Original Research Article

Comparison of intrathecal hyperbaric bupivacaine, isobaric levobupivacaine and isobaric ropivacaine with fentanyl as adjuvant in knee arthroscopy: A randomised controlled study

Neha Yadav¹,*, Sujata Chaudhary², Divya Gahlot³, Rashmi Salhotra²

¹Dept. of Anaesthesia, Maharishi Markandeshwar Institute of Medical Sciences and Research MMDU, Mullana, Haryana, India
²Dept. of Anaesthesia, University College of Medical Sciences & G.T.B. Hospital, Delhi, India
³Dept. of Anaesthesia, Maulana Azad Medical College(MAMC), New Delhi, India

ABSTRACT

Background and Aim: To compare the efficacy of intrathecal 0.5% hyperbaric bupivacaine, 0.5% isobaric levobupivacaine and 0.5% isobaric ropivacaine with fentanyl as adjuvant for outpatient knee arthroscopic surgeries.

Material and Methods: This prospective, randomized, double-blind study was conducted on 60 ASA I/II patients between 18-60 years, scheduled for knee arthroscopy under subarachnoid block. Patients were randomised into three groups; group BF: 10 mg 0.5% hyperbaric bupivacaine (2 ml), group LF: 10 mg 0.5% isobaric levobupivacaine (2 ml), group RF: 10 mg 0.5% isobaric ropivacaine (2 ml). In addition, each patient received fentanyl 25 μg (0.5 ml) as an adjuvant to the local anaesthetic (total intrathecal volume 2.5 ml in all three groups). The sensory and motor block characteristics, time to ambulation and discharge were recorded. Demographic profile, sensory and motor block characteristics were compared using one way ANOVA followed by Tukey’s test and hemodynamic parameters were compared using repeated measure ANOVA. Dunnett’s test was applied wherever required. Qualitative data was compared using Chi square or Fisher’s exact test. P-value <0.05 was considered significant.

Results: Mean time to ambulation and discharge was significantly less in group RF (10.10 ± 3.63 hr) compared to 14.80 ± 3.63 hr in group BF and 12.40 ± 2.30 hr in group LF (p<0.001). Mean time to complete motor recovery was significantly less in group RF (204.75 ± 34.39 min) compared to 260 ± 40.78 min in group BF and 280.25 ± 28.72 min in group LF (p<0.001). Duration of subarachnoid block was comparable in all the three groups (p=0.522).

Conclusion: Isobaric ropivacaine with fentanyl is better drug combination than isobaric levobupivacaine with fentanyl or hyperbaric bupivacaine with fentanyl as spinal anaesthetic for outpatient knee arthroscopic surgery.

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1. Introduction

Knee arthroscopy is a commonly performed outpatient procedure as there is minimal tissue damage and recovery is faster. Anaesthesia technique for outpatient procedure should provide excellent surgical anaesthesia, quick onset and offset of anaesthesia, smooth transfer to postoperative room with adequate pain control.¹

Neuraxial anaesthesia is preferred over general anaesthesia as it provides satisfactory post-operative analgesia with less incidence of nausea and vomiting.²,³

Hyperbaric bupivacaine is the most common local anaesthetic drug used for subarachnoid block (SAB). However, due to the longer duration of motor block, the drug is not suitable for ambulatory surgery.⁴

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¹ Corresponding author.
E-mail address: nehayadav05@gmail.com (N. Yadav).
Levobupivacaine is an S(-) enantiomer of bupivacaine, having less cardio toxic and neurotoxic effects in comparison with R(+) bupivacaine.\textsuperscript{5} Ropivacaine, another local anaesthetic, when used intrathecally for day care procedures provides adequate sensory block and early motor recovery\textsuperscript{6} due to greater degree of sensory motor differentiation.\textsuperscript{7–9} Addition of opioids, such as fentanyl, as adjuvant to local anaesthetic provides effective postoperative analgesia and helps in achieving optimal SAB at a much lower dose of local anaesthetic.\textsuperscript{5}

There is limited literature available comparing these drugs with each other.\textsuperscript{1,5,10} There is no published study comparing the effect of the three agents on ambulation. Hence, this study was planned with the primary objective to compare time to ambulation and discharge following the use of combination of fentanyl with either hyperbaric bupivacaine, isobaric levobupivacaine and isobaric ropivacaine for subarachnoid block in patients scheduled to undergo knee arthroscopy. In addition, sensory and motor block characteristics of all the three agents and their adverse effects were also studied.

2. Materials and Methods

After getting clearance from the institutional ethics committee, a written informed consent was taken from all the patients participating in the study. The study was a prospective randomized double blind trial. Sixty ASA I and II patients between 18-60 yrs age and 150-180 cm height undergoing knee arthroscopic procedures were included. Patients with contraindication to SAB, allergy to the drugs used in the study, BMI > 30, chronic opioid use, history of chronic pain, significant pre-existing severe systemic illness like cardiovascular, central nervous system, hepatorenal diseases and refusal to participate were excluded from the study.

A routine pre-anaesthetic assessment was performed and the technique of SAB was explained to the patients. During preanaesthetic check up, patients were made familiar to the concepts of visual analogue scale (VAS) for pain assessment. The patients were prescribed Tab. Alprazolam 0.25 mg night before surgery and in the morning of surgery. Patients were kept fasting overnight.

In the operation theatre, monitors were attached. Preloading with 15 ml/kg of intravenous infusion of Ringer’s lactate solution was done through 18 G iv cannula. Patients were randomly allocated into three groups with 20 patients in each group using a computerized random number table. Group BF patients received 10 mg 0.5% hyperbaric bupivacaine, Group LF patients received 10 mg 0.5% isobaric levobupivacaine and Group RF patients received 10mg 0.5% ropivacaine, each with 25 μg fentanyl respectively. Total volume of intrathecal drug was 2.5 ml in each group.

Subarachnoid block was performed under strict aseptic precautions with patient in sitting position and through midline approach, using a 25 G Quincke’s needle at L2 – L3 or L3 – L4 intervertebral space. Study drug solution was prepared by and injected intrathecally over a period of 10-12 seconds by an anesthesiologist who was not involved in the further conduct of the study. The person observing the outcome measures was blinded to the group allocation. The time of intrathecal drug injection was noted and all the observations were made using this time as ‘0’ min. Onset of sensory block (interval between drug injection and time to block T10 dermatome), duration of sensory block (time from drug administration until 2- segment regression) was assessed with pin prick method using 27 G hypodermic needle. Motor block was assessed using the Modified Bromage (6 point) Scale.\textsuperscript{11} Time to full motor block (Bromage 1, assessed every 2 min) was taken as onset, and time from onset to complete recovery (Bromage 6) was taken as the duration of motor block. Duration of motor block was recorded.

Heart rate, SBP, DBP, MAP, SpO\textsubscript{2} were recorded every 5 min for the first 15 min and then every 15 min for the rest of the intra-operative period and every 1 hour in postoperative period till complete recovery.

Pain score was assessed using a standard 10 cm linear Visual Analogue Scale (VAS)\textsuperscript{12} in post operative period every 30 min for first 2 hours, then at 4, 8, 12 and 24 hours. Duration of complete analgesia was defined as time from intrathecal injection to the time to first dose of rescue analgesia. Patients were given rescue analgesia with i.v. diclofenac 75 mg when VAS ≥ 3 and then every 8 hourly.

Patients were monitored for side effects like pruritus, shivering, nausea, respiratory depression, vomiting, headache and any other complications. If any of these side effects occurred appropriate management was done.

Time to ambulation and discharge was assessed by Post-anaesthesia discharge scoring system (PADSS) determining home readiness.\textsuperscript{13} Maximum score is 10 and score ≥9 was considered fit for discharge.

Minimum sample size calculated using power and sample size software was 15 cases with a power of study 80% and type 1 error of 5%. Accounting for failures and due to availability of resources 20 cases were included in each group. The data was analysed using SPSS v. 20.0. Quantitative data was presented as mean±SD. Time to maximum motor block was not normally distributed, so log transformation analysis was done. One way ANOVA followed by Tukey’s test was applied to compare demographic, sensory and motor block characteristics among the three groups. Repeated measure ANOVA was applied for hemodynamic parameters for inter and intragroup comparison. Chi square or Fisher’s exact test was used to compare the proportion of adverse effects among the three groups. P value of <0.05% was considered
as significant.

3. Results

Demographic profile of the patients and duration of surgery was comparable among the three groups (Table 1). Mean time of onset of sensory block was significantly delayed in Group RF compared to the other two groups. Time to achieve maximum sensory level was significantly longer in group RF but was comparable between the other two groups. Time to two segment regression was similar among the three groups (Table 2).

Mean time of onset of motor block was significantly delayed (p=0.007) in group RF. In group RF, 70% of patients achieved maximum motor block of Bromage 2 whereas in group BF 85% and in group LF 95% patients achieved maximum motor block of Bromage 1 (p<0.001). Time to achieve maximum motor block was longer in group RF and the time to recovery was significantly shorter than group BF and group LF (p<0.001) (Table 3). There was no significant difference in the time to request of first rescue analgesic and the total number of rescue analgesic doses required in 24 hr postoperative period (Table 4)

Hemodynamic variables were comparable from the baseline between the three groups till first 90 min (p>0.05) (Figures 1 and 2). However, within the group, there was a statistically significant fall in SBP at 10 min after intrathecal injection. No significant difference was found in any of the three groups with respect to hypotension, bradycardia and adverse effects (p>0.05). Shivering, headache, respiratory depression, nausea and vomiting, urinary retention was not observed in any of the patients. However, pruritus was observed in two patients in BF group but the incidence was not statistically significant.

4. Discussion

Early ambulation and discharge after lower limb procedures reduces the health care burden. Prolonged motor blockade with local anaesthetic drugs may limit early ambulation and discharge. So, the search for a local anaesthetic agent which is safe, efficacious and less toxic with early recovery profile and early ambulation is on. This study aimed to compare three local anaesthetics – ropivacaine, bupivacaine and levobupivacaine, for their efficacy as intrathecal agents with 25 mg fentanyl as an adjuvant in patients scheduled for knee arthroscopy surgery. Results of our study show that low dose (10 mg) ropivacaine with 25 mg fentanyl was best suited for anaesthesia for knee arthroscopy surgery. Results of our study show that low dose (10 mg) ropivacaine with 25 µg fentanyl was best suited for anaesthesia for knee arthroscopy surgery. Results of our study show that low dose (10 mg) ropivacaine with 25 µg fentanyl was best suited for anaesthesia for knee arthroscopy surgery. Results of our study show that low dose (10 mg) ropivacaine with 25 µg fentanyl was best suited for anaesthesia for knee arthroscopy surgery. Results of our study show that low dose (10 mg) ropivacaine with 25 µg fentanyl was best suited for anaesthesia for knee arthroscopy surgery.

Although levobupivacaine and bupivacaine are equipotent, the potency of ropivacaine is 2/3 that of bupivacaine. However, Nair et al reported that almost similar profile was noted with ropivacaine and bupivacaine in knee arthroscopy surgery in day care setting Therefore, in the present study equivalent doses of three drugs, i.e. 10 mg, were studied.

Bupivacaine is available in hyperbaric formulation in 0.5% concentration whereas levobupivacaine and ropivacaine are commercially available as isobaric formulations in the market. So to maintain sterility, we decided to take them in hyperbaric and isobaric forms, respectively (as commercial formulations).

In our study onset of sensory and motor block was significantly delayed in group RF as compared to groups LF and BF. Our results were similar to Chari et al who compared isobaric 0.75% ropivacaine with hyperbaric 0.5% bupivacaine and found that both sensory (42.6±11.39 sec) and motor onset (55.54±13.01 sec) was significantly delayed in ropivacaine group as compared to bupivacaine. Similar results were found in study done by Vani et al, Ravisankar et al. and Das et al. This can be attributed...
**Table 1:** Demographic profile

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group BF</th>
<th>Group LF</th>
<th>Group RF</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>32.10±8.23</td>
<td>30.35±8.06</td>
<td>31.05±9.62</td>
<td>0.814</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>64.20±7.63</td>
<td>62.90±5.76</td>
<td>62.15±8.08</td>
<td>0.665</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>164.20±6.75</td>
<td>164.00±7.10</td>
<td>160.75±7.69</td>
<td>0.243</td>
</tr>
<tr>
<td>Duration of surgery (min)</td>
<td>96.75±35.84</td>
<td>89.75±31.80</td>
<td>87.00±42.25</td>
<td>0.691</td>
</tr>
</tbody>
</table>

*p<0.05-Significant

**Table 2:** Sensory block characteristics

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group BF</th>
<th>Group LF</th>
<th>Group RF</th>
<th>p-value (one-way ANOVA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset (time to T10, min)</td>
<td>4.95±2.11</td>
<td>3.90±1.37</td>
<td>7.05±2.96</td>
<td>0.000*</td>
</tr>
<tr>
<td>Time to achieve maximum level (min)</td>
<td>9.40±4.40</td>
<td>7.50±1.46</td>
<td>10.35±3.48</td>
<td>0.030*</td>
</tr>
<tr>
<td>Time to 2 segment regression</td>
<td>107.45±20.35</td>
<td>104.75±22.73</td>
<td>97.25±19.01</td>
<td>0.282</td>
</tr>
</tbody>
</table>

*p<0.05-Significant

**Table 3:** Motor block characteristics

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group BF</th>
<th>Group LF</th>
<th>Group RF</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMB_Bromage 1</td>
<td>17 (85%)</td>
<td>19 (95%)</td>
<td>4 (20%)</td>
<td>0.000*</td>
</tr>
<tr>
<td>MMB_Bromage 2</td>
<td>3 (15%)</td>
<td>1 (5%)</td>
<td>14 (70%)</td>
<td></td>
</tr>
<tr>
<td>MMB_Bromage 3</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>2 (10%)</td>
<td></td>
</tr>
<tr>
<td>Time to MMB (log min)#</td>
<td>0.775±0.230</td>
<td>0.721±0.147</td>
<td>0.912±0.184</td>
<td>0.007*</td>
</tr>
<tr>
<td>Time to complete recovery (min)</td>
<td>260±40.78</td>
<td>280.25±28.72</td>
<td>204.75±34.39</td>
<td>0.000*</td>
</tr>
</tbody>
</table>

MMB: Maximum motor block; Values are expressed as number (percentage) or mean±SD; #Since the values were not normally distributed, for the purpose of analysis, log transformation has been done

**Table 4:** Rescue analgesic requirement and time to ambulation and discharge

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group BF</th>
<th>Group LF</th>
<th>Group RF</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to request of first rescue analgesic (min)</td>
<td>278.75 ± 57.46</td>
<td>279.25 ± 40.40</td>
<td>264.25 ± 41.11</td>
<td>0.522</td>
</tr>
<tr>
<td>Rescue analgesic doses required in 24 hrs</td>
<td>1.85 ± 0.58</td>
<td>1.80 ± 0.41</td>
<td>2.00 ± 0.56</td>
<td>0.461</td>
</tr>
<tr>
<td>Time to ambulation &amp; discharge (hr)</td>
<td>14.80±3.63</td>
<td>12.40±2.30</td>
<td>10.10±2.10</td>
<td>0.000*</td>
</tr>
</tbody>
</table>

*p<0.05-Significant

**Table 5:** Incidence of adverse effects

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group BF</th>
<th>Group LF</th>
<th>Group RF</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypotension</td>
<td>4 (20%)</td>
<td>1 (5%)</td>
<td>3 (15%)</td>
<td>0.505</td>
</tr>
<tr>
<td>Bradycardia</td>
<td>3 (15%)</td>
<td>1 (5%)</td>
<td>6 (30%)</td>
<td>0.129</td>
</tr>
</tbody>
</table>

Values are expressed as number (percentage)

In our study, we observed that time to reach maximum sensory block level was earliest in group LF as compared to groups BF and RF. This can be attributed to the isobaricity of levobupivacaine. But with isobaric ropivacaine, this was not noticed. This may be due to its lower potency. This is in contrast to studies done by D’souza et al, and Mantouvalou et al in which no significant difference was present in achieving the highest level of sensory block among the three groups.  

... to lesser lipid solubility of ropivacaine which may cause this drug to penetrate larger myelinated A fibres more slowly, thus resulting in delayed motor onset in comparison to the more lipid soluble bupivacaine. This is in contrast to a study done by D’souza et al, who compared 3 ml (15 mg) each of hyperbaric 0.5% bupivacaine, isobaric 0.75% ropivacaine, 0.5% levobupivacaine and concluded that hyperbaric bupivacaine produces a sensory block with an earlier onset compared to other two groups. 20
Mean time to two segment regression was comparable among the three groups. This is supported by a study done by Gautier et al, where duration of sensory block was found to be comparable among bupivacaine and ropivacaine which is in contrast to most of the studies done by D’souza et al, Chari et al where duration of sensory block was found to be longer in ropivacaine as compared to bupivacaine and levobupivacaine. This can be due to methodological differences like difference in baricity, dosage and demographic factors in these studies as compared to our study. In our study maximum motor block was found to be Bromage 1 in maximum number of patients in BF and LF groups but was Bromage 2 in 70% of patients in RF group. This difference in onset of dense motor blockade can be attributed to difference in baricity and differential blockade of nerve fibres where fibres involved in pain transmission (Ad and C fibres) are blocked to a greater extent than those for motor function (Ab fibres). Similar results were reported by Mantouvalou et al and Kumar et al where less intensity of motor block was seen in ropivacaine group than in bupivacaine group with the same dosage.

In our study, duration of motor blockade i.e. time to complete recovery was shortest in group RF as compared to BF and LF groups. Similarly, Jagtap et al reported that motor block was significantly shorter in ropivacaine group (242.8±47.06 min) as compared to bupivacaine group (268±49.9 min) thus favouring early ambulation and discharge.

Duration of spinal analgesia and the total number of rescue analgesics required in 24 hr postoperative period were found to be comparable among the three groups in our study. Time to ambulation and discharge was shortest in RF group as compared to groups BF and LF. Similar results were reported by Gupta et al who used fentanyl as adjuvant to 0.75% isobaric ropivacaine for infraumbilical surgery under SAB. They concluded that as intrathecal adjuvant to 0.75% isobaric ropivacaine for RF group as compared to groups BF and LF. Similar results were reported by Mantouvalou et al and Kumar et al where less intensity of motor block was seen in ropivacaine group than in bupivacaine group with the same dosage.

To conclude, the results of present study indicate that low dose (10 mg) of ropivacaine with fentanyl had a shorter duration of motor and sensory block and also a shorter time to ambulation and home discharge. Thus ropivacaine may prove to be a better and safer alternative in day care surgeries like knee arthroscopy.

5. Conclusion

To conclude, the results of present study indicate that low dose (10 mg) of ropivacaine with fentanyl had a shorter duration of motor and sensory block and also a shorter time to ambulation and home discharge. Thus ropivacaine may prove to be a better and safer alternative in day care surgeries like knee arthroscopy.

6. Source of Funding

None.

7. Conflict of Interest

There is no conflict of interest.

References


20. Souza ADD, Saldanha NM, Monteiro AD, Harshvardhan H. Comparison of intrathecal hyperbaric 0.5% bupivacaine, isobaric 0.5% levobupivacaine and isobaric 0.75% ropivacaine for lower abdominal surgeries. *Int J Health Sci Rev*. 2014;4:22–9.


Author biography

**Neha Yadav**, Assistant Professor

**Sujata Chaudhary**, Director and Professor

**Divya Gahlot**, Senior Resident

**Rashmi Salhotra**, Associate Professor

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