxial opioids have been increasingly used to augment the analgesia produced by local anaesthetics. Subarachnoid morphine has been widely used for this purpose to provide effective postoperative analgesia. Fentanyl may be advantageous over morphine because of its rapid onset of action, superior intra-operative conditions and lack of delayed respiratory depression. This study suggests that addition of 25µg of Fentanyl to 8.5 mg of 0.5% hyperbaric intrathecal Bupivacaine has no effect on the onset of analgesia to pinprick, height of the sensory block achieved and time to achieve maximum level. Fentanyl does not prolong the Bupivacaine sensory block but there is a significant prolongation of postoperative analgesia with addition of Fentanyl. Wang, et al. [4] found experimentally that there was a potential synergism between intrathecal Fentanyl and Bupivacaine. Our results are consistent with experimental effects of intrathecal opioids which showed that combination of opioids and local anaesthetics are synergistic for somatic analgesia. Intrathecal opioids can markedly enhance analgesia from subtherapeutic dose of spinal Bupivacaine. Intrathecal opioids appear to produce analgesia by inhibition of synaptic transmission in nociceptive afferent pathways (Aδ and C fibres) and yet, they donot inhibit conduction in sympathetic pathways or somatosensory evoked potentials. Thus, synergistic blockade of Aδ and C afferents allowed subtherapeutic concentration of hyperbaric Bupivacaine to maintain surgical anaesthesia during regression of spinal anesthesia. Thus our study results are consistent with an enhanced block of nociceptive afferents as a mechanism of improved analgesia with addition of Fentanyl to spinal Bupivacaine. In both the groups the mean onset of sensory block occurred between 2 minutes and 3 minutes in most of the patients (76%) and maximum level of sensory blockade at T_4 is achieved in 5 to 7 minutes. This observation shows that addition of Fentanyl to Bupivacaine does not influence Bupivacaine sensory block.

According to Hunt, et al. [5], the synergism between Fentanyl and Bupivacaine does not affect the onset of sensory block and the duration of motor block, but it facilitates an effective postoperative analgesia. Shende D, Cooper GM, Bowden [6] studied the effect of adding 15 µg Fentanyl to hyperbaric 0.5% Bupivacaine given intrathecally for elective caesarean section and concluded that onset times, neonatal outcomes were similar and duration of postoperative analgesia was prolonged in Fentanyl group. Roussel Jr., et al. [7] concluded that Fentanyl (25 µg) does not enhance the onset and duration of sensory and motor block produced by 12 mg of intrathecal Bupivacaine. In their study there was no significant difference between the 2 groups in two segment regression. Kan FC, T Sai YC, et al. [8] studied the effects of adding 25 µg Fentanyl to 5mg of hyperbaric Bupivacaine given intrathecally for caesarean section and disclosed that hemodynamic status was more stable in Fentanyl group, the incidence of nausea and vomiting appeared to be not statistically significant between groups, incidence of pruritus was apparently higher in Fentanyl group, but the incidence of shivering was much lower in Fentanyl group. The complete analgesia duration was longer in Fentanyl group. There was no significant difference in the anaesthetic and surgical status, 1 min and 5 min Apgar scores and the time of regression of sensory level to T_{10}.

In our study the mean duration of 2 segment regression in group FB was 100 minutes and in Group B was 94.8 minutes. So there was no significant difference in the duration of 2 segment regression in both the groups. This finding is in accordance with the Roussel Jr., et al. [7]. All the previous studies have shown that there is significant increase in the duration of postoperative analgesia with addition of Fentanyl to Bupivacaine. Our data shows that postoperative analgesia is better and longer lasting with addition of Fentanyl 25µg to Bupivacaine. The mean duration of postoperative analgesia in Group FB was 3 Hrs 58 Mins and Group B was 3 Hrs. This is a very

significant finding. This finding is in accordance with all other previous studies.

Ngiam SK, et al. [9], reported that pruritus would be frequently encountered after intrathecal opioid administration. According to Hunt, et al. [5] 25 to 50 µg Fentanyl in addition to intrathecal Bupivacaine increased the frequency of prutitis by 80%, which was statistically significant. According to our results the rate of pruritus is higher by 20% with intrathecal Bupivacaine and Fentanyl combination when compared to the control group. But it was well tolerated, none of the patients needed treatment.

The administration of intrathecal opioids carries the risk of respiratory depression. Fentanyl is much more lipid soluble than morphine and does not migrate intrathecally to fourth ventricle to cause respiratory depression. Liu, et al. [10] postulated that they did not observe any respiratory depression with the combination of intrathecal lidocane and 20µg Fentanyl, Hunt, et al. [5] and Varassi, et al. [11] did not report respiratory depression with intrathecal administration of Bupivacaine and 12.5µg Fentanyl.

In this study, we also did not observe respiratory depression. Our results are comparable with the results of Lin, et al. [10] and Varassi, et al. [11]. According to Chu, et al. [12], shivering subsided significantly with 12.5µg Fentanyl and Bupivacaine combination intrathecally. In our study shivering was not seen in Fentanyl group but 12% of patients in Bupivacaine group had shivering. In Bupivacaine group two patients had hypotension and one patient had bradycardia. Other complications with intrathecal Fentanyl in group FB was bradycardia (12%) nausea (12%), but none of the patient had vomiting, two patients had hypotension.

Conclusion

It was found that addition of 25 µg of Fentanyl to 8.5mg of 0.5% hyperbaric Bupivacaine has no effect on the onset of analgesia to pin prick, maximum level of analgesia and time to achieve maximum level. Fentanyl does not prolong the Bupivacaine sensory block but there was a significant prolongation of postoperative analgesia with addition of Fentanyl.

In conclusion, Fentanyl 25 µg does not enhance the onset and duration of sensory block produced by 8.5 mg of 0.5% hyperbaric intrathecal Bupivacaine. Fentanyl, however, prolongs postoperative analgesia and decreases the incidence of shivering, the incidence of pruritus is high, but it is usually mild. Intrathecal Fentanyl 25 µg along with 8.5 mg of 0.5% hyperbaric Bupivacaine is very much safer than other opioids like morphine which has more postoperative complications like intense pruritus and respiratory depression.

References

1. Alan R. Atkinkead, David J. Rowbotham, Graham Smith. Text Book of anaesthesia. Fourth edition, 2001.
2. Atkinson RS, Sushman GB, Davies NJH. Lee's synopsis of anaesthesia, Butterworth-Heinemann Medical, Eleventh edition, 1993.
3. Kuusniemi KS, Pihlajamäki KK, Pitkänen MT, Helenius HY, Kirvelä OA. The use of bupivacaine and fentanyl for spinal anesthesia for urologic surgery. Anesth Analg., 2000; 91: 1452–6.
4. Wang JK, Nauss LE, Thomas JE. Pain relief by intrathecally applied morphin in man. Anaesthesiology, 1997; 50: 149-51.
5. Hunt CO, Naulty JS, Bader AM. Perioperative analgesia with subarachnoid Fentanyl Bupivacaine for caesarean delivery. Anaesthesiology, 1989; 71: 535-540.
6. Shende D, Cooper GM, Bowden. The influence of intrathecal Fentanyl on the characteristics of subarachnoid block for caesarean section. Anaesthesia, 1998; 53: 706-710.

7. Roussel JR, Heindel L. Effects of intrathecal Fentanyl on duration of Bupivacaine spinal blockade for outpatient Knee Arthoscopy. AANAJ, 1999; 67(4): 337-43.
8. Kan FC, T Sai YC, Chang PJ, Chen TY. Subarachniod Fentanyl with diluted small dose Bupivacaine for caesarean delivery. Acta Anaesthesiol., 1998; 36(4): 207-14.
9. Ngiam SK, Chong JL. The addition of intrathecal sufentanil and Fentanyl to Bupivacaine for caesarean section. Singapore Med J., 1998; 39(7): 290.
10. Liu S, Chiu A, Carpenter RL, Mulroy MF, Allen HW, Neal JM, Pollock JE. Fentanyl prolongs lidocaine spinal anaesthesia without prolonged recovery. Anaesth Anlag., 1995; 80: 730-734.
11. Varrassi G, Celleno D, Capogna G, Costantino P, Emanuelli M, Sebastiani M, et al. Ventilatory effects of subarachnoid fentanyl in the elderly. Anaesthesia, 1992; 47: 558–62.
12. Chu CC, Shu SS, Liu SM. The effect of intrathecal Bupivacaine with combined Fentanyl in caesarean section. Acta Anaesthesiol., 1995; 33: 149-154.