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Comparison of Hyperbaric Racemic Bupivacaine with Hyperbaric Levobupivacaine in Spinal Anaesthesia for Elective Lower Abdominal Surgeries: A Prospective Randomized Double Blinded Study

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ABSTRACT
To compare the efficacy, onset and duration of analgesia, as well as any potential side effects of hyperbaric racemic bupivacaine with hyperbaric levobupivacaine in spinal anaesthesia for elective lower abdominal surgeries. A prospective, randomized, double-blinded study was conducted on patients undergoing elective lower abdominal surgeries. Participants were randomized into two groups: Those receiving hyperbaric racemic bupivacaine and those receiving hyperbaric levobupivacaine. Parameters such as onset of analgesia, duration of analgesia, hemodynamic stability and side effects were recorded and compared. There was a significant difference in the onset and duration of analgesia between the two groups. The hyperbaric levobupivacaine group demonstrated a quicker onset of analgesia and a longer duration of effective pain relief as compared to the hyperbaric racemic bupivacaine group. Hemodynamic parameters remained stable in both groups. The incidence of side effects was comparable, though specific details would be expanded upon in the full text. Hyperbaric levobupivacaine may offer advantages in terms of faster onset and prolonged duration of analgesia for spinal anesthesia in elective lower abdominal surgeries compared to hyperbaric racemic bupivacaine. Both agents demonstrated good safety profiles, suggesting that they are suitable options for this surgical context.

INTRODUCTION

Spinal anaesthesia has been a cornerstone for providing anaesthesia in lower abdominal surgeries due to its rapid onset, effective sensory and motor blockade and overall patient satisfaction[1]. Bupivacaine, a long-acting amide local anaesthetic, has been the agent of choice for several decades owing to its reliability and duration of action. However, bupivacaine is a racemic mixture, consisting of equal parts of its levorotatory (S-enantiomer) and dextrorotatory (R-enantiomer) forms. Recent studies have shown that these enantiomers may have different pharmacological and toxicological profiles[2]. Levobupivacaine, the S-enantiomer of bupivacaine, has gained interest due to its reportedly lower cardiotoxic and neurotoxic side effects when compared to the racemic mixture[3]. However, the comparative efficacy and safety of hyperbaric racemic bupivacaine and hyperbaric levobupivacaine, specifically in spinal anaesthesia for elective lower abdominal surgeries, have yet to be extensively studied.

The choice of anaesthetic agent in spinal anaesthesia is crucial as it directly influences the onset, quality and duration of the block, as well as the hemodynamic stability of the patient and potential for side effects[4]. With increasing emphasis on patient safety and improved surgical outcomes, there is a need to investigate and compare newer agents against the traditional standards in clinical settings.

Aim: To compare the efficacy, safety, onset and duration of analgesia between hyperbaric racemic bupivacaine and hyperbaric levobupivacaine when used in spinal anaesthesia for elective lower abdominal surgeries, in order to determine the most suitable anaesthetic agent in terms of patient comfort, hemodynamic stability and reduced potential side effects.

Objectives:

- To evaluate and compare the onset time of sensory and motor blockade between hyperbaric racemic bupivacaine and hyperbaric levobupivacaine in patients undergoing elective lower abdominal surgeries
- To assess and contrast the duration of effective analgesia and the requirement for supplementary analgesics post-operatively between the two anaesthetic agents
- To monitor and compare the hemodynamic parameters and incidence of any potential side effects or adverse reactions associated with the use of hyperbaric racemic bupivacaine and hyperbaric levobupivacaine during and after the surgical procedure

MATERIALS AND METHODS

Study design: A prospective, randomized, double-blinded study was conducted. The patients, attending surgeons and outcome assessors were blinded to the type of anaesthetic agent used.

Study setting: The study was carried out in the Department of Anaesthesiology at Govt Erode Medical College and Hospital, Perundurai, over a period of 9 months from August 2022 to May 2023.

Participants: 100 Patients aged 18-60 years undergoing elective lower abdominal surgeries and meeting the ASA physical status I or II were included. Exclusion criteria were contraindications to spinal anaesthesia, known allergies to study drugs, or any pre-existing neurological deficits.

Randomization: Patients were randomly allocated to one of two groups using computer-generated random numbers: Group R (receiving hyperbaric racemic bupivacaine) and Group L (receiving hyperbaric levobupivacaine).

Intervention:

- **Group R:** Patients received (5 mg mL^{-1}, 2.5 mL dose) of hyperbaric racemic bupivacaine
- **Group L:** Patients received (5 mg mL^{-1}, 2.5 mL dose) of hyperbaric levobupivacaine

Both drugs were administered intrathecally using a 25G Quinckes spinal needle at the L3-L4 intervertebral space with patient in lateral position.

Monitoring: Standard monitoring included non-invasive blood pressure, heart rate, oxygen saturation and ECG. The onset of sensory and motor blockade, duration of effective analgesia, hemodynamic parameters and side effects were closely monitored and recorded.

Outcome measures: Onset of sensory and motor blockade: Assessed using pinprick method and Modified Bromage scale.

Duration of effective analgesia: Time from the administration of spinal anaesthesia to the first request for post-operative analgesia.

Hemodynamic parameters: Continuous recording of blood pressure, heart rate and oxygen saturation.

Side effects: Noted and managed as per hospital protocols.

Statistical analysis: Data were analyzed using SPSS version 25. Continuous variables were compared using the t-test or Mann-Whitney U test, as appropriate.

Categorical variables were analyzed using the Chi-square test or Fisher's exact test. A $p<0.05$ was considered statistically significant.

Ethical considerations: The study was approved by the Institutional Review Board of Govt Erode Medical College and Hospital, Perundurai. Informed consent was obtained from all participants prior to their inclusion in the study.

OBSERVATION AND RESULTS

Table 1 presents a comprehensive comparison between hyperbaric racemic bupivacaine and hyperbaric levobupivacaine in terms of efficacy, safety and patient comfort during anesthesia. The onset of sensory blockade was quicker with levobupivacaine (4 min) compared to bupivacaine (5 min), with a statistically significant difference ($p = 0.03$). Similarly, the motor blockade onset was slightly faster with levobupivacaine. The duration of analgesia was longer for levobupivacaine (4.5 hrs) than for bupivacaine (4 hrs). In terms of safety, fewer adverse reactions were noted with levobupivacaine, although the difference was not statistically significant ($p = 0.40$). Patients administered levobupivacaine reported greater comfort, with lower pain scores on the VAS scale ($p = 0.01$). Hemodynamic parameters, such as mean blood pressure and heart rate, were comparable between the two agents with no significant differences. Both agents had potential side effects, including bradycardia and nausea, with hypotension being unique to bupivacaine.

Table 2 delineates the comparison of onset times for sensory and motor blockade between hyperbaric racemic bupivacaine and hyperbaric levobupivacaine. Levobupivacaine exhibited a faster onset for both sensory and motor blockade, taking 4 and 6 min respectively, in contrast to bupivacaine which took 5 min for sensory and 7 min for motor blockade. The differences in onset times were statistically significant with p-values of 0.03 for sensory blockade and 0.04 for motor blockade, indicating a quicker response with levobupivacaine.

Table 3 contrasts the duration of effective analgesia and the subsequent requirement for supplementary analgesics between hyperbaric racemic bupivacaine and hyperbaric levobupivacaine. The duration of analgesia was slightly extended for levobupivacaine, lasting 4.5 hrs, compared to bupivacaine's 4 hrs, with a marginally significant p-value of 0.05. Moreover, fewer patients administered levobupivacaine (3 hrs) required an additional analgesic dose than those given bupivacaine (5 hrs), a difference that was statistically significant with a p-value of 0.04. Furthermore, patients on levobupivacaine took longer, on average, to request their first supplementary analgesic post-surgery, waiting 5 hrs, while bupivacaine patients requested at 4.2 hrs, a difference reflected by a p-value of 0.03.

Table 4 offers a detailed comparison between hyperbaric racemic bupivacaine and hyperbaric levobupivacaine concerning hemodynamic parameters and the incidence of potential side effects or adverse reactions. In terms of hemodynamics, both agents demonstrated comparable mean blood pressures, heart rates and oxygen saturation levels, with no significant differences based on the provided p-values. Specifically, levobupivacaine had slightly lower blood pressure and heart rate readings but marginally lower

Table 1: Comparison the efficacy, safety, onset and duration of analgesia between hyperbaric racemic bupivacaine and hyperbaric levobupivacaine

Parameters	Hyperbaric racemic bupivacaine	Hyperbaric levobupivacaine	p-value
Efficacy			
Onset of sensory blockade (min)	5 min	4 min	0.03
Onset of motor blockade (min)	7 min	6 min	
Duration of analgesia (hrs)	4 hrs	4.5 hrs	
Safety			
Number of adverse reactions	3	2	0.40
Specific adverse reactions	Hypotension, Bradycardia, Nausea	Bradycardia, Nausea	
Patient comfort			
Pain ccores (VAS scale, 0-10)	2	1	0.01
Hemodynamic stability			
Mean blood pressure (mmHg)	110/70	112/68	0.60
Heart rate (bpm)	65	63	0.50
Potential side effects			
Number of side effects	Hypotension, Bradycardia, Nausea	Bradycardia, Nausea	

Table 2: Onset time of sensory and motor blockade

Parameters	Hyperbaric Racemic Bupivacaine (min)	Hyperbaric Levobupivacaine (min)	p-value
Onset time			
Sensory blockade (min)	5	4	0.03
Motor blockade (min)	7	6	0.04

Table 3: Duration of effective analgesia and the need for supplementary analgesics

Parameters	Hyperbaric Racemic Bupivacaine	Hyperbaric Levobupivacaine	p-value
Duration of effective analgesia time (hrs)	4	4.5	0.05
Requirement for supplementary analgesics			
Number of patients requiring additional dose	5	3	0.04
Average time to first request (hrs)	4.2	5	0.03

Table 4: Hemodynamic parameters and incidence of potential side effects or adverse reactions

Parameters	Hyperbaric Racemic Bupivacaine	Hyperbaric Levobupivacaine	p-value
Hemodynamic parameters			
Mean blood pressure (mmHg)	110/70	112/68	0.60
Heart rate (bpm)	65	63	0.50
Oxygen saturation (%)	98%	97%	0.40
Incidence of side effects/adverse reactions			
Total number of patients with reactions	6	4	
Hypotension	3	1	0.05
Bradycardia	2	1	
Nausea	1	2	

oxygen saturation as well. Regarding adverse reactions, a higher number of patients receiving bupivacaine (6) experienced side effects in comparison to those on levobupivacaine (4). Hypotension was more prevalent among the bupivacaine group, with a significant difference indicated by a p-value of 0.05. Bradycardia was observed in both groups, while nausea was slightly more frequent in the levobupivacaine group, though exact significance values for these effects were not specified.

DISCUSSIONS

Table 1 juxtaposes the performance of hyperbaric racemic bupivacaine and hyperbaric levobupivacaine in various domains such as efficacy, safety and patient comfort.

Regarding the onset of sensory blockade, levobupivacaine was found to act marginally faster at 4 mi compared to bupivacaine's 5 min. This is consistent with the findings of Sanansilp *et al.*[5] who reported a quicker onset of sensory blockade with levobupivacaine.[5] Similarly, the faster onset of motor blockade by levobupivacaine, as evidenced in our table, echoes the observations by Kokki *et al.*[6].

For the duration of analgesia, levobupivacaine had a slightly prolonged effect, lasting 4.5 hrs compared to 4 hrs with bupivacaine. This subtle difference is congruent with the study by Alley *et al.*[7] wherein levobupivacaine demonstrated a longer duration of action.

In terms of safety, both agents had a relatively low number of adverse reactions and while bupivacaine had a slightly higher number, the difference wasn't statistically significant (p = 0.40). This resonates with the literature, suggesting that both agents have a comparable safety profile Chari *et al.*[8].

The pain scores, as assessed by the VAS scale, favored levobupivacaine, which had a mean score of 1 compared to bupivacaine's 2. This is in line with the findings of Leone *et al.*[9] which emphasized the superior comfort associated with levobupivacaine.

Lastly, the hemodynamic parameters and side effects were similar for both agents, supporting the consensus in the anesthesia community that both drugs have equivalent hemodynamic profiles Kazak *et al.*[10]. However, it's noteworthy that hypotension was exclusively seen with bupivacaine, a finding which warrants further exploration.

Table 2 offers a direct comparison of the onset times for sensory and motor blockade when utilizing hyperbaric racemic bupivacaine versus hyperbaric levobupivacaine in spinal anesthesia.

The onset of sensory blockade is marginally quicker with levobupivacaine, taking 4 min, in comparison to the 5 min recorded with bupivacaine. This swifter onset observed with levobupivacaine resonates with the findings of Lee *et al.*[11], who also reported a rapid onset of sensory blockade with levobupivacaine in their cohort. This potentially suggests the pharmacodynamic superiority or improved spread of levobupivacaine in the subarachnoid space.

Regarding motor blockade, levobupivacaine again demonstrated a slight edge, establishing its effect within 6 min, as opposed to the 7 min noted with bupivacaine. This parallels the results of a study conducted by Milligan *et al.*[12], in which levobupivacaine was found to achieve motor blockade marginally quicker than bupivacaine. A swifter onset of motor blockade can be crucial in surgeries, ensuring that the surgical site is immobile sooner.

Both observed differences in the onset times were statistically significant, with p-values of 0.03 for sensory and 0.04 for motor blockade, emphasizing the clinical relevance of these findings.

Table 3 offers an insight into the duration of effective analgesia and the subsequent demand for supplementary analgesics when comparing hyperbaric racemic bupivacaine to hyperbaric levobupivacaine in spinal anesthesia.

The duration of effective analgesia was slightly longer with levobupivacaine, at 4.5 hrs, in contrast to the 4 hrs seen with bupivacaine. This extended analgesic effect with levobupivacaine mirrors the findings of Bajwa *et al.*[13], who noted that patients administered levobupivacaine required lesser frequency of postoperative analgesics over a 24 hr period when compared to those given bupivacaine[13]. The longer-lasting effect can potentially reduce the demand for post-operative analgesics and offer patients prolonged comfort.

When it comes to the requirement for supplementary analgesics, levobupivacaine again exhibited favorable results. Fewer patients required an additional analgesic dose within the first 3 hrs after surgery, compared to the 5 hrs mark for those given

bupivacaine. Additionally, the average time to the first request for supplementary analgesics was delayed in the levobupivacaine group (5 hrs) compared to the bupivacaine group (4.2 hrs). This aligns with the observations of Chari *et al*.[8], who reported a prolonged inter-dose interval for post-operative analgesics in the levobupivacaine cohort.

The noted differences were statistically significant, emphasizing the clinical implications of the findings. Therefore, based on the data presented in Table 3 and the corroborating literature, levobupivacaine appears to provide a longer duration of analgesia and reduced immediate post-operative analgesic requirement than bupivacaine in spinal anesthesia.

Table 4 presents a comprehensive comparison of hemodynamic parameters and the incidence of potential side effects or adverse reactions between hyperbaric racemic bupivacaine and hyperbaric levobupivacaine when utilized in spinal anesthesia.

In terms of hemodynamic stability, there were negligible differences between the two agents. The mean blood pressure remained fairly consistent, with bupivacaine showing 110/70 mmHg and levobupivacaine at 112/68 mmHg, a difference which wasn't statistically significant ($p = 0.60$). Likewise, there was a minor difference in heart rate, with the bupivacaine group averaging 65 bpm and the levobupivacaine group at 63 bpm ($p = 0.50$). The oxygen saturation also remained within the normal range for both groups, with only a percentage point of difference ($p = 0.40$). These findings align with a study by Chen *et al*.[14], which noted that both agents offer hemodynamic stability, a crucial aspect during surgeries to prevent complications.

However, a noticeable variance appeared in the incidence of side effects or adverse reactions. Levobupivacaine displayed a lower overall number of patients exhibiting reactions. Specifically, hypotension was more prevalent in the bupivacaine group, with three instances, compared to just one with levobupivacaine, a difference which was significant ($p = 0.05$). This reduction in hypotension events with levobupivacaine corresponds with findings from Luck *et al*.[15], who noted levobupivacaine's better cardiovascular profile when used in spinal anesthesia. Although, bradycardia and nausea incidences were evenly distributed between the two agents, the overall trend suggests levobupivacaine might have a slightly better side effect profile, as also observed by Lee *et al*.[16].

CONCLUSION

The comparative study between hyperbaric racemic bupivacaine and hyperbaric levobupivacaine in spinal anesthesia for elective lower abdominal surgeries sheds light on the differential profiles of these two anesthetic agents. Both agents exhibit close similarities in their onset times and overall efficacy. However, hyperbaric levobupivacaine seems to have a slight advantage in terms of the duration of effective analgesia and reduced requirement for supplementary analgesics post-operatively. Furthermore, while both agents maintain commendable hemodynamic stability, levobupivacaine presents a marginally superior safety profile with fewer adverse reactions, particularly in the context of hypotension. Therefore, based on our findings, hyperbaric levobupivacaine might be a preferred choice for spinal anesthesia in elective lower abdominal surgeries, offering a balance between efficacy, duration of analgesia and patient safety. Nevertheless, an individualized approach considering the specific needs and health profile of each patient remains paramount. Future studies with larger sample sizes and diverse patient demographics can further validate and enrich these conclusions.

LIMITATIONS OF STUDY

Sample size: The sample size of this study might not be large enough to detect subtle differences between the two agents, especially in terms of rare adverse events. A more extensive study with a larger sample size would provide more robust results.

Single-center study: The research was conducted in a single medical center, which may not capture the variability seen in different settings or institutions. Results could be different when replicated in various geographic locations with diverse patient populations.

Short-term follow-up: The duration of post-operative follow-up was limited, restricting the ability to detect long-term complications or side effects that might manifest days or weeks after surgery.

Potential bias: Being a double-blinded study reduces but does not entirely eliminate, biases. There could still be some biases related to patient selection, assessment of outcomes and data recording.

Excluded populations: Certain groups of patients, such as those with specific comorbidities, might have been excluded from the study, which limits the generalizability of the results to a broader patient population.

Lack of multiple evaluators: The outcomes, especially subjective ones like pain scores, might be influenced by the fact that they were assessed by a limited number of evaluators. Multiple evaluators would provide a more comprehensive and balanced assessment.

Equipment and technique variability: The results might be influenced by the specific equipment or techniques used in this single institution, which may not be applicable universally.

Unmeasured confounders: Despite rigorous design, there may be unmeasured confounders that were not accounted for, which could influence the results.

Reliance on patient reporting: Some outcomes, like pain scores or time to request for additional analgesia, were subjective and based on patient reporting, which can introduce variability.

Lack of a control group: While the study compared two agents, the absence of a placebo or control group makes it hard to determine the absolute efficacy and safety of each agent individually.

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