Original Research

A Randomized Comparative Study Between Hyperbaric Levobupivacaine (0.5%) And Hyperbaric Ropivacaine (0.75%) In Lower Limb Surgeries Under Spinal Anaesthesia

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Abstract
Aim: To compare efficacy of hyperbaric levobupivacaine (0.5%) and hyperbaric ropivacaine (0.75%) in lower limb surgeries under spinal anaesthesia.
Material and Methods: The present study was conducted in which 80 patients of American Society of Anesthesiologists (ASA) physical status I and II, aged 18-65 years, of either sex, who were admitted to SVBP Hospital associated with LLRM Medical College, Meerut, and undergoing lower limb surgeries under spinal anesthesia were enrolled. After obtaining Institutional Ethical Committee clearance, all included patients were explained about the study, and written informed consent was taken from them. The patients were randomized and divided into two groups, GROUP R in which we administered Hyperbaric Ropivacaine (0.75%) [3ml] and GROUP L in which we administered Hyperbaric Levobupivacaine (0.5%) [3ml]. Hemodynamic monitoring devices such as a non-invasive blood pressure cuff, pulse oximeter, and electrocardiogram (ECG) were employed to monitor patients' vital signs throughout the procedure. Pain assessment tools, such as a visual analog scale (VAS) or numeric rating scale (NRS) were used to evaluate the efficacy of the analgesia provided by each drug.
Results: The onset of sensory and motor block was early in group L. The duration of motor block was longer in Group L than Group R. The duration of Analgesia was longer in Group L than Group R. The hemodynamic parameters were comparable in both the groups but the SBP, DBP, MAP was on the lower side in Group L as compared to Group R. Hypotension, bradycardia, Nausea, Vomiting and Shivering were experienced by more patients in group L than group R, but no significant difference was observed.
Conclusion: Hyperbaric Levobupivacaine is more efficient than Hyperbaric Ropivacaine as it has early onset of sensory block, early onset of motor block, longer duration of analgesia and longer duration of motor block.
Keywords: Hyperbaric levobupivacaine, Hyperbaric ropivacaine, Lower limb surgeries, Spinal anaesthesia.
Biomarkers

Introduction:
"Cocainization of the spinal cord" was first described by August Bier in 1899.Cocaine, the drug which lead to the discovery of spinal anaesthesia, had many side effects and eventually Lignocaine became the preferred drug. Later 5% Lignocaine heavy was reported to cause transient neurological symptoms and it was withdrawn from regular use. Since then, Bupivacaine has been the most widely used drug for Spinal anaesthesia. Three decades ago, some patients who received Bupivacaine developed life threatening arrhythmias, which were refractory to treatment. On

notifying this life-threatening cardiotoxicity of Bupivacaine, the search for newer, safer local anaesthetic drugs began. An important aspect of this cardiotoxicity isthat it is related to the stereospecificity of Bupivacaine with the 'S' isomer having very less cardiotoxic potential compared to the 'R' form. The 1980s heralded the arrival of two new agents, ropivacaine and levobupivacaine, adding to the armamentarium of neuraxial blockade. The safety and effectiveness profile of spinal and epidural anesthesia were further improved by these agents, which also provided benefits like improved motor block characteristics and decreased cardiotoxicity [(1).]

Distinguishing between R and S enantiomers in pharmacology is crucial due to their varying affinities for different ion channels, particularly within the central nervous system (CNS) and cardiac myocytes. S enantiomers typically exhibit lower affinity towards these channels compared to their R counterparts. Levobupivacaine [(2)] has become a more secure option than its racemic parent chemical, bupivacaine, after being synthesized from the pure S (-) enantiomer. This attribute is especially vital in clinical scenarios where cardiac safety is paramount. Ropivacaine, introduced in 1996, represents another significant advancement in local anesthesia. Similar to levobupivacaine, ropivacaine is pure S enantiomer of a strongly protein-bound amide local anaesthetic. Its lower lipid solubility, relative to bupivacaine, results in reduced penetration into myelinated motor fibers. Consequently, ropivacaine offers a more favorable balance of sensory and motor blockade, providing greater differentiation between sensory and motor functions. Such knowledge empowers clinicians to make informed decisions regarding the selection and administration of local anesthetics[(3)] ultimately optimizing patient outcomes and enhancing the quality of care provided.

Intrathecal ropivacaine has emerged as a promising option in anesthesia practice due to its favorable safety profile, characterized by a shorter duration of action comparedto bupivacaine. When compared to intrathecal lignocaine, it also shows a lowerincidence of transient neurological symptoms (TNS). We conducted a thorough analysis to examine the effects of pure S-(laevo-rotatory) enantiomers, hyperbaric ropivacaine and hyperbaric levobupivacaine. We meticulously assessed various parameters including the onset and duration of both sensory and motor blockade, first rescue analgesia, induced by these agents.

This study aimed to provide clinicians with valuable insights into the comparative efficacy and safety profiles of hyperbaric levobupivacaine and hyperbaric ropivacaine. By elucidating these aspects, our study contributes to optimizing anesthesia management strategies, thereby enhancing patient care and minimizing the risks associated with lower limb surgeries. The aim and objectives of the study are as follows:

Aim: To study Hyperbaric Levobupivacaine (0.5%) versus Hyperbaric Ropivacaine (0.75%) in patients undergoing lower limb Surgeries under Spinal anesthesia.

Primary Objective: Primary Objective of the study is to determine the efficacy of the drug.

Secondary Objectives:

a. To compare and evaluate onset of sensory and motor block in both the groups.
b. To compare and evaluate duration of motor block in both the groups.
c. To compare and evaluate time of first rescue analgesia in both the groups.
d. Complications if any.

Material and Methods: In this prospective randomized comparative study, after obtaining Institutional Ethical committee approval and informed written consent from the patient, we enrolled 80 patients who were classified as American Society of Anesthesiologists (ASA) physical status I and II, aged between 18 to 65 years, of either gender, admitted to SVBP Hospital associated with LLRM Medical College, Meerut, and undergoing lower limb surgery under spinal anesthesia.

Inclusion Criteria:

a. Age: 18-65 years
b. ASA grade I &II
c. Weight: 40-80kg
d. No known history of drug allergy
e. Patients undergoing lower limb Surgeries

Exclusion Criteria:

a. Patient Refusal
b. Patients with history of coagulopathy
c. Patients with local skin infections at the site of injection.
d. Increased Intracranial Pressure
e. Patients with spine deformity
f. Patient having fever, history of drug allergy
g. Surgeries requiring >2.5hrs

Allocation and randomisation of study groups: Patients with ASA grade I and II included in the present study. The study was divided into two groups i.e.

Study drug [Group L]: Hyperbaric Levobupivacaine (0.5%)

Study drug [Group R]: Hyperbaric Ropivacaine (0.75%)

To keep the study unbiased, one of the Anesthetists who was unaware of the drug to be administered, prepared 80 coded slips and randomly allocated and divided 80 slips into 2 different groups and kept them inside a plastic box. The record was kept about which code belongs to which of the two groups. Before each study a slip was picked from the box and the respective drug given. The anesthetist's performing the spinal anesthesia had no knowledge about the drug solution. Records were made available

to us only after we completed the whole study of 80 patients.

Procedure: For this comparative study, several tools were employed to assess the efficacy of Hyperbaric Levobupivacaine (0.5%) and Hyperbaric Ropivacaine (0.75%) in patients undergoing lower limb surgeries under spinal anesthesia. The primary tool used was a standardized anesthesia protocol tailored to each patient's needs. Additionally, a spinal anesthesia kit containing the necessary drugs, needles, and syringes was utilized for administering the spinal anesthesia. Hemodynamic monitoring devices such as a non-invasive blood pressure cuff, pulse oximeter, and electrocardiogram (ECG) were employed to monitor patients' vital signs throughout the procedure. Pain assessment tools, such as a visual analog scale (VAS) or numeric rating scale (NRS) were used to evaluate the efficacy of the analgesia provided by each drug.

Sensory Block Assessment: It was tested by pin prick method using hypodermic needle by a three-point scale[4]:

0-Normal Sensation
1-Loss of Sensation of pin prick (Analgesia)
2-Loss of Sensation of Touch (Anesthesia)

Time of onset (time of intrathecal injection of drug to achieve T10 segment level block) was recorded.

Motor Block Assessment: Time of Onset (Time of Intrathecal injection of drug to modified Bromage Scale 3. It was tested using modified Bromage scale[5]:

0-No paralysis
1-Inability to raise the legs against the gravity but can flex the knee,
2-Inability to flex the knee but can flex ankle
3-Inability to flex the ankle.

Monitoring Parameters

1. Pulse Rate if<60 beat/min or fall more than 20% from baseline then I/V atropine 0.2 mg increments were given
2. Blood Pressure

a. Fall more than 20% from Baseline- I/V Mephentermine 6mg was given.
b. Fall more than 30-40% continuous ionotropic support.

3. Respiratory adequacy -SpO2 monitoring. If saturation<92% at room air, oxygen supplementation via simple face mask.
4. If the patient's VAS score is >4, then patient is supplemented with Inj. Tramadol 2mg/kg IV as Rescue Analgesia. All the parameters were recorded just after giving spinal anaesthesia, then at 3, 5,10,15 minutes and at an interval of 15 minutes till 120 minutes.

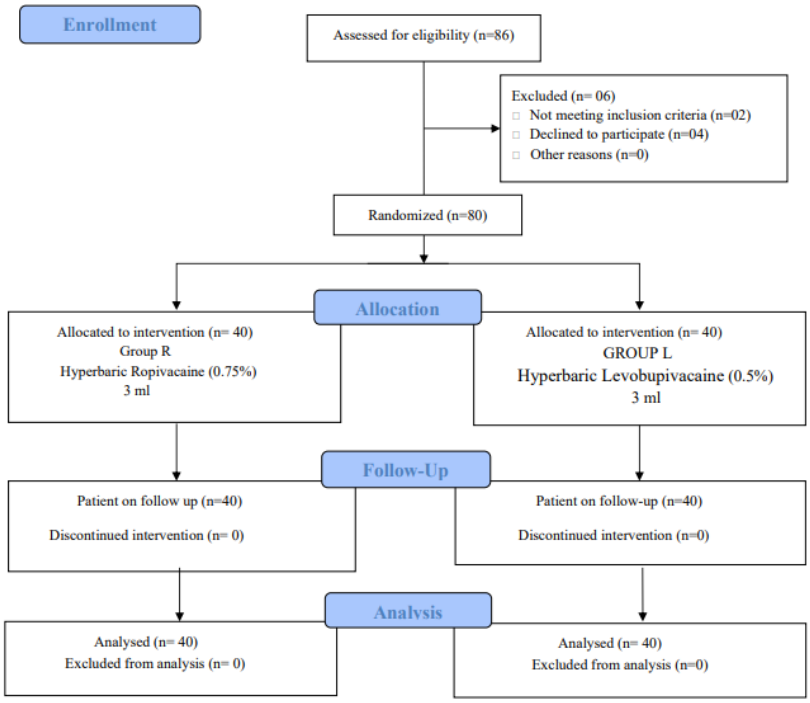
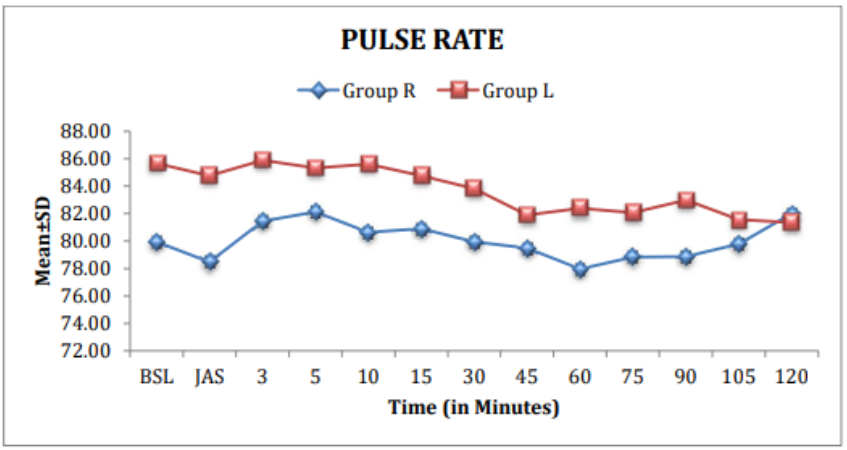


Figure 1: Consort diagram Data was collected and subjected to statistical analysis.

Statistical analysis: The statistical analysis was done using SPSS (Statistical Package for Social Sciences) Version 20.0 statistical Analysis Software. Statistical analysis was performed to compare the efficacy and safety of Hyperbaric Levobupivacaine and Hyperbaric Ropivacaine using appropriate statistical tests. Descriptive statistics were used to summarize demographic and clinical characteristics of the study population. Continuous variables such as onset and duration of sensory and motor blocks were compared between groups using t-tests or non-parametric equivalents. Categorical variables and adverse events

were analyzed using chi-square tests or Fisher's exact tests.

Results: In Group R, the maximum number of subjects were in the age group 25-34 and 35-44 years whereas in Group L maximum number of subjects were in the age group 25-34 and 18-24 years. In both the groups, male and female ratio was equal having (85%) of males and (15%) of females in each group. At baseline the mean pulse rate in Group R was 79.95±10.80 and in Group L it was 85.68±11.18 which was statistically insignificant (p>0.05). Group L has lower values as compared to Group R at 10 minutes and 60 minutes interval which were statistically significant (graph 1).



Graph 1: Mean Pulse rate in two Groups

At baseline the mean MAP in Group R was 99.68±6.62 mmHg while the same was observed to be 97.30±7.35 mmHg in Group L, showing no significant difference between the two groups(P>0.05). However, a statistically significant difference between the two groups was observed Just after spinal anesthesia and after 5 minutes of spinal anesthesia to 60 minutes with Group L showing significantly lower mean values as compared to Group R (table 1). No significant difference was observed between the two groups as regards the time taken for completion of surgery. However, for all the other landmarks, like Onset of Sensory block, Onset of Motor block, Mean time taken was higher in Group R as compared to Group L which was statistically significant. The mean duration of motor block was statistically significant with longer duration in Group L as compared to Group R. The demand for first Rescue Analgesia was early in Group R as compared to Group L which was statistically significant making it more effective (table 2).

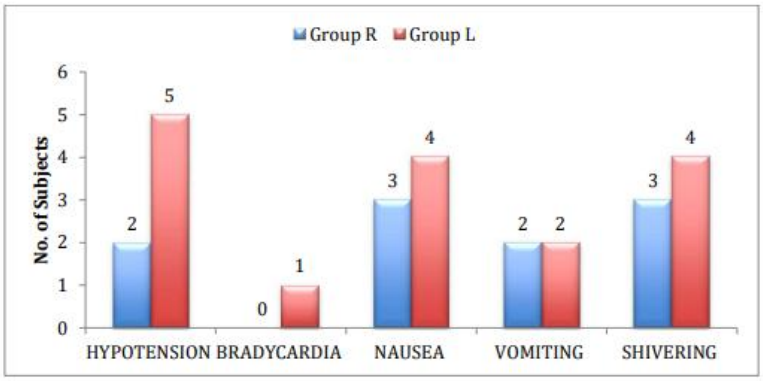
Table 1: Mean MAP in two groups at different time intervals

MEAN BP	Group R		Group L		P value
	Mean	SD	Mean	SD	
BASELINE	99.68	6.62	97.30	7.35	0.132
JAS	97.33	7.80	93.40	7.99	0.029
3min	90.20	6.94	89.03	7.61	0.476
5min	94.12	7.84	86.50	7.67	0.001
10min	93.23	6.28	85.48	7.14	0.001
15min	93.13	6.57	87.47	8.00	0.001
30min	93.78	6.09	87.42	7.86	0.001
45min	94.70	6.56	87.80	8.96	0.001
60min	89.23	7.40	83.72	8.44	0.302
75min	90.12	6.96	84.65	7.54	0.196
90min	89.55	7.33	83.18	6.68	0.134
105min	90.11	7.15	85.47	8.13	0.895
120min	86.12	7.4	85.55	7.13	0.353

Table 2: Mean Time taken to achieve various landmarks (min)

Sno.	Landmarks	Group R			Group L			"p" Value
		N	Mean (min.)	SD	N	Mean (min.)	SD	
1.	Onset of Sensory block(T10)	40	3.92	0.76	40	3.45	0.71	0.0053
2.	Onset of Motor block (Grade III)	40	5.49	0.95	40	4.52	0.81	0.0001
3.	Duration of Motor block	40	205.25	19.08	40	241.00	29.77	0.0001
4.	First Rescue Analgesia	40	270.5	14.75	40	310.2	10.71	0.04
5.	Duration of Surgery	40	84.25	23.66	40	90.75	22.69	0.214

On comparing the side effects of both the groups, it was seen that Group L has a greater number of patients with side effects as compared to Group R. Based on the analysis, there is no statistically significant difference in the proportion of patients showing hypotension between the two groups(p=0.23). In Group R, no Bradycardia episode is seen in any patient. This data shows that there are no significant differences in the occurrences of the above complications between the two groups (graph 2).



Graph 2: Complications among the study groups

Discussion: The study was conducted in 80 patients in the age group between 18-65 years, posted for various elective surgeries under spinal anaesthesia. There were no statistically significant differences seen in terms of demographic properties of the patients. The mean Age, Gender were comparable in both the groups.

Time of Onset of Sensory block was taken in minutes from the time of drug deposition to the evidence of analgesia to pinprick at T10 level. The Mean time for onset of sensory block in group R at T10 level was 3.92 ± 0.76 min & in group L at T10 level was 3.45 ± 0.71 min respectively which was comparable to the studies of Luck et al (2008)[6], Girish BK et al[7]., and Durgasheker et al[8]. Luck et al (2008)[6] compared Hyperbaric solutions of racemic bupivacaine, levobupivacaine, and ropivacaine by administering 3ml in each group for elective surgeries. The onset of sensory block at T10 was 5(2-15) min in Group Levobupivacaine and 5(2-15) min in Group Ropivacaine. Girish BK et al (2018)[7] compared Hyperbaric Levobupivacaine 0.5 % with Bupivacaine 0.5 % for spinal anesthesia in elective surgeries. The onset of Sensory Blockade in Levobupivacaine Group was 2.68 minutes. Durgasheker et al (2023)[8] in a comparative study between Levobupivacaine and Ropivacaine concluded that the onset of sensory block in group Levobupivacaine was 3.76 minutes and in Group Ropivacaine was 3.6 minutes which was comparable to our study.

Onset of Motor Block was taken in minutes from the time of drug deposition to the Modified Bromage scale 3 i.e. patient is unable to move the hip, knee and ankle joint is achieved. Mean time for onset of grade III motor block in group R was 5.49±0.95 min & in group L was 4.52±0.81 min respectively which was comparable to the studies of Girish BK et al[7] and Tamilisetti Vidya Sagar et al[9]. Girish BK et al[7] (2018) in the study found the onset of motor block was 4.21 minutes in Levobupivacaine Group. In Tamilisetti Vidya Sagar et al. (2023)[9],comparable results were found when comparing the period of onset of motor block in patients undergoing lower abdominal procedures using levobupivacaine against ropivacaine. In the former group, it was 3.65± 0.72 min, while in the latter group, it was 3.82±0.88 min.

The total duration of motor block was taken in minutes from commencement of block to the Bromage scale 0 i.e. patient can move limbs freely. The mean time of Duration of Motor Block in Group R was 205.25±19.08 and in Group L was 241.00±29.77 min respectively which was comparable to the study of P.S. Shanmugam et al[10], Tamilisetti Vidya Sagar et al[9] and Manazir Athar et al[11].Tamilisetti Vidya Sagar et al[9]. (2023) found the mean duration of motor block in Group Levobupivacaine was 201.15±22.06 and in Group Ropivacaine was 204±21.20 which was comparable to our study. P.S Shanmugam et al (2022)[10] concluded that the Duration of motor block in Ropivacaine Group was 209±7mins which was comparable to our study. Manazir Athar et al (2016)[11] in a randomized double-blind controlled trial study found that Group Levobupivacaine duration of motor block was 290.50±34.67 min and in Group Ropivacaine was 222.50±23.00 min which was similar to our findings.

The total duration of Analgesia was taken in minutes from commencement of the block to the patients first request for rescue Analgesia. The mean time of the first Rescue Analgesia in Group R was 270.5±14.75 min and in Group L was 310.2±10.71 min respectively which was comparable to the study of P.S. Shanmugam et al[10], Tamilisetti Vidya Sagar et al[9]. and Manazir Athar et al[11]. Tamilisetti Vidya Sagar et al[9] found that the time of rescue analgesic administration in Group Levobupivacaine was 262.22±36.60 min and in Group Ropivacaine was 261.20±32.71 min which was comparable to our study. P.S. Shanmugam et al concluded that the time of First Rescue Analgesia in Ropivacaine Group was 278±5mins.

Similar complications were seen in both groups, including bradycardia, hypotension, nausea, vomiting, and shivering. In both groups, these were similar and not statistically significant. Similar results were observed in the other existing literature[12-13]. Decrease in Blood pressure and Pulse rate are commonly encountered during Neuraxial blockade.

The outcomes of the study yielded intriguing findings, indicating that levobupivacaine exhibited a significantly longer duration of both motor block and analgesia compared to ropivacaine. This observation suggests that while both levobupivacaine and ropivacaine are effective for intrathecal anesthesia, levobupivacaine may hold a distinct advantage, particularly in surgical settings requiring prolonged anesthesia and postoperative pain management. This personalized approach has the potential to optimize patient comfort, enhance surgical outcomes, and contribute to overall healthcare quality.

Limitations: The study was limited to only one tertiary Centre. Maintenance of the temperature of drugs was a challenge in tropical countries. Utmost care and vigilance were taken to make this study randomized and bias free. However, limitations and biases can occur during any new research and this study is not an exception.

Conclusion: We have considered the potential confounding factors such as patient demographics, comorbidities, and surgical variations in our analysis to ensure that our results accurately reflect real-world clinical practice. This study has the potential to significantly contribute to the optimization of anesthesia management strategies for lower limb surgeries. By generating high-quality evidence on the comparative efficacy and safety of levobupivacaine and ropivacaine in spinal anesthesia, we aim to improve patient outcomes and enhance the quality of perioperative care in this demographic. So, we can conclude from our study that both the drugs are good options for spinal anesthesia for lower limb surgeries, and considering not only efficacy but also safety and side effect profiles when tailoring anesthetic protocols to meet the unique need of each surgical patient, Hyperbaric Levobupivacaine is more efficient than Hyperbaric Ropivacaine as it has early onset of sensory block, early onset of motor block, longer duration of analgesia and longer duration of motor block.

Reference:

1. Clinical trial NCT03142880. Spinal Marginally Hyperbaric Ropivacaine forCesarean Delivery. http://clinicaltrials.gov/ct2/show/NCT03142880.
2. Stefania Leone, Stefania Leone, Simone Di Cianni, et al. Pharmacology, toxicology and clinical use of new long-acting local anaesthetics,ropivacaine and levobupivacaine. Acta Biomed 2008; 79:92-105.
3. Luck JF, Fettes PDW, Wildsmith JAW. Spinal anaesthesia for elective surgery: acomparison of hyperbaric solutions of racemic bupivacaine, levobupivacaine, andropivacaine. British journal of Anaesthesia. 2008;101(5):705-10.
4. Hadzic A. Hadzic's Peripheral Nerve Blocks and Anatomy for Ultrasound-Guided Regional Anesthesia. 2nd ed. New York, NY: McGraw-Hill Education;2011.
5. Miller RD, Eriksson LI, Fleisher LA, et al. Miller's anesthesia e-book. Elsevier Health Sciences; 2014.
6. Luck JF, Fettes PD, Wildsmith JA. Spinal anaesthesia for elective surgery: a comparison of hyperbaric solutions of racemic bupivacaine, levobupivacaine, and ropivacaine. British journal of anaesthesia. 2008;101(5):705-10.
7. Girish BK, Srinivas HT, Shwetha M. Reddy et al. A Comparative Study ofHyperbaric 0.5% Levobupivacaine with Bupivacaine 0.5% for Spinal Anaesthesiain Elective Surgeries. Indian J Anesth Analg.2018;5(12):2013-20.
8. Dikkala DB, Guntreddy AS. A Comparative Study Between 0.5% Levobupivacaine And 0.75% Ropivacaine in Patients Undergoing Elective Lower Limb Surgeries Under Subarachnoid Block. Asian J Pharm Clin Res [Internet]. 2023;16(11):98-102.
9. Sagar TV, Byndoor Y. Levobupivacaine versus ropivacaine in patients undergoing lower abdominal surgeries. Indian Journal of Pharmacy and Pharmacology. 2023;10(2):111-5.

10. Shanmugam DP, Ravi M. Comparison Study Of Intrathecal 0.75% Ropivacaine Heavy Versus 0.5% Bupivacaine Heavy For Safety & Efficacy Of Patients Posted For Elective Lower Abdominal Surgeries: A Randomized Comparative Study. Journal of Pharmaceutical Negative Results. 2022:605-11.
11. Athar M, Ahmed SM, Ali S, et al. Levobupivaca ín ropivacaína: un ensayoaleatorio doble ciegocontrolado condosisequipotentesen la anestesiaespinal. Rev Colomb Anestesiol. 2016;44:97–104.
12. Sen H, Purtuloglu T, Sizlan A, et al. Comparison of intrathecal hyperbaric and isobaric levobupivacaine in urological surgery. Minerva Anestesiologica. 2010;76(1):24.
13. Barash PG, Cullen BF, Stoelting RK, Cahalan MK, Stock MC (eds). Philadelphia; Lippioncot Williams & Wilkins New York; 2010:927-950.