INTRATHECAL FENTANYL WITH HYPERBARIC BUPIVACAINE IMPROVES ANALGESIA DURING CAESAREAN DELIVERY AND IN EARLY POST-OPERATIVE PERIOD

Dr. B. N. Biswas¹ Dr. A. Rudra² Dr. B. K. Bose³ Dr. S. Nath⁴ Dr. S. Chakrabarty⁵ Dr. S. Bhattacharjee⁶

SUMMARY

The use of neuraxial opioids has gained popularity over the last few years; they may augment the analgesia produced by local anaesthetic through direct binding with the specific spinal receptors. Fentanyl, a lipophilic opioid has rapid onset of action, it does not tend to migrate intrathecally to the 4th ventricle in sufficient concentration to cause delayed respiratory depression.

Forty healthy women of ASA grade I scheduled for elective Caesarean section were randomly allocated to receive either 2 ml of 0.5% inj bupivacaine with 0.25 ml of normal saline (group A, n=20) or 0.25 ml (12.5 microgram) fentanyl with 2 ml of 0.5% inj bupivacaine (group B, n=20). Vital signs, sensory level, motor block, pain score and side effects were observed every 2 min for first 20 min, then at 15 min interval for remainder of operation, thereafter at 30 min interval until the patient complained of pain.

Complete analgesia (time from injection to first report of pain) lasted longer in group B (183±9) than group A (129±9.5). The duration of effective analgesia (time from injection to first parenteral analgesic) was increased with the dose of intrathecal fentanyl 12.5 microgram (248±11.76). Pruritus was only 15% in fentanyl group.

Hence, addition of fentanyl to bupivacaine improves the quality of spinal anaesthesia.

Keywords : Spinal anaesthesia, Bupivacaine, Caesarean section, Intrathecal fentanyl, Postoperative analgesia.

Opioid added to local anaesthetic for spinal anaesthesia was first introduced into clinical practice in 1979 with intrathecal morphine as a forerunner. Neuraxial administration of opioids along with local anaesthetics improves the quality of intraoperative analgesia and also provide postoperative pain relief for longer duration.¹²

Animal studies have also demonstrated antinociceptive synergism between intrathecal opioids and local anaesthetics during visceral and somatic nociception.³⁴

Morphine is a hydrophilic agent, may not be optimal as an intrathecal drug for intraoperative analgesia because of its slow onset of action. It has prolonged duration of action, and delayed respiratory depression is not infrequent following spinal administration.

Fentanyl, a lipophilic opioid, has rapid onset of action following intrathecal administration. It does not tend to migrate to the fourth ventricle in sufficient concentration to cause delayed respiratory depression when administered intrathecally.⁵

Therefore, fentanyl provides better intraoperative analgesia and a safer alternative than morphine for management of early postoperative pain (4 hrs after intrathecal injection).

This study was designed to evaluate, the effects of intrathecally administered fentanyl (12.5 microgram) on the onset and duration of hyperbaric bupivacaine induced sensory and motor spinal block, quality of intraoperative surgical anaesthesia and requirements of analgesia during early postoperative period.

Methods

Following ethical committee is approval, patients were thoroughly explained regarding the nature of study. A written informed consent was obtained from all the patients.

Forty healthy women of ASA status I, scheduled for elective Caesarean section were randomly allocated to received either 2 ml of 0.5% inj. bupivacaine (hyperbaric) with 0.25 ml of normal saline (group A, n=20) or 0.25 ml (12.5 microgram) fentanyl, (using a tuberculin syringe)
with 2 ml of 0.5% inj. bupivacaine hyperbaric (group B, n = 20). All the study agents were introduced intrathecally and the total volume of agents administered was 2.25 ml.

The patients in whom regional anaesthesia was contraindicated or patients with foetal abnormalities and patients with allergies to the study medication were excluded from the study.

In the operating room an intravenous cannula (18 G) was inserted and patients received IV pre-hydration with 15 ml kg⁻¹ Ringer’s lactate solution. Pulse rate, blood pressure, rate of respiration and foetal heart rate were recorded before spinal anaesthesia.

Under all aseptic precautions lumbar puncture was performed with 25 gauge Quincke’s needle in the L₃ L₄ space in the sitting position and the study drugs were injected as per group of the patient according to random assignment. After noting the time of injection, patient was immediately placed in supine position. A wedge was placed under the right hip. All patients received supplementation of O₂ (3 litre per minute) via polymask. Immediately after administration of spinal anaesthesia, foetal heart rates were noted for any bradycardia. Pulse rate, blood pressure and rate of respiration, pain score, discomfort and occurrence of side effects i.e., pruritus, nausea, vomiting, shivering were recorded every 2 min for first 20 min, then at 15 min interval for remainder of the operation and thereafter at 30 min interval until the patient complained of pain. SpO₂ was monitored continuously in the operating room. In any patient who began to scratch or who complained of itching, intensity was assessed as either mild (itching was only a minor concern), moderate (itching was a primary concern, although bearable, and the patient said she would rather itch than hurt) or severe (unbearable, patient requested treatment).

The onset and duration of sensory block was assessed by pinprick method and time taken from intrathecal injection to the highest level of sensory block and sensory regression to the L₁ dermatome were recorded.

The onset and duration of motor block was noted. Grading of motor block was done as per scale Bromage.

O = No paralysis
1 = Inability to raise extended leg
2 = Inability to flex the knee
3 = Inability to flex the ankle (complete motor block)

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. The duration of complete analgesia (time from subarchoid injection to first reports of pain) (pain score greater than 0) and effective analgesia (time from subarchoid injection to first dose of rescue analgesic) were recorded.

Apgar scores were recorded at 1 and 5 min after delivery of baby.

Data were analysed by using unpaired ‘t’ test P value <0.05 was considered statistically significant. Data are presented as mean values ± SD and numbers (percent).

**Results**

The two groups were comparable with respect to ASA status, age, weight, height, intrathecal injection to delivery interval or surgical time as shown in table I.

<table>
<thead>
<tr>
<th>Table I: Demographic profile of two groups with mean S.D. values</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group A</strong> (Control)</td>
</tr>
<tr>
<td>------------------------</td>
</tr>
<tr>
<td>Number of patients</td>
</tr>
<tr>
<td>Age (years)</td>
</tr>
<tr>
<td>Weight (kg)</td>
</tr>
<tr>
<td>Height (inch)</td>
</tr>
<tr>
<td>Intrathecal injection</td>
</tr>
<tr>
<td>Surgical time (min)</td>
</tr>
<tr>
<td>Delivery interval (min)</td>
</tr>
<tr>
<td>SpO₂ (%)</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>

The highest sensory level achieved were T₇ (T₆–T₈) and T₅ (T₄–T₆) in group A and B.

The onset of bupivacaine induced spinal block was not enhanced in fentanyl group as shown in table II. The time intervals (duration) for sensory level to regress to L₁ dermatome were prolonged in fentanyl group but duration of motor blocks was not prolonged in fentanyl group as shown in table II.

<table>
<thead>
<tr>
<th>Table II: Characteristics of sensory and motor block</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group A</strong> (Control)</td>
</tr>
<tr>
<td>Higher sensory level (range)</td>
</tr>
<tr>
<td>Time for injection to highest sensory level (min)</td>
</tr>
<tr>
<td>Time for sensory regression to L₁ from highest sensory level (min)</td>
</tr>
<tr>
<td>Onset of grade III motor block (min)</td>
</tr>
<tr>
<td>Duration of grade I motor block (min)</td>
</tr>
</tbody>
</table>

*P<0.05 considered significant (unpaired ‘t’ test)

No statistically significant difference in motor block.
12.5 microgram fentanyl with 0.5% hyperbaric bupivacaine markedly improved the quality of intraoperative surgical anaesthesia as none of the patients in this group complained of discomfort compared with seven patients in control group, as shown in table III.

Table - III : Complaint of discomfort in intraoperative period and duration of complete analgesia and effective analgesia

<table>
<thead>
<tr>
<th></th>
<th>Group A (Control)</th>
<th>Group B (Fentanyl 12.5 microgram)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complaint of discomfort by patients</td>
<td>7 (35%)</td>
<td>0 (Nil)</td>
</tr>
<tr>
<td>Complete analgesia (min) (from subarachnoid injection to first complain of pain)</td>
<td>129±9.5</td>
<td>183±9*</td>
</tr>
<tr>
<td>Effective analgesia (min) (time from injection to rescue analgesic)</td>
<td>150±10.48</td>
<td>248±11.76*</td>
</tr>
</tbody>
</table>

Values are mean±S.D.  
*P<0.05 considered significant (unpaired 't' test)

Complete analgesia lasted longer in group B (fentanyl group) for 183 ± 9 min compared with group A (control group) 129 ± 9.5 min, as shown in table III. The duration of effective analgesia (time from subarachnoid injection to rescue analgesia) was prolonged in group B, as compared with group A, as shown in table III.

Three patients out of twenty in group B complained of mild pruritus, however symptoms were self limiting.

There was no difference in the number of patients experiencing episodes of bradycardia (HR<60/min), hypotension (fall of systolic BP>20% from base level), Respiratory depression (RR<9 breaths min⁻¹ or SaO₂<90%), desaturation (SpO₂<90%) in all groups of patients as shown in table IV. Hypotension was treated with rapid infusion of fluids and giving Trendelenburg position. None of the patients required vasoactive drugs to raise their blood pressure. And bradycardia was treated with administration of atropine 0.2mg intravenously. Incidence of emetic episodes were less in fentanyl group than in control group. Fewer patients requested for rescue analgesic in early postoperative period in fentanyl group than in control group as show in table IV.

Discussion

Administration of fentanyl intrathecaly is an established method for intraoperative anaesthesia and to supplement postoperative anagesia. The Spread of fentanyl after administration into cerebrospinal fluid include, movement from the cerebrospinal fluid into the opioid receptors or other non-specific binding sites in the spinal cord and rostral migration via the cerebrospinal fluid to supraspinal sites. Because of the high affinity of fentanyl with nonspecific binding sites on the lipid surface only a small proportion of the administered dose migrates to the cervical region.

Use of morphine, via subarachnoid route in the routine postoperative pain management has been limited for greater incidence of side effects, particularly respiratory depression.

Fentanyl is more lipid soluble than morphine, which is more readily eliminated from the cerebrospinal fluid than morphine making late respiratory depression less likely.

Advantage of using intrathecal fentanyl is its extremely rapid onset of action. Analgesia has been reported to occur within 5-10 min.

Epidurally administered fentanyl in doses of 50-100 microgram has been shown to provide postoperative analgesia of 3-4 hr duration. This was similar to our duration of effective analgesia following 12.5 microgram doses of subarchoid fentanyl.
Results of this study showed that fentanyl 12.5 microgram prolongs the duration of bupivacaine induced sensory blockade (sensory regression to L1 dermatome). This suggests a potential synergism between fentanyl and bupivacaine, as reported in animal study by Wang et al.4

In our study, three patients (15%) belonging to group B, receiving 12.5 microgram fentanyl complained of pruritus which corroborated with reported result of Hunt et al.2 We assessed the intensity of pruritus as mild, moderate or severe, according to previous worker Herman et al11 study.

Use of any drug in the subarachnoid space is the cause for its neurotoxicity. Animal studies have demonstrated the safety of fentanyl in this regard.12,13 None of the patients in this study experienced any neurological complication during postoperative follow-up.

There have been reports of life threatening respiratory depression when intrathecal lipophilic opioids have been used for labor analgesia.14,15 During Caesarean delivery, however, significant sedation or respiratory depression has not been observed.2,16 In our study no patient in either group experienced respiratory depression (RR<9min-1 or SpO2<90) or sedation.

Intraoperative nausea and vomiting occurs in as many as 66% of Caesarean deliveries mainly related to peritoneal traction and exteriorization of the usterus performed with regional anaesthesia.17 In this study emetic episodes were less than control (group A), which corroborated with observations of Manullang et al18 and Dahlgren et al16 study.

There were no differences in neonatal Apgar scores among the groups, which were similar with observations of Hunt et al2 and Shende et al19 study.

The dose of fentanyl 12.5 microgram had been chosen in our study, because it was mid range for doses quoted in the literature.2,20

In conclusion, the results of our study indicated that 12.5 microgram of fentanyl added with hyperbaric 0.5% bupivacaine for spinal anaesthesia would markedly improve intraoperative anaesthesia, and significantly reduced the demand for postoperative analgesics with good maternal satisfaction and foetal well being.

Reference
1. Abouleish E, Rawal N, Shaw J, Lorenz T, Rashad MN. Intrathecal morphine 0.2 mg versus epidural bupivacaine 0.125% or their combination; effects on parturients. Anesthesiology 1991; 74; 711-6.