An Observational Study between Intrathecal Fentanyl and Butorphanol with Low Dose Bupivacaine to Facilitate Early Ambulation in Perineal Surgeries

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Abstract

Background: Neuraxial opioids are widely used with local anaesthetics as they allow lower dose of local anaesthetics while providing adequate anaesthesia and faster recovery from spinal anaesthesia because of their sympathetic and motor nerve sparing activities. In the last few years the number of surgeries performed on an ambulatory basis has increased worldwide because of many advantages like short hospital stay, less chance of wound infection and less chances of deep vein thrombosis.

Methods: 64 patients of ASA- I or II of either gender who underwent perineal surgeries were divided into two groups of 32 each:- Group BF patients received 1ml of 0.5% hyperbaric bupivacaine with 20µg fentanyl(0.4ml) and Group BB patients received 1ml of 0.5% hyperbaric bupivacaine with 200µg butorphanol(0.2ml) and normal saline(0.2ml).Patients were observed for onset of sensory and motor blockade, duration of sensory and motor blockade, duration of analgesia and time to unassisted ambulation. There was no difference in onset of sensory and motor blockade between the two groups(P> 0.005).Patients receiving butorphanol had statistically significantly longer duration of sensory and motor blockade and duration of analgesia than fentanyl(p-0.001).Patients receiving fentanyl were observed to ambulate unassisted significantly early compared to butorphanol (p-0.001).

Conclusion: Patients receiving intrathecal fentanyl 20µg can ambulate earlier compared to patients receiving butorphanol 200µg when used as an adjuvant with low dose hyperbaric bupivacaine 0.5% without any complication.

Keywords: Ambulation, bupivacaine, butorphanol, fentanyl, spinal anaesthesia.

Introduction

According to Farlex, pain is defined as bothersome feeling which is conveyed to the brain via sensory neurons.1 Pain is not just the sensation of physical awareness, it also includes the perception and the subjective interpretation of discomfort.2

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Spinal anaestheia is popular and safe procedure for infraumbilical surgeries, however it is not without complications, such as hypotension, bradycardia, urinary retention and neurological injuries. Most of them depend on dose and volume of injected drug and height of subarachnoid block.3 These complications can be reduced by adding adjuvants to local anaesthetics without unduly affecting the quality of analgesia.4

Opioids when used intrathecially with local anaesthetics, provide adequate anaesthesia and analgesia even when small dose of local anaesthetic is used.5 The synergism between intrathecal opioids in addition
to local anaesthetics is due to the drugs' separation mechanism of action; blockade of Na⁺ channel by local anaesthetics⁶ and voltage gated Ca²⁺ channels with opioids.⁷ Intrathecal opioids used as adjuncts with lower dose of local anaesthetics allow early ambulation of patients because of their sympathetic and motor nerve sparing activities.

Fentanyl, a highly lipid soluble, pure μ agonist opioid with rapid onset and short duration of action, has been used with local anaesthetics (LA) for various surgeries.⁸ Fentanyl added to LA agents seems to be the most frequently used combination to enhance and increase the duration of sensory analgesia without increasing the motor blockade or prolonging recovery from spinal anaesthesia.⁹ Over the years various studies have shown that low dose bupivacaine when diluted with fentanyl can provide anaesthesia with the added advantage of rapid recovery and ambulation in patients undergoing minor surgical procedures.¹⁰

Butorphanol is a lipophilic opioid agonist-antagonist analgesic with an affinity for opioid receptors in vitro of 1:4:25 (μ:δ:κ).¹¹ Butorphanol has been used for epidural as well as intrathecal administration.¹²

In the last few years the number of surgical procedures performed on an ambulatory basis has increased worldwide because of many advantages like maintaining normal breathing and blood flow, less chances of wound infection, less chances of deep vein thrombosis, pressure sores and improvement of muscle tone.¹³

So we planned to carry out an observational study between intrathecal fentanyl and butorphanol with low dose hyperbaric bupivacaine for early ambulation in perineal surgeries.

**Materials & Methods**

The observational study was carried out at Dhiraj Hospital in Department of Anaesthesiology after clearance from ethical committee.

64 patients between the ages of 20 and 60 years of Grade I or II American Society of Anesthesiologists (ASA) classification, scheduled for elective perineal surgeries were included in the study after properly explaining the procedure to the patient and obtaining a written informed consent.

The patients were allocated into two groups, BF and BB of 32 each.

- **Fentanyl group (BF):** 0.5% hyperbaric bupivacaine (1ml) + 20µg fentanyl (0.4 ml). Total volume- 1.4ml
- **Butorphanol group (BB):** 0.5% hyperbaric bupivacaine (1ml) + 200µg butorphanol (0.2 ml) + Normal saline (0.2ml). Total volume- 1.4ml

Site of Study - Department of Anaesthesiology, Dhiraj Hospital, S.B.K.S Medical Institute and Research Centre, Piparia, Waghodia, Vadodara, Gujarat.

Study Duration- 18 months

Sample Size- 64. n=32 per group

P value <0.05 was considered statistically significant.

Sample size was calculated using formula

\[ N_A = \frac{k n_B}{1 + (1/k)(\delta z_{1-\alpha/2} + z_{1-\beta}/\mu_A - \mu_B)}^2 \]

Where

\[ K = n_A/ n_B \text{ is the matching ratio} \]

\[ \delta \text{ is standard deviation, } \alpha \text{ is Type 1 error, } \beta \text{ is Type 2 error} \]

Selection criteria

**Inclusion Criteria**

- ASA I or II patients
- Patients requiring spinal anaesthesia
- Age group 20-60 years.
- No history of allergy or reaction to any drug
- Patient willing to sign informed consent.

**Exclusion Criteria**

- Patient not willing for spinal anaesthesia.
· Patients allergic to any drugs including study drugs.
· History of seizure disorder.
· Patients with renal, hepatic, cardiovascular and respiratory diseases.
· Patients with neurological disorders and neuropathies or receiving medications known to influence neuromuscular junction.
· ASA III, IV, V Patients.

Routine pre-operative examination and investigations were carried out for all the patients. Written informed consent was obtained.

In the pre-anaesthesia room, patient’s baseline vital parameters (temperature, pulse, blood pressure and SpO2) were recorded. IV line was secured with 20 G cannula and preloaded with ringer lactate 10ml/kg/hr. On arrival in operation theatre, standard monitors were applied including ECG, noninvasive blood pressure (NIBP), pulse rate and oxygen saturation. Patients were premedicated with Inj. glycopyrrolate 0.2mg I.V and Inj. ondansetron 4mg I.V.

Patients were classified into two groups according to the type of adjuvant added to the low dose 0.5% hyperbaric bupivacaine.

Spinal anaesthesia was administered in the sitting position following all aseptic precautions with a 25G spinal needle. Drug was injected according to the group (BF or BB) after free flow of cerebrospinal fluid and supine position was given.

The onset and duration of sensory and motor blockade, duration of analgesia, time to unassisted ambulation was noted. Time of unassisted ambulation is the time period from the spinal injection till the patient can walk unassisted. Pain score was assessed by Visual Analogue Scale. Diclofenac sodium 1.5 mg/kg was administered when VAS ≥ 4 and study terminated.

Side effects and complications was noted and treated. Bradycardia defined as pulse rate < 60/min and was treated with IV atropine sulfate 0.6mg. Hypotension defined as systolic BP ≥ 20% from the base level and was treated with IV mephenteramine 6mg.

After completion of surgery, patients were shifted to recovery room and vitals noted.

**Results and Discussion**

The demographic data were comparable between the two groups which was statistically insignificant (p value > 0.05).

**Table 1:** Shows the distribution of patients undergoing different perineal surgeries between the two groups.

<table>
<thead>
<tr>
<th>Types of surgery</th>
<th>Group BF</th>
<th>Group BB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemorrhoidectomy</td>
<td>14</td>
<td>17</td>
</tr>
<tr>
<td>Fistulectomy</td>
<td>18</td>
<td>15</td>
</tr>
</tbody>
</table>

**Table 2:** Various parameters recorded following spinal anaesthesia (in minutes) between the groups

<table>
<thead>
<tr>
<th>Parameters in minutes</th>
<th>BF</th>
<th>S.D.</th>
<th>BB</th>
<th>S.D.</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td></td>
<td></td>
<td>Mean</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Onset of sensory block</td>
<td>5.59</td>
<td>4.34</td>
<td>7.47</td>
<td>4.02</td>
<td>0.078</td>
</tr>
<tr>
<td>Duration of sensory block</td>
<td>138.81</td>
<td>10.84</td>
<td>151.47</td>
<td>7.11</td>
<td>0.001</td>
</tr>
<tr>
<td>Onset of motor block</td>
<td>2.72</td>
<td>1.22</td>
<td>4.84</td>
<td>1.55</td>
<td>0.001</td>
</tr>
<tr>
<td>Duration of motor block</td>
<td>156.19</td>
<td>8.19</td>
<td>164.91</td>
<td>5.16</td>
<td>0.001</td>
</tr>
<tr>
<td>Duration of analgesia</td>
<td>144.72</td>
<td>10.55</td>
<td>156.19</td>
<td>7.11</td>
<td>0.001</td>
</tr>
</tbody>
</table>
The mean onset of sensory block was statistically insignificant between the two groups (P value- 0.078). The mean time for two segment regression was faster with fentanyl compared to butorphanol which was statistically highly significant (P value-0.001). The mean duration of sensory block, onset of motor block, duration of motor block and the duration of analgesia was significantly highly longer with butorphanol group compared to fentanyl group (P value- 0.001).

There was no significant difference in mean pulse rate, mean systolic and mean diastolic blood pressure, mean arterial oxygen saturation between the groups in the intraoperative and postoperative period.

Table 3: Mean time to unassisted ambulation (in minutes) between the groups

<table>
<thead>
<tr>
<th></th>
<th>BF</th>
<th>BB</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>188.16</td>
<td>7.80</td>
<td>198.88</td>
<td>9.40</td>
</tr>
</tbody>
</table>

Mean time to unassisted ambulation was quicker in the fentanyl group compared to butorphanol which was highly significant (P value-0.001).

No incidence of side effects was observed in any of the study groups.

The effects of low dose intrathecal bupivacaine with fentanyl or with butorphanol for early ambulation in perineal surgeries were compared.

20µg fentanyl and 200µg butorphanol with 5mg hyperbaric bupivacaine 0.5% was used as low dose of bupivacaine causes early ambulation which is beneficial in preventing deep vein thrombosis, wound infection and pressure sores.

In our study the difference in the mean onset of sensory block between the two groups was statistically non-significant (p- 0.078). However the mean duration of sensory block was significantly longer in the butorphanol group (p-0.001) as compared to fentanyl group. The mean time of two segment regression was faster in the fentanyl group (p-0.001) compared to butorphanol group.


In contrast to our study, Arora N et al (2018)21 in their study reported that the duration of sensory block and two segment regression (p-0.002) was longer with fentanyl compared to butorphanol group.

The onset of motor block was faster with fentanyl compared to butorphanol (p-0.001) and the duration of motor block was longer in the butorphanol group compared to fentanyl group in our study which was statistically significant (p-0.001).


In contrast to our study, Arora N et al (2018)21 observed that the onset was faster with butorphanol (p-0.06) and duration of motor block was longer with fentanyl compared to butorphanol (p-0.001).

Mean duration of analgesia was significantly longer in the butorphanol group compared to fentanyl group (p-0.001) in our study.


The difference in the mean heart rate, mean systolic and diastolic blood pressure and mean oxygen saturation in the intraoperative as well as postoperative period was found to be statistically insignificant (p>0.05) between the two groups.

Reddy NG et al (2015)16, Bhatia U et al (2017)18, Gupta V et al (2017)19 in their studies also observed comparable haemodynamic parameters in intraoperative and post-operative period (p>0.05) between the groups.
Fentanyl, a µ-receptor agonist acts principally by the interaction with receptors at the supraspinal site. To a lesser degree it also binds to κ-receptors in the substantia gelatinosa of spinal cord. The addition of fentanyl (20-25µg) to low dose bupivacaine improves the perioperative quality of spinal blocks with fewer cardiovascular changes. Intrathecal addition of fentanyl with bupivacaine produces synergism between the two drugs. Opioids and local anaesthetics exert their antinociceptive effect in the spinal cord. There is an opening of the K⁺ channels and reducing Ca ++ influx causing inhibition of neurotransmitter release. It also has a direct post synaptic effect, causing hyperpolarization and reduction in neuronal activity.

Butorphanol is a partial agonist and antagonist at μ and κ-receptors. Butorphanol causes inhibition of adenylate cyclase, decrease in calcium influx and hyperpolarization of neurons thus suppressing the action potential. It has better effects on somatic than visceral pain. Action on pain is primarily due to action on κ-receptors.

In our study patients in the fentanyl group were able to ambulate unassisted significantly faster compared to butorphanol (p-0.001).

Kumar A et al (2016)17, David BB et al (1996)22 also observed faster recovery in the group receiving intrathecal fentanyl compared to butorphanol.

Opioids used along-with low dose local anaesthetics exhibit synergism between the two, which is the result of the drugs’ separation mechanism of action, with the Na⁺ and voltage gated Ca ++ channels being blocked by LA and opioids respectively. This allows early ambulation due to the sympathetic and motor nerve sparing activities.

In our study we did not observe any adverse effects in either of the group.

Arora N et al (2018)21 also found no drug related side effects in the study groups.


**Conclusion**

It is concluded that with the administration of intrathecal fentanyl as an adjuvant to low dose bupivacaine, the patients were able to ambulate unassisted in a shorter period of time compared to intrathecal butorphanol. However it was also observed that the onset of sensory and motor block as well as the duration of analgesia was significantly longer in the patients receiving intrathecal butorphanol. Both the drugs were very well tolerated by the patients undergoing surgery.

**Source of Funds**- Nil

**Conflict of Interest**- None

**References**

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