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COMPARISON OF INTRATHECAL BUPIVACAINE, LEVOBUPIVACAINE AND ROPIVACAINE FOR TRANSURETHRAL RESECTION OF PROSTATE: A DOUBLE BLINDED RANDOMISED CONTROLLED STUDY

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ABSTRACT

Background: A common treatment for "BPH (Benign Prostatic Hyperplasia)", specifically in older individuals with numerous comorbidities, is "TURP (Transurethral Resection of The Prostate)". Spinal anesthesia is preferred due to its hemodynamic benefits and timely detection of issues such as TURP syndrome and bladder perforation. Bupivacaine is widely used for spinal anesthesia but has potential cardiovascular side effects. Levobupivacaine and ropivacaine are safer alternatives with comparable efficacy, but their use in elderly TURP patients requires further evaluation. This study aims to assess and compare the effects of intrathecal bupivacaine, levobupivacaine, and ropivacaine with respect to hemodynamic stability, postoperative pain alleviation, sensory and motor blockade, and related side effects.

Materials and Methods: 150 patients scheduled for elective TURP under "SA (Spinal Anesthesia)" participated in a randomized, double-blind controlled experiment. Bupivacaine (15mg), levobupivacaine (15mg), or ropivacaine (22.5mg) were given to participants at random. Postoperative pain alleviation, the start and duration of sensory and motor blockade, hemodynamic parameters, and any side effects had also noted. "Sensory and motor blockade" features were the primary end measures, whereas hemodynamic stability as well as side effects were the supplementary outcomes. The results' statistical significance had been evaluated by employing the chi-square and ANOVA tests.

Results: In addition to producing the longest sensory and motor block durations, bupivacaine also had the quickest onset of sensory blockade. Levobupivacaine and ropivacaine came next. Because of its a bit shorter duration of motor blockade, ropivacaine facilitated early postoperative mobilization. Hemodynamic stability was significantly better with ropivacaine, which had the lowest incidence of bradycardia and hypotension, while bupivacaine showed the highest rates of these complications. Levobupivacaine demonstrated a balance between prolonged analgesia and cardiovascular safety. Postoperative analgesia was longest with bupivacaine, followed by levobupivacaine and ropivacaine. Shivering, nausea, as well as vomiting were among the side symptoms noted least common with ropivacaine and most common with bupivacaine.

Discussion: The findings suggest that while bupivacaine provides prolonged anesthesia, it is associated with higher hemodynamic instability and adverse

effects. Ropivacaine, with its superior hemodynamic profile and early recovery characteristics, is preferable for procedures requiring early ambulation. Levobupivacaine offers a balanced alternative with improved cardiovascular safety, making it suitable for elderly patients with comorbidities. Despite the study's valuable insights, its single-centre design and limited sample size warrant further multicentre trials to confirm these findings and evaluate long-term outcomes.
Keywords: Spinal anesthesia, hemodynamic stability, sensory blockade, motor blockade, postoperative analgesia, elderly patients, benign prostatic hyperplasia, local anaesthetics.

INTRODUCTION

TURP is a frequently performed procedure for the management of BPH, primarily affecting elderly. This patient group often presents with multiple coexisting medical conditions, that involve “hypertension”, “diabetes mellitus (DM)”, “chronic obstructive pulmonary disease (COPD)” and “coronary artery disease (CAD)”, which can pose challenges in perioperative care. The selection of an appropriate anaesthetic technique is critical in ensuring optimal surgical outcomes while minimizing complications associated with systemic comorbidities.[1,2]

Spinal anesthesia is widely favoured for endoscopic urological procedures, particularly in elderly patients, due to its ability to promote peripheral blood pooling, thereby reducing the risk of circulatory overload and related complications. Additionally, it enables early detection of critical conditions such as transurethral resection prostate (TURP) syndrome, characterized by fluid overload and electrolyte imbalances, as well as bladder perforation. By maintaining patient awareness during the procedure, spinal anesthesia facilitates timely recognition of symptoms, allowing for prompt intervention and improved perioperative management, ultimately enhancing patient safety and surgical outcomes.[3]

Intrathecal 0.5% heavy bupivacaine,. an amide-type local anaesthetic frequently employed in spinal anesthesia, remains a reliable choice for surgical procedures. However, in elderly or weak patients, careful dose selection is crucial to prevent excessive plasma concentrations and systemic side effects. One of the key concerns during spinal anesthesia is the drop in blood pressure caused by decreased sympathetic nervous system activity. The block can be extended by 2 to 6 dermatomes above the level of sensory blockade with this chemical sympathectomy. In older patients who are suffering from cardiac disease, “systemic vascular resistance” might drop by up to 25%, whereas in normovolemic people, it can drop by 15 to 18%.[4] Therefore, judicious dosing and vigilant hemodynamic monitoring are essential to ensure patient safety.

Levobupivacaine, the S (-)-enantiomer of racemic bupivacaine, is indeed recognized as a safer alternative to the racemic form. It retains similar anaesthetic potency but has a lower risk of cardiotoxicity and neurotoxicity, making it particularly beneficial in greater-risk populations—that involve elderly patients or those with underlying cardiac disease. At lower intrathecal doses, it induces less motor blockade than bupivacaine, making it advantageous for early postoperative mobilization. Its favourable cardiovascular and central nervous system safety profile further supports its use in spinal anesthesia, particularly in geriatric patients with cardiovascular disorders.[5]

In comparison to bupivacaine, ropivacaine, an S-enantiomer and propyl derivative of bupivacaine, is long-acting amide local anesthesia that is less potent, less lipid soluble, and less likely to cause cardiovascular and central nervous system damage. A smaller degree of motor block results from its primary targeting of pain-transmitting nerve fibers (Aδ and C fibers) while sparing those that participate in motor control (Aβ fibers). Because of this feature, as well as its briefer duration of action and faster recovery of motor function, ropivacaine is especially useful for ambulatory operations and intermediate-length surgeries in day-care surgical units.[6]

While Ropivacaine has demonstrated efficacy and safety in other regional anesthesia techniques, its specific application via intrathecal administration requires further exploration and validation. Given the distinct pharmacological profiles of bupivacaine, levobupivacaine, and ropivacaine, a comprehensive comparison is essential to determine the optimal local anaesthetic agent for neuraxial anesthesia in elderly patients undergoing TURP.

Despite individual studies on these agents, direct comparative research in elderly urological patients is limited. Important factors like the onset of “sensory and motor block”, cardiovascular stability, post-operative pain management, and side effects are all methodically evaluated in this study. The results will provide evidence-based guidance for anaesthetic selection, improving patient safety and perioperative outcomes in this high-risk population.

MATERIALS AND METHODS

This double-blinded, randomized, prospective study was conducted at our institute over 18 months after obtaining ethical committee approval. 150 patients scheduled for elective TURP under SA had been

divided into 3 groups at random: i) "Group B received bupivacaine (15mg)", ii) "Group L received levobupivacaine (15mg)", and iii) "Group R received ropivacaine (22.5mg)".

Computer-generated, sequentially numbered, opaque, sealed envelopes were employed for randomization. The following patients were excluded: those with known allergy to local anesthesia, coagulation abnormalities, morbid obesity, spinal deformities, or local infection at the lumbar puncture site; patients 50yrs. of age or older, ASA Grade I or II, scheduled for elective TURP had been involved.

Following written informed consent, each patient underwent a preanesthetic assessment. The night before surgery, patients had been given oral ranitidine (150mg) and alprazolam (0.5 mg) as premedication. "Heart rate (HR)", "non-invasive blood pressure (NIBP)", "electrocardiography (ECG)", and "oxygen saturation (SpO_2)" were all part of the routine intraoperative monitoring. Patients were given a preload of crystalloid solution at a dose of 10mL/kg before to spinal anesthesia. Under aseptic precautions, Lumbar puncture had been conducted at L3–L4 interspace utilizing "25-gauge Quincke needle", and assigned research drug had been administered intrathecally. To maintain blinding, two anaesthesiologists were involved—one prepared and administered the drug, while the other was responsible for intraoperative monitoring and patient care.

Hemodynamic parameters were monitored at baseline, every 2.5minutes during first 10minutes, subsequently every 10minutes until surgery ends. Hypotension, defined as a greater than 20% drop in average arterial pressure from systolic blood pressure or baseline below 90mmHg, had been treated with 6mg of mephentermine. Bradycardia, identified as a heart rate below 50bpm, had been managed with 0.6mg atropine. Sensory block was assessed using pinprick method at one-minute intervals; onset was recorded as the time for achieving a T10 sensory level, Moreover, duration had been measured unless regression to S2 dermatome.

Motor block had been evaluated utilizing Modified Bromage Scale. Onset had been noted as the time required for reaching complete block (score3), while duration had been measured from full block to complete recovery (score of 0). Pain post-operation was monitored hourly utilizing the VAS (Visual Analog Scale), rescue analgesics were administered when VAS score reached 4 or higher.

In order to determine the most safe and efficient anesthesia for this high-risk group, the study offers a systematic comparison of "sensory and motor block" characteristics, hemodynamic responses, postoperative pain control, along with side effects related to intrathecal bupivacaine, levobupivacaine, ropivacaine in elderly patients undergoing TURP.

RESULTS

The study included 150 patients equally divided into three groups receiving intrathecal bupivacaine (Group B), levobupivacaine (Group L), and ropivacaine (Group R). As shown in Table 1, baseline demographic characteristics such as age, weight, height, and ASA status were comparable among the groups ($p > 0.05$), ensuring homogeneity.

Table 1: Baseline Demographic and Clinical Characteristics

Demographic	Group B (Bupivacaine)	Group L (Levobupivacaine)	Group R (Ropivacaine)	p-value
Age (years)	55.13 ± 4.25	59.53 ± 4.55	60.23 ± 4.25	0.500
Weight (kg)	62.5 ± 4.17	62.13 ± 4.57	63.4 ± 4.02	0.433
Height (cm)	156.57 ± 4.35	158.47 ± 5.10	157.93 ± 4.14	0.372
ASA classification	1.46 ± 0.50	1.43 ± 0.50	1.43 ± 0.50	0.900

Regarding sensory blockade (Table 2), bupivacaine demonstrated the fastest onset (2.40 ± 0.48 min) and longest total duration of analgesia (138.17 ± 10.46 min) compared to levobupivacaine and ropivacaine ($p < 0.05$). Ropivacaine showed a significantly slower onset and shorter sensory duration, though it achieved the highest sensory level among the three.

Table 2: Onset and Duration of Sensory Blockade

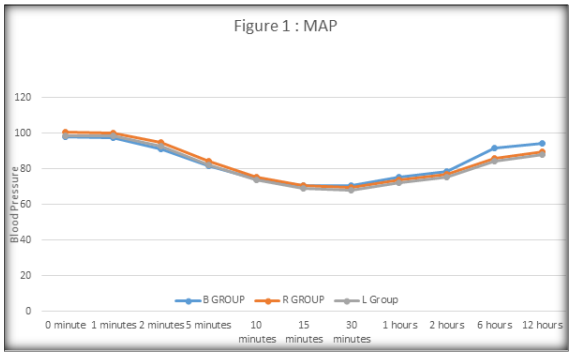
Parameters	Group B (Bupivacaine)	Group L (Levobupivacaine)	Group R (Ropivacaine)	P	Group B vs L	Group B vs R	Group L vs R
Onset of sensory blockade (min)	2.40 ± 0.48	2.55 ± 33.91	3.22 ± 0.48	0.32	0.0001	0.0001	0.0001
Highest sensory level achieved	4.4 ± 0.621	5.2 ± 0.76	5.33 ± 0.60	0.0001	0.0001	0.0001	0.46
Two segment regression time from highest block (min)	108 ± 10.77	98.67 ± 18.30	91.83 ± 9.01	0.06	0.0001	0.0001	0.046
Time of regression (min)	161.67 ± 12.78	143.33 ± 23.68	118.33 ± 12.01	0.45	0.0001	0.0001	0.0001
Total duration of analgesia (min)	138.17 ± 10.46	137.67 ± 16.95	126.67 ± 15.55	0.9	0.0001	0.01	0.01

Motor blockade analysis (Table 3) revealed levobupivacaine had the quickest onset (6.8 ± 1.3 min), while bupivacaine provided the longest duration (156.5 ± 25 min), followed by levobupivacaine and ropivacaine, respectively ($p < 0.05$ for duration).

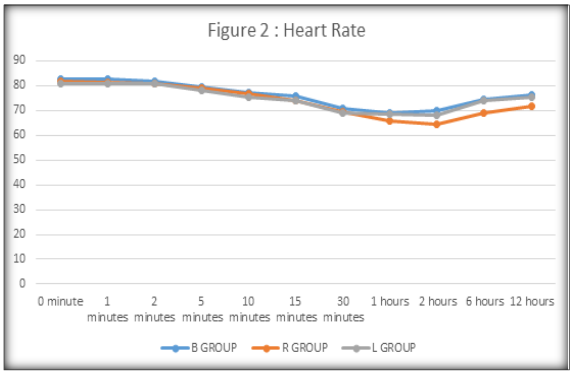
Table 3: Duration of Motor Blockade

Group	Onset of Motor Block (min, mean ± SD)	p-value (Onset)	Duration of Motor Block (min, mean ± SD)	p-value (Duration)
Bupivacaine (Group B)	7.0 ± 1.2	0.421	156.5 ± 25	0.001
Ropivacaine (Group R)	7.5 ± 1.4	0.305	122.3 ± 20	0.014
Levobupivacaine (Group L)	6.8 ± 1.3	0.632	137.1 ± 22	0.025

Hemodynamic stability findings (Figure 1) indicated ropivacaine had the lowest MAP drop and hypotension incidence, highlighting its superior cardiovascular profile, although intergroup differences were not statistically significant ($p > 0.05$).



Heart rate variations over time (Figure 2) became significant after the 2-hour mark, with Group R showing a lower mean heart rate compared to Groups B and L ($p < 0.01$ at 2, 6, and 12 hours).



Postoperative analgesia results (Tables 4) showed the longest duration in the bupivacaine group (12 ± 2 hours). Levobupivacaine (11 ± 2 hours) and ropivacaine (10 ± 1.5 hours) had shorter durations, with significant differences in analgesic requirement and time to first request ($p < 0.05$).

Table 4: Analgesia Requirements Post-Surgery

Group	Time to First Analgesia Request (min, mean ± SD)	p-value for Time	Total Doses of Analgesia in 24h (mean ± SD)	p-value for Total Doses
Bupivacaine (Group B)	240 ± 30	0.032	2.5 ± 0.8	0.045
Ropivacaine (Group R)	230 ± 35	0.032	2.8 ± 0.7	0.032
Levobupivacaine (Group L)	250 ± 28	0.032	2.3 ± 0.9	0.045

Complication rates were slightly higher with bupivacaine (15%) compared to levobupivacaine (10%) and ropivacaine (12%), primarily due to hypotension and nausea. [Table 5]

Table 5: Incidence and Types of Complications

Complication Type	Bupivacaine (Group B)	Ropivacaine (Group R)	Levobupivacaine (Group L)	p-value
Patients Affected (%)	15% (7/50)	12% (6/50)	10% (5/50)	0.819
Hypotension (n, % of total)	10 (20%)	8 (16%)	7 (14%)	0.761
Nausea (n, % of total)	5 (10%)	0 (0%)	4 (8%)	0.100
Pruritus (n, % of total)	0 (0%)	0 (0%)	1 (2%)	0.605

As shown in Table 6, the mean time to full motor recovery was shortest in ropivacaine (160 ± 25 min), followed by levobupivacaine (165 ± 20 min) and bupivacaine (170 ± 30 min). The incidence of delayed recovery (>180 min) was highest in the ropivacaine group, though not statistically significant ($p > 0.05$).

Table 6: Return of Motor Function Post-Surgery

Group	Mean Time to Full Motor Recovery (min)	Standard Deviation	Patients with Delayed Recovery (>180 min) (n, %)	p-value
Bupivacaine (Group B)	170 ± 30	30	5 (10%) [5/50]	0.05
Ropivacaine (Group R)	160 ± 25	25	7 (14%) [7/50]	0.08
Levobupivacaine (Group L)	165 ± 20	20	6 (12%) [6/50]	0.06

DISCUSSION

In this investigation, elderly patients slated for TURP had their clinical safety and efficacy for intrathecal bupivacaine, levobupivacaine, and ropivacaine compared. A balanced comparison was ensured by the statistical similarity of the baseline demographics, which included age, weight, height, ASA classification, across all groups.[Table 1]

Bupivacaine was the first to cause sensory blockade, followed by levobupivacaine and ropivacaine ($p<0.05$, significant). Bupivacaine had the longest duration of sensory blocking, levobupivacaine had a somewhat shorter length, and ropivacaine had a much shorter duration ($p < 0.05$, significant). These outcomes are consistent with an investigation by Jagtap et al. that found that ropivacaine and bupivacaine in urological operations had comparable sensory block properties.[7]

Furthermore, Glaser et al. found levobupivacaine to have a sensory blockade duration similar to bupivacaine, supporting its efficacy as an alternative.[8]

The duration of postoperative analgesia was longest with bupivacaine, followed by levobupivacaine and ropivacaine. [Table 2] This trend is according to investigations by Varun et al. and Malinovsky et al,[9,10] who reported that while bupivacaine provides prolonged pain relief, it requires careful monitoring due to potential hemodynamic instability.

Levobupivacaine had the earliest onset of motor blockade, followed by bupivacaine and ropivacaine. In contrast, ropivacaine had the lowest duration of motor blockade ($p<0.001$), whereas bupivacaine had the longest [Table 3]. These findings align with Luck et al. and Lee et al,[11,12] who observed that ropivacaine facilitates early postoperative mobilization due to its shorter motor block duration compared to bupivacaine.

Hemodynamic stability was notably better with ropivacaine, which had the lowest incidence of hypotension, followed by levobupivacaine and bupivacaine ($p < 0.05$). Additionally, bradycardia was more frequent with bupivacaine, occurring less with levobupivacaine and ropivacaine ($p<0.05$, significant). The "mean arterial pressure (MAP)" reduction was most significant with bupivacaine, while ropivacaine demonstrated the highest stability ($p < 0.05$, significant). These findings are supported by Malinovsky et al,[10] and Graf BM et al,[13] who emphasized that ropivacaine has a more favourable cardiovascular profile compared to bupivacaine, reducing perioperative risks in elderly patients. (Figure 1& 2)

The duration of postoperative "numeric rating scale (NRS)" varied among the three anaesthetics, with bupivacaine providing the longest pain relief, followed by levobupivacaine and ropivacaine. [Table 4] Varun et al,[9] who noted that bupivacaine provided persistent analgesia but need further dosages within 24 hours, concurred with these findings.

Similarly, Glaser et al,[8] observed that levobupivacaine demonstrated an analgesic duration comparable to racemic bupivacaine, suggesting it as a viable alternative with a potentially better safety profile.

An investigation by Compagna et al. compared levobupivacaine and bupivacaine for post-surgical pain management and found that the time to first request for analgesia was slightly longer with bupivacaine (367 min) than levobupivacaine (226 min), but this difference was not statistically significant. Additionally, the number of patients requiring analgesia within 24 hours was similar between levobupivacaine and bupivacaine.[14]

The incidence of complications, including nausea, vomiting, as well as shivering, was significantly greater in the bupivacaine group in contrast to levobupivacaine and ropivacaine. [Table 5] Studies by Glaser et al,[8] and Opas Vanna et al,[15] noted similar findings, highlighting that levobupivacaine and ropivacaine are associated with fewer adverse effects than bupivacaine.

These results suggest that while bupivacaine provides a prolonged anaesthetic effect, it is related to a higher risk of hemodynamic instability as well as complications. Ropivacaine, with its shorter duration of motor blockade, favourable hemodynamic profile, and early recovery characteristics, is a preferable choice for procedures requiring early ambulation. Levobupivacaine, with its balanced sensory and motor blockade profile, offers a viable alternative with improved cardiovascular safety, making it particularly useful for elderly patients.

Despite the valuable insights from this study, some limitations should be noted. As a single-centre study with a limited sample size, findings may not be entirely generalizable.

Additionally, long-term outcomes and patient satisfaction were not assessed. Future Multi-center trials that involve larger sample sizes and longer follow-up durations have been recommended to validate these findings. Research focusing on cost-effectiveness, postoperative recovery quality, and long-term analgesic efficacy will further refine the role of these anaesthetics in clinical practice.

CONCLUSION

In summary, this study validates that levobupivacaine and ropivacaine are good substitutes for bupivacaine in spinal anesthesia for older TURP patients, offering better hemodynamic stability and a quicker recovery after surgery. The selection of an appropriate anaesthetic must be personalized to the patient's comorbidities, hemodynamic response, and surgical requirements.

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