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A prospective comparative study of levobupivacaine hydrochloride 0.5% with ropivacaine hydrochloride 0.75% for peri-operative epidural anesthesia in infra- umbilical surgeries

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ABSTRACT

Background: Epidural anesthesia is a neuraxial regional anesthesia used to provide surgical anesthesia, to supplement general anesthesia, and to provide intra and post-operative analgesia. Levobupivacaine and ropivacaine are local anesthetic agents used in an epidural. **Aims and Objectives:** The aim of this study is to evaluate the onset and duration of sensory and motor block, duration of analgesia, hemodynamics, and adverse effects of levobupivacaine and ropivacaine given epidurally for infra-umbilical surgeries. **Materials and Methods:** This prospective randomized study was conducted in a total of 142 patients undergoing an infra-umbilical surgery, divided into two groups of 71 patients each. Group L received 15 mL of 0.5% levobupivacaine and Group R received 15 mL of 0.75% of ropivacaine. The onset and duration of sensory and motor blockade, duration of analgesia, hemodynamics, and side effects were assessed. **Results:** The mean time of onset of sensory and motor block is faster with ropivacaine ($P<0.05$). The duration of sensory and motor block and analgesia was longer with ropivacaine ($P<0.05$), whereas the incidence of side effects such as hypotension was more with ropivacaine. **Conclusion:** Our study concluded that ropivacaine produced a superior quality of epidural block but levobupivacaine had a more stable hemodynamic profile.

Key words: Levobupivacaine; Ropivacaine; Epidural

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INTRODUCTION

Epidural anesthesia is a versatile technique used for both primary surgical anesthesia and as a source for post-operative pain management. Often combined with general anesthesia in surgical procedures across various patient demographics with moderate to severe comorbid disease, epidural analgesia not only provides effective pain relief but also reduces the need for other anesthetics and analgesics, thereby minimizing their side effects. In addition, it has been shown to lower cortisol levels, hasten the return of bowel function post-surgery, decrease the incidence of pulmonary embolism and venous thromboembolism, and shorten the length of in-hospital stays.[1-3]

Over recent decades, the clinical applications of epidural anesthesia and analgesia have expanded significantly. In combination with general anesthesia in surgeries, epidurals are being used to provide analgesia in the intraoperative and post-operative periods.

Levobupivacaine, a local anesthetic belonging to the amide group and an S (-)-enantiomer of bupivacaine, is increasingly being preferred in regional anesthesia

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for its improved pharmacokinetic profile over racemic bupivacaine, enhancing safety. Displaying its action through reversible blockade of neuronal sodium channels, it has shown equivalent efficacy but better tolerability in regional anesthesia techniques.

Ropivacaine, a long-acting amide local anesthetic, structurally related to bupivacaine, produces its effects similarly to other local anesthetics by reversibly blocking sodium ion influx in nerve fibers. While bupivacaine is a racemic mixture, ropivacaine happens to be a pure S (-) enantiomer, chosen for its lower toxicity and enhanced sensory and motor block characteristics.[4] In comparison to bupivacaine, ropivacaine has lesser lipophilicity due to which it is associated with decreased potential for central nervous system toxicity and cardiotoxicity. This characteristic makes it particularly suitable for epidural infusion to manage post-operative pain effectively.[5]

It is widely used in epidural blocks for surgeries such as cesarean sections, lower limb surgeries, major nerve blocks, and local infiltration.[6]

In this prospective study, we compared levobupivacaine hydrochloride 0.5% with ropivacaine hydrochloride 0.75% for perioperative epidural anesthesia in infra-umbilical surgeries.

Aims and objectives

The aim of the study was to compare and evaluate the efficacy of epidural levobupivacaine hydrochloride 0.5% with ropivacaine hydrochloride 0.75%.

Primary objective

The objective of the study was to compare the onset and duration of sensory and motor block and the duration of analgesia between the two groups.

Secondary objective

The objective of the study was to compare intraoperative hemodynamic parameters and side effects between the two groups.

MATERIALS AND METHODS

This study was conducted on 142 patients admitted in JA group of hospitals, Gajra Raja Medical College, Gwalior, during September 2022–May 2024, belonging to the physical status of American Society of Anesthesiologists (ASA) Grades I and II, aged 18–60 years, undergoing an infra-umbilical surgery, after obtaining approval from the Ethical Committee of the Institute.

Inclusion criteria

- Patient giving informed and written consent to participate in the study
- Age between 18–60 years
- ASA Grades I and II.

Exclusion criteria

- Patients with cardiovascular, hepatic, and renal diseases, and obesity
- Any coagulation disorder and patients taking anticoagulant medications
- Neurological and musculoskeletal disease
- Local infection at the injection site.

Sample size

From the study done by Maheshwari et al.,[7] using the formula,

$$n=\frac{(Z\alpha/2\sqrt{2}pq+Z1-\beta\sqrt{p1q1}+p2q2)2}{(p1-p2)2}$$

p1=14.3
p2=34.3
$Z\alpha/2=1.96$ (at 5% level of significance) $Z1-\beta=0.84$ (at 80% power of the test).

Hence, n=70.91~71, 71 patients were allotted in each group.

Total sample size=142.

Grouping

Patients were randomized into two groups by sealed envelope method.

Group L (n="71")	15 mL of 0.5% levobupivacaine epidurally
Group R (n="71")	15 mL of 0.75% ropivacaine epidurally

Pre-anesthetic assessment was done a day before the surgery for a complete general, physical, and systemic examination. All the required routine and special investigations, including a complete blood count, random blood sugar, blood urea, serum creatinine, and electrocardiogram (ECG). (Above 35 years of age) and chest X-ray (above 40 years of age) was carried out as per hospital protocol.

All patients were kept nil orally for at least 12 h before the procedure. On the patients' arrival in the operating theatre, an 18 G cannula was secured in their forearm for intravenous (IV) access. All routine monitors, including the pulse oximeter, blood pressure (BP) cuff, and ECG were connected, and observations were recorded by multipara

monitor (Drager Infinity Kappa). Pre-loading was done with approximately 15 mL/kg of ringer lactate solution.

Under all available aseptic precautions, with the patient in a sitting position, a skin wheal was raised in the L1-2 or L2-3 inter-vertebral space with 2 mL of 2% lignocaine. An 18-gauge Tuohy needle was introduced through a space around 1 cm and the stylet was removed. A 10 mL loss of resistance (LOR) syringe with 5 mL of 0.9% normal saline was firmly fastened to the hub of the Tuohy needle. The needle was slowly advanced till it entered the epidural space, which was identified by the LOR technique. The epidural catheter was threaded cephalad with 5–6 cm into the epidural space. 3 mL of 2% lignocaine with epinephrine 1:200,000 was injected as a test dose. The study drug was injected, and then the patient was positioned in the supine position. Following parameters were recorded and entered into pro forma for statistical analysis.

1. The time for onset of sensory level of the block (in minutes) (up to T8) was assessed by pin prick method
2. The evaluation of motor blockade was assessed by the modified Bromage scale (up to Bromage score 3)

Modified bromage score

0	No motor block
1	Able to bend the knee (hip blocked)
2	Able to dorsiflex the foot (hip and knee blocked)
3	Complete motor block (hip, knee, and ankle blocked).

The time for onset of motor block (Bromage 3) in minutes was recorded after the injection of the study drug.

3. The duration of sensory block was assessed in the patients as the time from induction up to regression to L1 and motor block was regression to modified Bromage score 0
4. The duration of analgesia, defined as the time from the onset of analgesia after epidural anesthesia to the onset of pain, was recorded
5. Hemodynamic parameters, including pulse rate (PR), systolic BP (SBP), diastolic BP (DBP), and mean arterial pressure (MAP), were recorded at B0, S3, S5, S10, S15, S30, S60, S90, S120, and S150 min after the injection of the study drug. During surgery, any fall in MAP below 20% of the baseline value was treated with a bolus dose of injection mephentermine 6 mg IV, PR <50 beats/min was treated with injection atropine sulfate 0.3–0.6 mg IV
6. Post-operative pain was assessed by Visual Analogic Score (VAS) Scale consisting of a 10 cm horizontal scale with gradations marked as "0" (VAS), which means no pain at all and 10 (VAS) means the worst pain imaginable.

VAS score rating:

Figure showing VAS Score

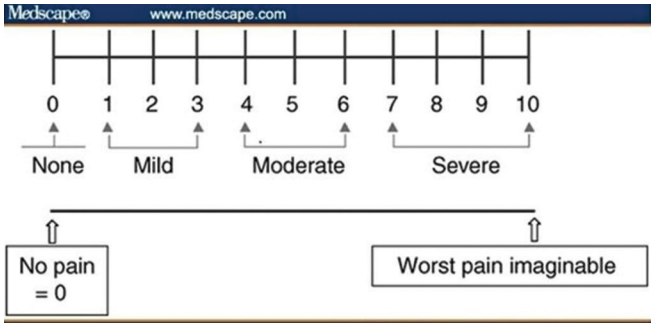

Table showing VAS Score

0	No pain
1–3	Mild pain
4–6	moderate pain
7–10	Severe pain

VAS score was noted at the time for the first rescue analgesic (TRA1). VAS score >3 was managed with rescue analgesia with injection tramadol 2 mg/kg IV in 100 mL of normal saline to relieve post-operative pain.

7. TRA1 is defined as the time interval from the induction of epidural anesthesia to the patient requiring the first dose of rescue analgesic, that is, a VAS score >3
8. Observation and recording of side effects and complication of the study drugs and technique.

Statistical analysis

The study data in electronic format needed additional statistical analysis, and it was formatted in appropriate spreadsheets such as EXCEL and Statistical Packages for the Social Sciences (SPSS). After the compilation of the data, it was analyzed statistically by SPSS software version 20.0. To compare the two groups, after checking the assumption for the normality, either the Chi-square test or the unpaired t-test were applied. The significance level was 95% confidence level ($P<0.05$).

RESULTS

As shown in Table 1, age, gender, weight, and ASA grade were comparable between the groups, $P>0.05$ which was statistically insignificant.

Table 2 shows that mean PR was lower in Group R at 5, 10, 15, 30, and 45 min and the difference was statistically significant.

Figure 1 shows that the comparison of MAP between 3 min and 90 min was statistically significant ($P<0.05$), with MAP being lower in Group R than Group L.

Table 1: Demographic profile (Mean±SD) associated with the groups

Demographic parameter	Group R (n=71)	Group L (n=71)	P-value
Age (years)	38.79±12.94	40.41±10.61	0.41
Gender	Male=49 Female=22	Male=53 Female=18	0.45
Weight (kg)	56.24±7.73	55.48±4.98	0.48
ASA grade	Grade I-50 Grade II-21	Grade I-22 Grade II-49	0.54

SD: Standard deviation, ASA: American society of anesthesiologists

Table 2: Intraoperative intergroup statistical analysis of mean pulse rate (bpm)

PR (bpm)	Group R	Group L	P-value
Basal	80.06±8.99	79.32±9.39	0.636
0 min	79.3±8.4	78.9±9.09	0.78
3 min	74.93±8.49	77.61±9.21	0.074
5 min	71.52±8.92	77.69±9.24	<0.001**
10 min	67.94±9.01	77.92±8.92	<0.001**
15 min	66.62±8.44	78.34±8.61	<0.001**
30 min	71.24±7.73	78.68±8.53	<0.001**
45 min	74.51±7.24	78.93±8.9	0.002**
60 min	77.21±8.48	78.97±8.74	0.234
90 min	78.17±7.69	79.53±9.11	0.406
120 min	77.78±7.97	80.07±8.91	0.273
150 min	80±7.48	80.67±5.83	0.82

bpm: beats per minute, PR Pulse rate. **P<0.001: Highly significant

Figure 2 shows that the onset and time to reach T10 were less in Group R as compared to Group L, whereas the duration was more in Group R, and the difference was statistically significant (P<0.05).

Figure 3 shows that the onset of motor blockade was less in Group R whereas the duration of motor blockade was more in Group R and the difference was statistically significant (P<0.05).

Table 3 shows that post-operative VAS score was comparatively better in Group R compared to Group L and was statistically significant (P<0.05).

Table 4 shows that the time taken for the TRA1 for Group R was 253.61±5.13 min and for Group L was 220.97±5.98 min, signifying that Group R has a longer duration of analgesia and the difference is statistically significant.

Figure 4 shows that the incidence of hypotension was 63.38% in Group R and 1.14% in Group L and the difference was statistically significant. However, the incidence of other side effects mentioned above was statistically insignificant between the two groups.

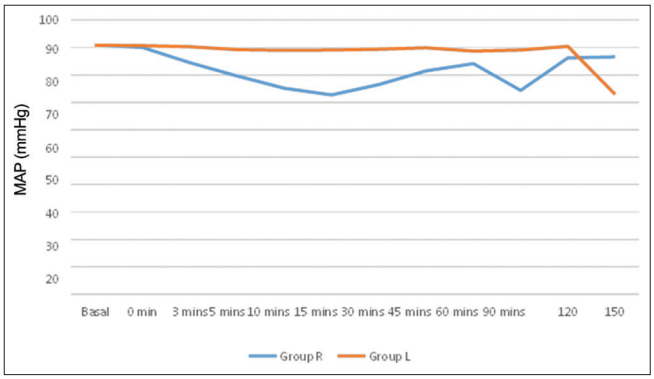

Figure 1: Intraoperative intergroup statistical analysis of mean arterial pressure (mmHg)

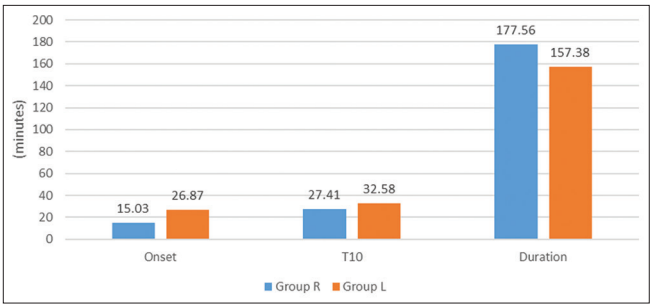

Figure 2: Parameters of sensory blockade

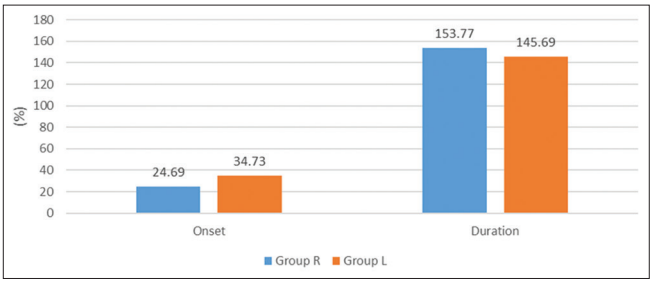

Figure 3: Parameters of motor blockade

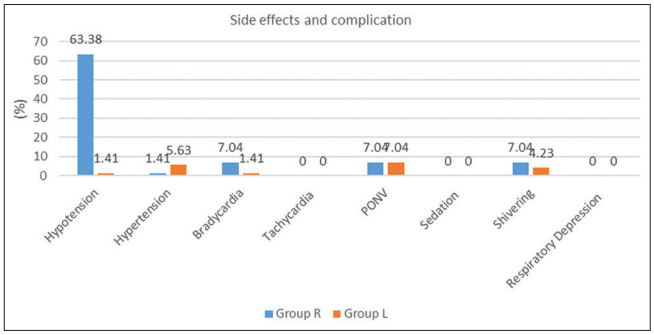

Figure 4: Side effects

DISCUSSION

Epidural anesthesia and analgesia have expanded their clinical uses over the past several decades.

Table 3: Post-operative intergroup statistical analysis of VAS score

VAS (hours)	Group R	Group L	P-value
0 h	0.49±0.5	0.69±0.47	0.017*
4 h	1.25±0.44	1.46±0.5	0.008**
8 h	1.62±0.49	2.65±0.76	<0.001**
12 h	2.55±0.5	3.96±0.64	<0.001**
20 h	3.39±0.49	5.21±0.41	<0.001**
24 h	4.39±0.49	6.21±0.41	<0.001**

VAS: Visual analogic score, h: hours. *P<0.05: Significant. **P<0.001: Highly significant

Table 4: Time taken for first rescue analgesic

TRA (m in) 1st rescueanalgesia	Group R	Group L	P-value
	253.61±5.13	220.97±5.98	<0.001**

TRA: Time for first rescue analgesia, m: Time in minutes. **P<0.001: Highly significant

Levobupivacaine, the pure S (-)-enantiomer of bupivacaine, has been successfully used in providing epidural anesthesia and analgesia for surgical procedures, with effects similar to those produced by equal doses of bupivacaine.

Ropivacaine, a long-acting local anesthetic belonging to the amino amide family, when used at clinically relevant concentrations (0.5–0.75%) for epidural anesthesia, produces a blockade that is similar to that produced by the same concentrations and doses of bupivacaine.

In our study, we compared the efficacy of two local anesthetics, levobupivacaine, and ropivacaine in epidural anesthesia.

In our study, demographic characteristics such as age gender, and weight (Table 1) were comparable between both groups and were statistically insignificant (P>0.05) similar to the studies of Maheshwari et al.,[7] Garg et al.,[8] Karki et al.,[9] and De Negri et al.[10]

The time of onset of sensory blockade (Figure 2) for Group L was 26.87±2.88 min and for Group R was 15.03±1.85 min, with a P<0.001, which was highly significant. Thus, ropivacaine has a faster sensory block onset compared to levobupivacaine similar to the study conducted by Maheshwari et al.,[7] and Peduto et al.[11]

The duration of sensory block (Figure 2) in Group L was 157.38±4.74 min whereas in Group R it was 177.56±3.73 min, P<0.001 and the difference was highly significant.

Similar results were observed in the study conducted by Maheshwari et al.,[7] and Peduto et al.,[11] also observed similar results in their study, where they compared 15 mL of 0.5% levobupivacaine and 15 mL 0.75% of ropivacaine for epidural anesthesia among patients undergoing elective lower limb procedures. They observed that the duration of sensory block was longer in the patients who received ropivacaine as compared to those who received levobupivacaine.

The time of onset of motor block (Figure 3) in Group L was 34.73±2.23 min, whereas in Group R it was 24.69±2.16 min. The P<0.001 and thus the difference was highly significant. Thus, ropivacaine had a faster onset of motor block compared to levobupivacaine. Similar results were observed in the study conducted by Maheshwari et al.,[7] and Peduto et al.,[11] where ropivacaine had a faster onset of motor block.

The duration of the motor block (Figure 3) in Group L was 145.69±3.66 min and 153.77±3.5 min in Group R. The P<0.001 and the difference was statistically significant. Thus, ropivacaine had a longer duration of motor block compared to levobupivacaine.

A similar observation was obtained in the study conducted by Maheshwari et al.,[7] where ropivacaine demonstrated a longer duration of motor block as opposed to levobupivacaine.

Various parameters such as heart rate, SBP, DBP, MAP, and SpO_2 were analyzed perioperatively, and it was observed that the comparison of the mean PR (Table 2) between 5 min and 45 min was statistically significant with mean PR being lower in Group R than Group L. Difference of MAP (Figure 1) between 3 min and 90 min was statistically significant (P<0.05), with MAP being lower in Group R than Group L. Maheshwari et al.,[7] also observed results in accordance with our study where the mean PR and MAP were significantly lower in patients who received ropivacaine compared to levobupivacaine.

Bajwa et al.,[12] also observed similar results with epidural 0.75% ropivacaine where they demonstrated a declining trend in the mean PR following administration.

The duration of analgesia, as assessed by the time taken for the 1st rescue analgesia (Table 4), in Group L was 220.97±5.98 min and 253.61±5.13 min in Group R. The P<0.001 and the difference was statistically significant. VAS score (Table 3) was higher in Group L than Group R and was statistically significant, (P<0.05) showing more effective pain control with ropivacaine than levobupivacaine.

At 8th, 12th, 20th, and 24th h, due to the VAS score being higher, rescue analgesic was administered in Group L, but not in Group R.

Thus, ropivacaine improved the duration and quality of analgesia more in comparison to levobupivacaine, patients in Group R had lower VAS scores throughout the intraoperative and post-operative periods and the administration of rescue analgesia was also delayed in Group R as compared to Group L.

Maheshwari et al.,[7] and Peduto et al.,[11] observed a longer duration of analgesia with epidural ropivacaine as compared to levobupivacaine, findings consistent with our present study.

The incidence of hypotension (Figure 4) was 63.38% in Group R (45 patients) and 1.41% in Group L (1 patient). The $P<0.001$ and the difference was statistically significant. Thus, the incidence of hypotension was higher in Group R in comparison to Group L. Hypertension, bradycardia, shivering, and ponv were comparable between the groups, and the difference was statistically insignificant ($P>0.05$).

Tachycardia, shivering, and respiratory depression were not observed in any of the patients in either of the two groups.

Similar results were observed in the study conducted by Maheshwari et al.,[7] where they observed that hypotension was significantly higher in patients who received ropivacaine in comparison to levobupivacaine.

Limitations of the study

Nil.

CONCLUSION

Ropivacaine, when given through the epidural route, had a faster onset of sensory and motor blockade as compared to levobupivacaine, also it increased the duration of sensory and motor blockade and prolonged the duration of analgesia as compared to epidural levobupivacaine. However, epidural levobupivacaine produced a stable hemodynamic profile following induction as compared to epidural ropivacaine.

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Authors Contribution:
SSY- Concept and design of the study, prepared the first draft of manuscript; **SP-** Interpreted the results; reviewed the literature and manuscript preparation; **AG-** Concept, coordination, statistical analysis, and interpretation; **RG-** Preparation of manuscript and revision of the manuscript.

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