Original Clinical Research

Clinical Efficacy of Isobaric Ropivacaine Alone and with Dexmedetomidine in Spinal Anesthesia for Abdominal Hysterectomy: A Prospective Randomised Double Blind Study

Devendra Verma MD, Ravindra Kr. Gehlot MD, Basant Kr. Dindor MD, Babulal Jat MD, Manoj Chaudhary MBBS, Dinesh Didwania MD

Abstract

Background: Ropivacaine is a levo-isomer of bupivacaine, with better safety profile. Data are sparse for use of ropivacaine in spinal anesthesia for abdominal hysterectomy and effect of adding Dexmedetomidine to it is also not much reported. This study was designed to assess the clinical efficacy of isobaric ropivacaine 30 mg in spinal anesthesia for abdominal hysterectomy and the effect of adding 5 µg of Dexmedetomidine to ropivacaine was also evaluated.

Methods: In this prospective, randomised double blind, comparative study, 90 patients of American Society of Anesthesiologists (ASA) grade I-II, aged between 30-60 years, weight 40-80 kg and height >140cm, posted for elective abdominal hysterectomy in spinal anesthesia were randomly divided into two groups; Group R(n=45): patients received 4 ml of 0.75% ropivacaine (30 mg) and Group RD(n=45): patients received 4ml of 0.75% ropivacaine (30 mg) + Dexmedetomidine(5 µg). The sensory–motor block characteristics, hemodynamic profile, postoperative analgesia and adverse effects were recorded and compared.

Results: Both groups were statistically comparable regarding vital parameters. Time to sensory block regression to S1 was significantly longer in group RD (285.03±39.03 min) as compared to group R(238.49±32.90 min) (p<0.001). Time to first rescue analgesic was significantly longer in group RD (278.71±38.48min) as compared to group R(224.97±42.43min) (p<0.001). Duration of motor block (time to regression to B0) was significantly longer in group RD (295.42±39.60 min) as compared to group R (252.68±33.69 min) (p<0.001).

Conclusion: Addition of 5µg of dexmedetomidine to 4ml of 0.75% Ropivacaine administered intrathecally to patients undergoing total abdominal hysterectomy results in a prolongation of sensory block, motor block and duration of analgesia when compared to Ropivacaine alone. The addition of dexmedetomidine 5µg does not result in any increase in adverse effect.

Keywords: Isobaric Ropivacaine; Dexmedetomidine; Spinal Anesthesia; Abdominal Hysterectomy.

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Introduction

Spinal anesthesia is an established mode of anesthesia for lower abdominal surgeries because it blunts the “stress response” to surgery, decreases intra-operative blood loss and lowers the incidence of postoperative thromboembolic events.\textsuperscript{1-3} Many techniques and drug have been tried to calm the patients and eliminate the anxiety component during regional anesthesia.\textsuperscript{4} Subarachnoid block (SAB) has inherent advantages like intense motor and sensory blockade with faster onset, good relaxation, reliability, avoidance of side effects of multiple drugs used in GA, no postoperative respiratory depression, nausea, vomiting and drowsiness.

Ropivacaine shares many physiochemical properties with bupivacaine but has shown a better safety profile over bupivacaine due to the reduced central nervous system and cardiac toxicity.\textsuperscript{5,6} Recent clinical data have shown that ropivacaine is clinically effective and safe for regional anesthetic techniques with good tolerability. Ropivacaine has been successfully used in spinal anesthesia for caesarean section, urological surgery and lower limb orthopedic surgery. However, there is scarcity of data in which ropivacaine has been used in spinal anesthesia for abdominal hysterectomy in which the surgery is more extensive, needing more relaxation than above mentioned surgeries. Local anesthetic when used alone is associated with short duration of action. Various adjuvants have been used intrathecially to improve the quality and duration of the spinal anesthesia along with better postoperative analgesia like epinephrine, neostigmine, midazolam, ketamine, opioids and alpha-2 receptor agonists (clonidine, dexmedetomidine).\textsuperscript{7,9} When dexmedetomidine is added to intrathecal ropivacaine better clinical profile was noted as compared to ropivacaine alone. No study comparing the efficacy of ropivacaine 4ml of 0.75% versus ropivacaine 0.75% plus 5µg dexmedetomidine in spinal anesthesia has been conducted to our knowledge. Therefore, the aim of the current study is to compare 4 ml of 0.75% ropivacaine alone and 4ml of 0.75% ropivacaine with 5µg dexmedetomidine in spinal anesthesia for abdominal hysterectomy regarding sensory and motor block characteristics, success rate, postoperative analgesia, hemodynamic profile and complications.

Methods

After approval from the institutional ethical committee and obtaining Clinical Trials Registry-India (CTRI/ 2017/11/010704) registration, this randomised, double blinded, comparative study was conducted in the Department of Anesthesiology at our institute. 90 patients with 45 in each group having American Society of Anesthesiologists (ASA) grade I-II, aged between 30-60 years, weight 40-80 kg and height >140cm, posted for abdominal hysterectomy under spinal anesthesia were included in the study. The exclusion criteria included patient’s refusal, contraindication to regional anesthesia, history of significant co-existing diseases (like ischemic heart disease, hypertension, diabetes, psychiatric illness & thyroid disease), impaired renal functions, severe liver disease, morbid obesity and allergy to study drugs.

This study was conducted in a prospective randomised double blind fashion. All patients under study were subjected to a detailed pre-anesthetic examination and investigations were carried out during this evaluation. Patients who fulfill inclusion criteria were enrolled in the study. They were randomly divided into two groups of 45 patients in each group using sealed envelope technique Group R (Ropivacaine) (n=45) consisted of patients who received 4ml (30mg) of 0.75% Isobaric Ropivacaine hydrochloride. Group RD (Ropivacaine-Dexmedetomidine) (n=45) consisted of patients who received 4ml (30mg) of 0.75% Isobaric Ropivacaine with 5µg Dexmedetomidine hydrochloride (0.05ml).

The study solutions were prepared in 5 ml syringe by an anesthesiologist who also performed the subarachnoid block and was not involved further in the study. In Group RD, Dexmedetomidine 100µg was taken in insulin syringe (1ml=40 part=100 µg) and 2 parts (5µg) instilled in 5cc syringe containing 4ml ropivacaine so resulting volume was 4.05 ml (Same volume of drug was not prepared by adding saline as it can change the baricity of solution).

The anesthesiologist who was conducting the study and recording all data, was not aware of group allocation. Patients, surgeons and postoperative nurses were also not aware of group allocations.

Patients were preloaded with 10 ml/kg Ringer
lactate via 20G peripheral IV cannula and injection of midazolam 1 mg i.v and injection of ondansetron 4 mg i.v were given as pre-medication. Patients were monitored with non-invasive blood pressure (NIBP), heart rate (HR) and peripheral oxygen saturation (SpO₂). After taking full aseptic precautions spinal puncture was done using 25 G quincke spinal needle in L3-L4 or L4-L5 space via midline approach in lateral position and drugs were injected in subarachnoid space as per group allocation.

The end time of intrathecal injection was considered as “time 0” for further data recording. The motor block was assessed using the Modified Bromage Score with No motor block = 0, Inability to raise extended legs = 1, Inability to flex knees = 2 and Inability to flex ankle joints = 3.

Sensory-motor block assessment (using spirit soaked cotton swab) was started 3 min after spinal injection (zero time) and repeated every 2 min thereafter till 11 min (3, 5, 7, 9 and 11 min). SBP, DBP, HR, SPO₂ were recorded every 3 min till 15 min then every 10 min till the end of surgery.

The onset time of sensory block was defined as the time between injection of intrathecal anesthetic and absence of sensation at T6 dermatome level. The highest level of sensory block (peak sensory level) and time to reach peak sensory level, the maximum motor block (Maximum Bromage score) and onset time of motor block (time to reach maximum Bromage score), the durations of motor block from the end of spinal injection to complete motor recovery (Bromage score 0) and sensory block from end of injection to sensory regression to S1 and duration of analgesia to first pain were recorded.

Surgery was allowed to commence after spinal anesthesia if T₆ sensory level and bromage score of 2 or 3 were achieved. If not achieved in 11 minutes after SAB than the case was converted to GA and declared as failed case. Intra-operatively if patient complains of pain, supplementation in the form of ketamine /propofol /fentanyl was given. If pain continues, case was converted to GA with intubation and declared as failed case. If SBP falls below 90 mm of Hg it was considered as hypotension and 6 mg inj. mephentermine was given; if HR falls below 60 beats/min it was considered as bradycardia and 0.4 mg of atropine was given. If nausea and/or vomiting occur, inj. ondansetron 4mg was given.

Other complications like shivering, headache and arrhythmias were noted and treated accordingly.

The clinical efficacy (success rate) was graded as completely successful if no supplementation was given, partially successful if ketamine / propofol /fentanyl were given and failure if surgery was converted to general anesthesia. The success rate in each group was defined as the number of cases in which surgery could be completed without supplementation.

For post-operative data recording of sensory and motor blocks and vital signs were recorded every 30 min, till complete recovery of sensory and motor blocks.

**Statistical analysis**

Data were entered into MS EXCEL and analyzed using SPSS version 20. Categorical (qualitative) data were presented as number (proportion) and compared using chi square test. Continuous variable (quantitative) were presented as mean ±SD and compared using t-test as per need. P< 0.05 was considered as statistically significant.

Sample size was calculated on the basis of previous study conducted by Naithani et al. in 2015. To detect a difference of 0.5 min in onset of sensory block with a power of 80% (β) and confidence interval of 95% (α=0.05), a minimum sample size of 40 in each group was required. We enrolled 45 patients in each group to compensate for dropouts.

**Results**

Patients’ characteristics are presented in Table 1.

**Table 1**

<table>
<thead>
<tr>
<th>Demographic parameters</th>
<th>Group R (n=45)</th>
<th>Group RD (n=45)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>45.29±5.94</td>
<td>43.20±6.77</td>
<td>0.274</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>54.27±10.02</td>
<td>54.69±08.87</td>
<td>0.36</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>155.5±03.90</td>
<td>154.16±03.54</td>
<td>0.725</td>
</tr>
</tbody>
</table>

Data are expressed as mean±SD

Both groups were statistically comparable regarding mean age, mean weight and mean height.
Fig. 1
Comparison Of Mean Systolic Blood Pressure In Both Group

Fig. 2
Comparison Of Mean Diastolic Blood Pressure In Both Group

Fig. 3
Comparison Of Mean Heart Rate In Both Group
All hemodynamic parameters (HR, SBP, and DBP) showed no significant changes from baseline during intraoperative period in both groups (Figure 1-3).

Table 2 shows that both groups were statistically comparable regarding mean time to reach T6 and peak sensory level. However the time to sensory block regression to S1 (duration of sensory block) was significantly longer in group RD (285.03±39.03 min) as compared to group R (238.49±32.90min). Time to first rescue analgesic was also significantly longer in group RD (224.97±42.43min) as compared to group R (224.97±42.43min).

Table 3 shows that both groups were statistically comparable regarding mean time to reach bromage score 3. Duration of motor block (time to regression to B0) was significantly longer in group RD (295.42±39.60 min) as compared to group R (252.68±33.69 min).

Incidences of side effects such as hypotension, bradycardia and vomiting were not different between the two groups (Table 4).

The clinical efficiency profile of spinal anesthesia was not different between the two groups (Table 5).

### Table 2

<table>
<thead>
<tr>
<th>Sensory block characteristics</th>
<th>Group R (n=45)</th>
<th>Group RD (n=45)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to reach T6 (min)</td>
<td>7.35±1.93</td>
<td>6.69±1.68</td>
<td>0.396</td>
</tr>
<tr>
<td>Time to peak sensory level (min)</td>
<td>7.71±2.98</td>
<td>8.51±3.11</td>
<td>0.795</td>
</tr>
<tr>
<td>Duration of sensory block (min)</td>
<td>238.49±32.90</td>
<td>285.03±39.03</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Duration of analgesia (Time to first rescue analgesic) (min)</td>
<td>224.97±42.43</td>
<td>278.71±38.48</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Data are expressed as mean±SD.

### Table 3

<table>
<thead>
<tr>
<th>Motor block characteristics</th>
<th>Group R (n=45)</th>
<th>Group RD (n=45)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to Bromage score 3 (min)</td>
<td>4.34±1.46</td>
<td>3.87±1.43</td>
<td>0.909</td>
</tr>
<tr>
<td>Time to regression to Bromage score 0 (min)</td>
<td>252.68±33.69</td>
<td>295.42±39.60</td>
<td>0.000</td>
</tr>
</tbody>
</table>

Data expressed as mean±SD.

### Table 4

<table>
<thead>
<tr>
<th>Side effects</th>
<th>Group R (n=45)</th>
<th>Group RD (n=45)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypotension, n (%)</td>
<td>4 (8.88)</td>
<td>10 (22.2)</td>
<td>0.227</td>
</tr>
<tr>
<td>Bradycardia, n (%)</td>
<td>7 (15.55)</td>
<td>7 (15.55)</td>
<td>0.773</td>
</tr>
<tr>
<td>Vomiting, n (%)</td>
<td>1 (2.22)</td>
<td>2 (4.44)</td>
<td>.984</td>
</tr>
</tbody>
</table>

### Table 5

<table>
<thead>
<tr>
<th>Success rates of spinal anesthesia in the two groups</th>
<th>Group R (n=45)</th>
<th>Group RD (n=45)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Completely successful (no supplementation given), n (%)</td>
<td>34 (75.6%)</td>
<td>35 (77.8%)</td>
<td>0.944</td>
</tr>
<tr>
<td>Partially successful (supplementation of ketamine / propofol / Fentanyl was given), n (%)</td>
<td>03 (6.7%)</td>
<td>03 (6.7%)</td>
<td>0.673</td>
</tr>
<tr>
<td>Failure (converted to general anesthesia), n (%)</td>
<td>08 (17.8%)</td>
<td>07 (15.6%)</td>
<td>0.968</td>
</tr>
</tbody>
</table>
Discussion

We measured time taken for sensory regression to S1 (sensory block duration) which was 238.49±32.90min in Group R and 285.03±39.03min in Group RD, the difference was statistically significant (P=0.000). This was primary outcome of the study. Time to return to Bromage 0 (motor block duration) was 252.68±33.69min in Group R and 295.42±39.60min in Group RD, which was statistically significant (P=0.000). We observed that there was a significant prolongation in duration of both sensory as well motor blockade in the group receiving intrathecal dexmedetomidine along with ropivacaine. Similar sensory block characteristics were found by Gupta R et al.11, Parmar et al.8. In another study conducted by Gupta et al12, they observed that the total duration of motor blockade was prolonged in dexmedetomidine group as compared to fentanyl group (421±21 min vs. 149.3±18.2 min, P value<0.0001). The local anesthetics act by blocking sodium channels, whereas the α2 adrenoceptor agonist acts by binding to pre-synaptic C-fibres and post-synaptic dorsal horn neurons. The analgesic action of intrathecal α2 adrenoceptor agonist is by depressing the release of C-fibre transmitters and by hyperpolarisation of post-synaptic dorsal horn neurons. It may be an additive or synergistic effect secondary to the different mechanism of action of the local anesthetic and the α2 adrenoceptor agonist as studied by Salgado et al.13. This antinociceptive effect may explain the prolongation of sensory block when added to spinal anesthetics.

In present study time of first complaint of pain in postoperative period was considered as duration of analgesia, which was significantly longer in group RD (278.71±38.48min) as compared to group R (224.97±42.43min) (p = 0.000). Similar to our study, Parmar et al.8 reported that duration of analgesia was significantly longer in Group RD (270.00±38.75 min) as compared to group R (174.77±22.31 min) (p< 0.01). Gupta R et al.11 also reported that duration of analgesia was significantly longer in Group D (478.4±20.9 min) compared to Group R(241.7±21.7 min) and there was a significant difference (P < 0.001).

In our study, HR, SBP DBP and SpO2 showed no significant change from baseline during intraoperative period in both groups. Both two groups were statistically comparable regarding vital parameters like heart rate, systolic blood pressure, diastolic blood pressure and SpO2 during intra-operative period (p > 0.05). Previous studies by Gupta R et al.11, Naithani U et al.10, Singh A.K. et al.14, Parmar et al.8, who studied Ropivacaine alone and with Dexmedetomidine also reported that there was no significant difference in hemodynamic data including SBP, DBP, HR, SpO2 (p > 0.05), between two Groups. This showed that isobaric Ropivacaine alone and with Dexmedetomidine in spinal anesthesia produces effective sensory motor blockade without affecting hemodynamic variables significantly.

In present study, only observed side effects were hypotension and bradycardia after spinal anesthesia which were minimal. Hypotension was noted in 4 patients and bradycardia in 7 patients that occurred in Group R and 10 patients had hypotension and 7 bradycardia in Group RD which was successfully managed with single dose of 6 mg of mephentermine i.v and 0.4 mg of atropine i.v. There was no significant difference regarding side effects between two groups (p > 0.538). Gupta R et al.11 reported that incidence of hypotension was 3.3% in Group R and 6.6% in Group RD and incidence of bradycardia was 0% and 6.6% in group R and RD respectively.

Conclusion

The addition of 5µg of dexmedetomidine to 4ml of 0.75% Ropivacaine administered intrathecally to patients undergoing total abdominal hysterectomy results in a prolongation of sensory block, motor block and duration of analgesia when compared to Ropivacaine alone. The addition of dexmedetomidine 5µg does not result in any increase in adverse effects.

Financial disclosures: None

Conflicts of interest: None
References:


