To Evaluate Fentanyl as an Adjuvant to Intrathecal Bupivacaine for Lower Segment Cesarean Section

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Abstract
Objective: To compare efficacy of subarachnoid block with bupivacaine alone and low dose bupivacaine with fentanyl as adjuvant in terms of, onset and duration of anaesthesia and post-operative analgesia.
Materials and Methods: Present prospective randomized case control study was conducted in 60 patients undergoing elective caesarean section. They were randomly divided into two groups of 30 each. Subarachnoid block was standardized. Haemodynamic parameters, onset and duration of sensory and motor blockade, post-operative analgesia and side effects (if any) were compared. Data was analysed using student’s unpaired t-test.
Results: Onset of analgesia was earlier in Group BF (1.36±1.30 min) compared to Group B (1.81±1.61 min) which was statistically significant (p<0.05). Duration of two segment regression in Group BF (81.21±9.40 min) was significantly prolonged than Group B (62.4±14.81 min) which was statistically significant (p<0.05). Duration of sensory blockade in Group BF (124±9.36 min) was significantly more than Group B (104.7±6.40 min) which was statistically significant (p<0.05). In Group BF, onset of motor blockade was delayed and duration of motor blockade was less as compared to Group B, which was statistically not significant (p>0.05). Postoperative analgesia in Group BF (194±16.82 min) was significantly prolonged than Group B (108.57±7.90 min) which was statistically significant (p<0.05).
Conclusion: Addition of fentanyl to bupivacaine resulted in faster onset of action and effective spinal anaesthesia with a lower dose of bupivacaine.

Keywords: Bupivacaine, Caesarean section, Fentanyl, Subarachnoid block

Introduction
Subarachnoid block is a preferred technique for caesarean delivery, as it is easy to perform, economical, produces rapid onset of anaesthesia and complete muscle relaxation with lower incidence of failed block, neonatal depression and aspiration pneumonitis¹. Intrathecal bupivacaine during caesarean section produce dose dependent sensory and motor block and cardiac toxicity². It is more potent than lignocaine and has a longer duration of action. It has been used in obstetric anaesthesia with remarkable safety³ but has slow onset of action and less motor blockade⁴. Therefore, intrathecal opioids are commonly added to it for potentiating their effects, reducing their doses and thereby side effects and complications. Opioids also prolong the duration of postoperative analgesia⁵. Fentanyl is a lipophilic opioid with a rapid onset following Intrathecal injection. It improves quality of anesthesia without producing significant side effects and prolongs post-operative analgesia⁶-¹⁰.

Aim of present study was to compare efficacy of subarachnoid block with bupivacaine alone and low dose bupivacaine with fentanyl as adjuvant in terms of, onset of analgesia, duration of two segment regression time, duration of sensory blockade, onset of motor blockade, duration of motor blockade and duration of post-operative analgesia.

Material and Methods
After approval from institutional ethical committee, present prospective randomized case control study was conducted in Department of Anaesthesiology, Tertiary care hospital, during July 2009 to August 2010 in 60 patients posted for elective caesarean section.

Inclusion Criteria: Women between 18 to 30 years with ASA grade I and II posted for elective cesarean section were included.

Exclusion Criteria: Patients with ASA grade III and above, those posted for emergency cesarean section, allergic to study drugs, having contraindications to regional anaesthesia and those refused to participate in study were excluded.

After a thorough pre-anaesthetic evaluation of all patients, a written and informed consent was obtained, both for conduct of study as well as administration of subarachnoid block. They were kept nil by mouth for...
eight hours before surgery. Intravenous access was established with 18G intravenous canula and preloading was done with 15 ml/kg Lactated Ringer’s (RL) solution and they were premedicated with intravenous ondansetron 4mg and ranitidine 50mg half-hour before the procedure. Anaesthesia machine, accessories, monitors and drugs were checked.

All patients were randomly divided into two groups using computer generated randomization technique.

- Group B (Bupivacaine group) (n=30)
- Group BF (Bupivacaine + Fentanyl group) (n=30)

Under strict aseptic precautions, in lateral position, subarachnoid block was performed at L3-L4 intervertebral space with a 25G spinal needle. Group B: Patients received 10mg of 0.5% heavy Bupivacaine (2ml) and Group BF: Patients received 7.5 mg of 0.5% heavy Bupivacaine (1.5ml) with 25μg preservative free Fentanyl (0.5ml).

Onset and duration of sensory blockade, duration of two segment regression, onset and duration of motor blockade (by modified Bromage scale), hemodynamic parameters like heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure at 2 minute intervals for first 10 minutes, then at 5 minute intervals for next 30 minutes and at 15 minute intervals till 2 hours after giving study drug, ECG, SpO2 and post-operative complications (nausea, vomiting, shivering, pruritis) if any were noted. Duration of sensory blockade was taken from time of intrathecal injection to Visual Analogue Scale (VAS) > 2; at this point patients received rescue analgesia. Postoperatively, they were monitored for analgesia using VAS for 24 hours. Sample size was calculated using Open Epi, Version 3, open source calculator – SS mean on internet with confidence interval of 99%, power of 95% and ratio of two groups at 1:1; which was minimum 26 participants per group. All data was expressed as Mean±Standard deviation(SD). Statistical analysis was done by student’s unpaired t-test, p value <0.05 was considered significant.

### Results

Demographic profile was comparable in both the groups (p-value > 0.05) (Table 1). Onset of analgesia was earlier in Group BF (1.36±1.30 min) compared to Group B (1.81±1.61 min) which was statistically significant (p<0.05). Duration of two segment regression in Group BF (81.21±9.40 min) was significantly prolonged then Group B (62.4±14.81 min) which was statistically significant (p<0.05). Duration of sensory blockade in Group BF (124±9.36 min) was significantly more than Group B (104.7±6.40 min) which was statistically significant (p<0.05). In Group BF, onset of motor blockade was delayed (1.78±3.70 vs 1.26±4.21 in Group B) and duration of motor blockade was less as compared to Group B (Group BF 73.4±12.70, Group B 96.4±8.21), which was statistically not significant (p>0.05). (Table 2)

Postoperative analgesia in Group BF (194±16.82 min) was significantly prolonged then Group B (108.5±7.90 min) which was statistically significant (p<0.05). (Table 3)

Nausea and pruritis were seen in both the groups whereas vomiting and shivering was seen only in Group B. (Table 4)

### Table 1: Distribution according to Demographic profile (N=60)

<table>
<thead>
<tr>
<th>S. No</th>
<th>Parameters</th>
<th>Group-BF (n=30) (Mean ± SD)</th>
<th>Group-B (n=30) (Mean ± SD)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Age (year)</td>
<td>21.56±3.42</td>
<td>21.00±2.50</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>2</td>
<td>Height (cm)</td>
<td>148.70±4.41</td>
<td>150.40±3.88</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>3</td>
<td>Weight (kg)</td>
<td>52.63±4.95</td>
<td>54.96±5.30</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>4</td>
<td>Duration of Surgery (min)</td>
<td>53.95±8.95</td>
<td>56.28±4.30</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

p-value<0.05 is taken as significant

### Table 2: Comparison of study parameters in both groups (N=60)

<table>
<thead>
<tr>
<th>S. No</th>
<th>Parameters(Min)</th>
<th>Group-BF (n=30) (Mean ± SD)</th>
<th>Group-B (n=30) (Mean ± SD)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Mean onset of sensory blockade</td>
<td>1.36±1.30</td>
<td>1.81±1.61</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>2</td>
<td>Mean two segment regression time</td>
<td>81.21±9.40</td>
<td>62.4±14.81</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>3</td>
<td>Mean duration of sensory blockade</td>
<td>124±9.36</td>
<td>104.7±6.40</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>4</td>
<td>Mean onset of motor blockade</td>
<td>1.78±3.70</td>
<td>1.26±4.21</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>5</td>
<td>Mean duration of motor blockade</td>
<td>73.4±12.70</td>
<td>96.4±8.21</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

p-value<0.05 is taken as significant
p-value<0.05 is taken as significant

**Table 3: Comparison of post-operative analgesia (N=60)**

<table>
<thead>
<tr>
<th>S. No</th>
<th>Complication</th>
<th>Group-BF (n=30) (Mean ± SD)</th>
<th>Group-B (n=30) (Mean ± SD)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Post-operative analgesia(Min)</td>
<td>194±16.82</td>
<td>108.57±7.90</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

**Table 4: Comparison of postoperative complications (N=60)**

<table>
<thead>
<tr>
<th>S. No</th>
<th>Complication</th>
<th>Group-BF (n=30)</th>
<th>Group-B (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Nausea</td>
<td>1(3.33%)</td>
<td>2(6.66%)</td>
</tr>
<tr>
<td>2</td>
<td>Vomiting</td>
<td>Nil</td>
<td>1(3.33%)</td>
</tr>
<tr>
<td>3</td>
<td>Shivering</td>
<td>Nil</td>
<td>4(13.33%)</td>
</tr>
<tr>
<td>4</td>
<td>Pruritis</td>
<td>5(16.66%)</td>
<td>2(6.66%)</td>
</tr>
</tbody>
</table>

**Discussion**

Many studies have shown that combination of opioids and local anesthetic agents administered intrathecally has a synergetic analgesic effect. Intrathecal fentanyl has faster onset of action, it improves quality of intraoperative analgesia and also helps to reduce intrathecal doses of local anaesthetic agents. It is associated with less side effects and provides good postoperative analgesia.

Demographic profile and hemodynamic parameters were comparable in both the groups.

Onset of sensory blockade in BF groups was early then bupivacaine group, which is statistically significant (p<0.05). This shows fentanyl has accelerated onset of sensory blockade, this is in accordance with prior studies.

Duration of two segment regression and duration of sensory blockade was significantly prolonged in Group BF(p<0.05). Sergio DB concluded that duration for regression below T12 dermatome was longer and increased with increasing dose of fentanyl.

In Group BF, onset of motor blockade was delayed and duration of motor blockade was less as compared to Group B, which was statistically not significant (p>0.05) which is similar to previous studies.

Onset of motor blockade was earlier in Group B as 10 mg of 0.5% hyperbaric bupivacaine was used compared to only 7.5 mg in group BF and fentanyl has no effect on motor blockade. Early motor recovery in group BF decreases incidence of side effects like deep vein thrombosis, thereby reducing morbidity. Early mobilization also increases patient’s comfort and reduces the emotional as well as psychological disturbance.

Intrathecal bupivacaine causes dose dependent inhibition of both Aδ and C nerve fibers and there is no selectivity for either afferent or efferent pathways whereas intrathecal fentanyl selectively enhances the effects of bupivacaine on afferent nociceptive pathway, but without any effect on efferent pathway.

Post operative analgesia was monitored using VAS Score. In Group BF, it was significantly prolonged then Group B which was statistically significant (p<0.05). This suggests synergy between fentanyl and bupivacaine.

Side effects like nausea, vomiting, shivering and pruritis were observed during study period. Nausea following subarachnoid fentanyl is presumably due to their interaction with opioid receptors of the chemoreceptor trigger zone (CTZ) located on floor of fourth ventricle. However, 25μg fentanyl which is highly lipophilic do not remain free in the cerebrospinal fluid long enough when administered in the subarachnoid space at the lumbar level to reach CTZ in sufficient concentration to induce vomiting. However, it sufficiently augments local anesthesia mediated block to decrease nociceptive stimulation which occurs during maneuvers like peritoneal traction and thus reduces nausea and vomiting.

Shivering was observed only in Group B. Reduction in shivering with fentanyl could be due to decreased thermal inputs at the spinal cord. Opioids also stimulate cAMP formation which increases the thermo sensitivity in warm sensitive and moderate slope temperature insensitive neurons.

Pruritis was noticed more in Group BF but was of short duration and low intensity and did not require any treatment. It could be due to activation of μ opioid receptors located in the dorsal horn of spinal cord.

**Conclusion**

Fentanyl has synergistic action with bupivacaine. It provides excellent sensory blockade and prolongs postoperative analgesia. It also helps in reduction of the dose of bupivacaine for spinal anesthesia, thus reduces side effects associated with it and helps in early ambulation of patients thus assures better quality of anaesthesia.

**References**