Original article:

Effect of Intrathecal Fentanyl on subarachnoid block with 0.5% hyperbaric bupivacaine

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Abstract:

Background and objectives: Subarachnoid block is most versatile regional block commonly employed for infraumbilical surgeries. The use of neuroaxial opioids has gained widespread popularity as they potentiate the analgesia produced by local anesthetics. Hence the present study was undertaken to evaluate the effects of intrathecally administered fentanyl (25mcg) on the characteristics of hyperbaric bupivacaine induced subarachnoid block and adverse effects of fentanyl.

Methods: In this prospective randomized study eighty ASA grade I and II patients scheduled for elective gynecological surgeries were assigned to receive either 3ml of 0.5% hyperbaric bupivacaine with0.5ml of CSF (Group I) or 3ml of 0.5%hyperbaric bupivacaine and 0.5ml of fentanyl(25mcg,Group II). Vital signs, sensory, motor block and side effects were observed every 1 minute for first 30 minutes, at 10 minutes for an hour and at every 30 minutes till recovery.

Results: Onset of sensory and motor block was comparable in both groups. Two segment regression and the duration of analgesia was significantly prolonged in group II i.e. 134.12±10.81 and 207±17.57 minutes respectively compared to group I i.e-89.85±10.98 and 192.12±21.04minutes respectively. Intraoperatively 75% [30] of patients in group I needed sedation and 10 % (4) patients had to be administered GA, however none required supplementation in group II, which was statistically highly significant. There was no significant statistical difference in the incidence of side effects in both the groups.

Conclusion: This study confirmed that addition of fentanyl (25mcg) to 0.5% hyperbaric bupivacaine for spinal anesthesia would markedly improve the quality of intraoperative analgesia with minimal side effects.

Key words: Spinal anesthesia, 0.5% hyperbaric bupivacaine, Gynecological surgery, Intrathecal fentanyl, Side effects.

1. Introduction

The unmatchable reliability and simplicity of subarachnoid block has made spinal anesthesia a very useful and successful technique in managing all surgical cases undergoing infraumbilical procedures. Currently it has become more popular because of addition of opioids to local anesthetics in centroneuroaxial blockade which provides better intraoperative analgesia and early postoperative analgesia.

Bupivacaine was introduced by Eckenstam in 1957 and used clinically by Telivno in 1963. Currently hyperbaric bupivacaine is being used with opioids for almost all surgical cases. Bupivacaine an amide type of local anesthetic has high potency, slow onset (5-8 minutes) and long duration of action. Although intrathecal bupivacaine alone offers good sensory blockade, a substantial number of patients experiences some pain and discomfort and may require analgesic supplements intraoperatively. Addition of fentanyl not only improves quality of intraoperative analgesia but it also extends to early postoperative period.

The advantages of spinal anesthesia not only includes the simplicity of the technique and the rapid onset of anesthesia but it also has an option of using spinal opioids for pain relief. Morphine is a forerunner of spinally instilled opioids and was introduced in the clinical practice in 1979.
neuroaxial administration of opioids along with local anesthetics improves the quality of intraoperative analgesia and also provides postoperative pain relief for longer duration\textsuperscript{8,9}. However morphine is hydrophilic agent and may not be optimal opioid intrathecally because of its slow onset of action, also its delayed respiratory depression is not infrequent\textsuperscript{10}. Compared to morphine, fentanyl is lipophilic, has rapid onset of action and it does not tend to migrate to the fourth ventricle in sufficient concentration when administered intrathecally\textsuperscript{11}. Fentanyl not only improves the quality of intraoperative analgesia but also reduces the need of supplemental sedation\textsuperscript{12}. Hence, the purpose of this study was to evaluate the effects of intrathecally administered fentanyl (25mcg) on the onset and duration of hyperbaric bupivacaine induced sensory and motor block, quality of intraoperative analgesia and side effects associated with its intrathecal use.

2. Materials and Methods:
2.1 - Study protocol
Present study was conducted at Government Medical College, Nagpur during the period of February 1997 to June 1999 in the residency programme of the author as a topic of thesis, it was started with approval of institutional ethical committee and written informed consent was taken from all the patients willing to participate in the study.

Inclusion criteria
- ASA I and II
- Age 20-60 years of either sex.
- Willingness for spinal anesthesia

Exclusion criteria
- Patient with spinal deformity
- Cardiopulmonary diseases
- Coagulation disorder
- Local sepsis
- Patient with psychiatric or neurological disorder
- Not willing for spinal anesthesia

2.2 - Study plan
Preanesthetic examination was carried out in detail which included general, systemic, airway and spine examination. All baseline investigations were done including Hb, CBC, basal blood sugar, blood urea, sr. creatitinine and urine routine. ECG and X chest may advised if indicated.

The patients were divided randomly with the help of random number table into two groups containing 40 patients in each group.

Group I patients received 3ml of 0.5% hyperbaric bupivacaine plus 0.5ml of CSF and Group II patients received 3ml of 0.5% hyperbaric bupivacaine and 0.5ml of fentanyl (25mcg preserved free).

2.3 - Materials
- Inj. Bupivacaine 0.5% heavy preservative free (Sensorcaine Astra)
- Inj. Fentanyl 50mcg/ml-2ml ampoule preserved free (Trofenta Astra)
- Autoclaved spinal tray
- 23G spinal needle
- 5cc syringe
- Emergency drugs and equipments of resuscitation.

After shifting the patient on the OT table, monitors like NIBP and ECG monitors were applied. Baseline Pulse rate, respiratory rate and blood pressure were recorded. IV access was gained using 18G canula and preloading with 10ml/kg RL was done. Premedications Inj. Metoclopramide 10mg and Ranitidine 50mg were given IV. Table position was kept neutral.

Under all aseptic precautions with patient placed in lateral position spinal was given with 23G spinal needle in L3-4 interspace with midline approach.
The patients were immediately turned supine following injection.

2.4 - Monitoring
Intraoperatively pulse rate, respiratory rate and blood pressure monitoring was done at 1 minute interval for 30 minutes and then at every 10 minutes. Pulse oximeter was not available for \( \text{SpO}_2 \) monitoring.

2.5 - Sensory block assessment
Sensory level was tested by using blunt 21G needle by pin prick method. The onset of sensory analgesia was defined as a time interval from completion of intrathecal injection to the loss of pinprick at dorsum of foot. Highest sensory level was tested in midclavicular line at every minute until the level stabilized for two consecutive tests. Then it was tested every 10 minutes till complete recovery.

Two segment regression and complete sensory recovery were recorded as duration of anesthesia. Time taken to achieve peak sensory level, two segment regression and complete sensory recovery was noted for each patient.

2.6 - Motor block assessment
The onset of motor block was defined as a time from injection of drug in subarachnoid space till the patient was unable to raise the extended leg (grade I). The degree of motor block was assessed with modified Bromage scale. Motor blockade recovery was recorded every 10 minutes. Duration was again calculated from injection time to recovery of motor block.

2.7 - Monitoring and treatment of side effects
Intraoperative side effects such as hypotension, bradycardia, respiratory depression, nausea, vomiting, shivering and pruritus were looked for till complete recovery.

Hypotension was defined as a fall in systolic blood pressure of more than 30% of baseline value, it was treated with \( \text{O}_2 \) supplementation, fast IV fluid or inj. Mephenytoin 6mg IV if needed.

Bradycardia was defined as a fall in pulse rate below 60 beats/minute. Inj. Atropine 0.6mg was given if needed. Respiratory depression was defined as respiratory rate less than 10/minute. Inj. Naloxone was kept ready if required.

2.8 - Assessment for additional sedation
IV. Pentazocine 30mg was administered if patients complained about any discomfort or pain. GA was supplemented if the discomfort is intolerable.

2.9 - Assessment of analgesia
Postoperatively the patients were evaluated for pain at operation site and rescue analgesia was advised.

2.10 - Observations for postoperative side effects
All patients were observed 24 hours for postoperative complications like nausea, vomiting, pruritus, respiratory depression, post spinal headache, hypotension, bradycardia and any neurodeficient.

2.11 - Statistical analysis
\( Z \) test was applied to test statistical significance between the means of two groups. The Chi-Square test was used to find dependencies between two groups. A value of \( P<0.05 \) was considered to be significant.

3. Results
There was no statistical difference among both the groups as far as age, height and duration of surgery concerned.
Table 1: Demographic profile among two groups

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Mean ± SD values</th>
<th>Group I</th>
<th>Group II</th>
<th>( p &gt; 0.05 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td></td>
<td>38.30 ± 3.14</td>
<td>36.82 ± 3.66</td>
<td></td>
</tr>
<tr>
<td>Height (cm)</td>
<td></td>
<td>161.17 ± 8.8</td>
<td>160.9 ± 9.12</td>
<td>( p &gt; 0.05 )</td>
</tr>
<tr>
<td>Duration of surgery (min)</td>
<td></td>
<td>119.5 ± 25</td>
<td>122.6 ± 22</td>
<td>( p &gt; 0.05 )</td>
</tr>
</tbody>
</table>

\[ \text{p} > 0.05 \text{- nonsignificant, } \text{p<0.05} \text{- significant, } \text{p<0.01} \text{- highly significant} \]

The time required for onset of sensory analgesia, maximum cephalic spread and maximum analgesic block (segment) were comparable in both groups. The onset of motor block and time taken for complete motor block were also statistically insignificant. All patients in both groups had complete motor block (grade 3). Mean time for two segment regression in group I was 89.85 ± 10.98 minutes and in group II was 134 ± 10.81 minutes (\( p < 0.01 \)) which is highly significant. (Figure 1)

Duration of analgesia was evaluated as from time of spinal injection to the time when patient had discomfort or pain. Mean duration of analgesia in group I was 192.12 ± 21.04 minutes while in group II it was 207.5 ± 17.57 minutes (\( p < 0.01 \)) which is statistically highly significant (figure 5).

Table 2: Characteristics of spinal blockade seen in both the groups

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean ± SD values</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group I</td>
<td>Group II</td>
</tr>
<tr>
<td>Onset of sensory analgesia (min)</td>
<td>2.27 ± 0.372</td>
<td>2.2 ± 0.372</td>
</tr>
<tr>
<td>Time for maximum cephalic spread (min)</td>
<td>12.17 ± 3.75</td>
<td>11.72 ± 3.5</td>
</tr>
<tr>
<td>Maximum analgesic block (segment)</td>
<td>( T_{5.7} )</td>
<td>( T_{5.7} )</td>
</tr>
<tr>
<td>Onset of motor block (min)</td>
<td>3.41 ± 0.99</td>
<td>3.5 ± 0.94</td>
</tr>
<tr>
<td>Time for complete motor block (min)</td>
<td>7.15 ± 2.39</td>
<td>7.37 ± 2.41</td>
</tr>
<tr>
<td>Time for two segment regression (min)</td>
<td>89.85 ± 10.98</td>
<td>134.12 ± 10.81</td>
</tr>
<tr>
<td>Mean duration of analgesia (min)</td>
<td>192.12 ± 21.04</td>
<td>207 ± 17.57</td>
</tr>
</tbody>
</table>

\( P > 0.05 \) not significant, \( P < 0.05 \) significant, \( P < 0.01 \) highly significant.

Intraoperatively the systolic blood pressure, heart rate and respiratory rate of the patients were monitored. The incidence of hypotension, fall in mean intraoperative systolic blood pressure, changes in pulse rate (figure 2, 3) and comparison of mean respiratory rate in preoperative and intraoperative period were comparable.

Incidences of intraoperative side effects were also comparable. Mild pruritus was complained by 2(5%) patients in group II but did not required any treatment.
Table 3: Comparison of hemodynamic variables intraoperatively between both groups.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean±Sd values</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimal systolic BP (mm of Hg)</td>
<td>96.90 ± 6.30</td>
<td>94.20 ± 5.07</td>
</tr>
<tr>
<td>Minimal pulse rate (min)</td>
<td>87.13 ± 5.03</td>
<td>86.47 ± 3.30</td>
</tr>
<tr>
<td>Mean respiratory rate (breath per min)</td>
<td>16</td>
<td>16.07</td>
</tr>
</tbody>
</table>

p>0.05 not significant, p<0.05 significant, p<0.01 highly significant.

Assessment for requirement of additional sedation was done. 30(75%) patients of group I were supplemented with IV sedation (i.e. titrated doses of Pentazocine or Ketamine IV) and 4(10%) patients required GA, however none of the patients of group II needed any sedation or GA. (figure 4)

Postoperatively vomiting and nausea was complained by 2(5%) patients of group I and was treated with inj. metoclopramide 10mg. Other side effects such as shivering, itching, hypotension, bradycardia, respiratory depression, postspinal headache, backache were not seen in either groups.

4. Discussion

In the context of ‘Augmentation strategies’ for epidural and intrathecal analgesia, the discovery of opioid receptors and subsequent development of the technique of epidural and intrathecal opioid administration is undoubtedly one of the most significant advances in pain management of last four decades. plethora of studies has shown that spinal opioids can provide profound analgesia with fewer central and systemic adverse effects than the opioids administered systemically. Segmental analgesia induced by spinal administration of opioids is being used successfully.

The present study was conducted in 80 patients of ASA I and II undergoing elective gynecological (abdominal and vaginal hysterectomy) surgeries. All of them received spinal anesthesia. Patients in both groups were comparable in respect of age, sex, height and duration of surgery.

4.1 Effect on sensory and motor blockade

In this study the mean time for the onset of sensory analgesia and maximum cephalic spread were similar in both groups. Peak analgesic block attained varied between T5-7. The addition of fentanyl to bupivacaine did not alter the onset of sensory analgesia or height of the block. Jaishri Bogra et al4, Agrawal et al5, B.N. Biswas et al14, Hunt Co etal6, Catherine O et7, Harbhej Singh etal8 and G. Dahlgren et al9 also found similar results in their studies. In our study, the time to reach peak sensory level was comparable among the groups in contrast to study by P.R. Dhumal et al12, it is expected because opioids have synergistic effect with local anesthetics10. Shende D etal14 found in their study that sensory block to T4 was achieved after 6.5 min in those who received fentanyl compared to 8 min in the control group. This trend in above two groups was not observed in the present study. Results similar to present study were found with Harbhej Singh et al10, Bruce Ben David et al13 and Catherine O et al7. Better degree of analgesia in Group II seen in our study was due to synergism of fentanyl and bupivacaine and effectiveness of fentanyl in abolishing visceral pain. Jaishri Bogra et al4 found in their study that bupivacaine alone could not completely remove the visceral pain. Bupivacaine-Fentanyl combination was effective in abolishing visceral pain. Onset of motor blockade was comparable in both the groups and fentanyl has no action on motor blockade9,10,12,13. All patients had grade III motor block. The addition of fentanyl had no effect to
enhance the onset or degree of motor blockade. Jaishri Bogra et al\textsuperscript{4} and Dahlgren G et al\textsuperscript{9} also found that onset and degree of motor blockade was comparable in their study groups.

4.2 - Effects on vitals

Virtually all hemodynamic variables including heart rate, arterial blood pressure, respiratory rate remain unchanged. None of the patients experienced bradycardia (i.e. pulse rate <60bpm) in group I and in only 2(5%) patients had bradycardia in group II and these patients responded to injection atropine 0.6mgIV. Studies conducted by Agrawal A et al\textsuperscript{5}, Jaishri Bogra et al\textsuperscript{4} and various authors\textsuperscript{6,7,8,14}) also showed same results. Belzerena et al\textsuperscript{15} studied the effects of different dosage of intrathecal fentanyl and observed no difference in the incidence of hypotension. Wang C et al\textsuperscript{10} also concluded that the hypotension may develop with sympathetic blockade of bupivacaine, in present study 8(20%) patients of group and 9(22%) of group had hypotension and were comparable, these patients were treated with 6mg of IV mephentermine and rapid infusion of IV fluids.

The mean values of pulse rate changes per minute recorded in group I and group II were almost similar. This was statistically not significant. There was no incidence of significant bradycardia in studies conducted by Agrawal A et al\textsuperscript{5}, Jaishri Bogra et al\textsuperscript{4}, Hunt CO et al\textsuperscript{6}, Catherine O\textsuperscript{7}, Belzerena et al\textsuperscript{15}, Harbhej Singh et al\textsuperscript{8} and of hypotension in the studies done by B.N. Biswas\textsuperscript{14} and Belzerena et al\textsuperscript{15}.

In present study low dose (25mcg) fentanyl was used and all patients were observed closely, no respiratory depression was noted. Reuben SS et al\textsuperscript{18} and Varrasi G. et al\textsuperscript{19} found that although no patient developed respiratory depression, respiratory rate changes increased with the dose of fentanyl and they suggested that larger doses probably will be associated with respiratory depression. Late rostral spread with small dose intrathecal fentanyl is less and studied by Neil Roy et al\textsuperscript{20}, Echevarria et al\textsuperscript{21}, Harbhej Singh et al\textsuperscript{8}, Dalhgren G et al\textsuperscript{9} and Olofsson et al\textsuperscript{22} and they concluded that 25mcg fentanyl is the safest dose.

4.3 - Incidence of side effects

Side Effects such as nausea, vomiting, itching and shivering were observed. The overall incidence was 15% in group I and 17.5% in groupie which was statistically comparable. In group I and II only 2(5%) had nausea while in group I 2(5%) patients had vomiting and 3(7.5%) patients of group had vomiting. All of this patients had hypotension. Bohannon T.W.et al\textsuperscript{23}, Harbhej Singh et al\textsuperscript{8} and Dahlgern et al\textsuperscript{9} concluded that there was no difference in the incidence of nausea and vomiting in their studies. In contrast to this, Barbara L et al\textsuperscript{24} and Catherine O et al\textsuperscript{7} observed higher incidence of nausea and vomiting in their studies.

Mild itching was observed in 2(5%) patients of group II without any rash and it subsided without any treatment. These patients received blood transfusion so it may be mild reaction to blood transfusion. Pruritus may a commonest side effect after intrathecal opioid and was observed by Bohannon et al\textsuperscript{23}, Ng Yt et al\textsuperscript{25} and Ngiam et al\textsuperscript{26} in their studies, however in contrast to this Hunt CO et al\textsuperscript{6}, Harbhej Singh et al\textsuperscript{8}, Olofsson et al\textsuperscript{22} and Palmer et al\textsuperscript{27} reported that there was no difference in the incidence of itching in their studies. Shivering was seen in only 2(5%) patients of group I and responded well to sedation.

There were no significant postoperative side effects in our study.

4.4 - Two segment sensory recovery and intraoperative supplementation

Opioids have synergistic effect with local anesthetics; Mean time for two segment regression and mean duration of analgesia was significantly
prolonged in group II. Belzerena Sergio\textsuperscript{15} concluded that time taken to regression below T\textsubscript{12} dermatome was longer in treated group and increased with increasing dose of fentanyl. Prolonged sensory block suggest synergism between fentanyl and bupivacaine as seen with other opioids and local anesthetics\textsuperscript{5,6,7,8,9}. Intraoperatively if any patient complains of discomfort or pain additional analgesia and general anesthesia was provided. In present study 75% patients of group were given IV. Pentazocine 30 mg in divided doses. General anesthesia was administered in 10% patients near to end of surgery. No patients of group II needed any supplementation which was statistically highly significant. P.R. Dhumal et al\textsuperscript{12} assessed intraoperative comfort score by using V A S and this was slightly better in bupivacaine plus fentanyl group. Shende D et al\textsuperscript{17} observed that quality of intraoperative surgical anesthesia improved significantly in fentanyl group compared with control group. Comfort scores were better in fentanyl group(8.2) compared with control group (6.8)This is due to efficacy of fentanyl in abolishing visceral pain better quality of surgical analgesia, good hemodynamic stability and fewer complications like nausea, vomiting and shivering. Jaishri Bogra et al\textsuperscript{4}, Shende D et al\textsuperscript{17} and Hunt OC et al\textsuperscript{6} found prolonged duration of analgesia and less analgesic requirement in early postoperative period. All these results were consistent with present study.

**Conclusions**

Thus fentanyl (25mcg) mixed as an adjuvant to intrathecal 0.5\% hyperbaric bupivacaine offers various advantages; i.e. better surgical analgesia, prolongs the duration of analgesia, reduces the intraoperative need of analgesic supplement, delays time of postoperative rescue analgesic and minimal side effects. Hence it may be recommended that, 25mcg fentanyl is a safe and promising drug to be added with 0.5\% hyperbaric bupivacaine for spinal anesthesia in infraumbilical surgeries.

![Figure 1 Two Segment Regression](image-url)
Figure 2 - Change in Systolic Blood Pressure

Figure 3: Change in Pulse Rate

Figure 4: Intro operative supplementation
References:
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