

Effect on the cardiovascular system by Hyperbaric Bupivacaine and Isobaric Ropivacaine given by sub-arachnoid block in planned lower extremity surgery

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Abstract

Objectives: To study the efficacy of two local anaesthetics drugs Ropivacaine and Bupivacaine were compared when they were administered intrathecally during elective lower limb surgery. Furthermore, the side effects of both drugs were also studied in similar research.

Methods: The study was done double-blinded, unbiased and a randomized control trial. One hundred patients of the American Society of Anesthesiologists with physical statuses 1 and 2 satisfying all inclusion and exclusion criteria after the informed consent were recruited. Patients were randomly allocated into 2 groups i.e., who received intrathecal 0.5% hyperbaric bupivacaine were allocated to Group B, and the study participants who received 0.5% isobaric ropivacaine fell in Group R. Cardiovascular system parameters such as average heart rate and average systolic blood pressure were monitored after the medication is given. Decreased blood pressure, nausea, vomiting, shivering, and headache were the parameters used to assess the side effects of the patients receiving both drugs.

Results: The action of these two drugs on cardiovascular system parameters were monitored and there was no valuable dissimilarity seen. No statistical significance was found in the occurrence of the side effects such as duration of nausea, vomiting, headache, and bradycardia. However, shivering was observed in the patients that were administered Bupivacaine as compared to Ropivacaine.

Conclusion: Ropivacaine is comparatively a better drug of choice as compared to Bupivacaine while considering the hemodynamic parameters as well as the different post-operative symptoms.

Keywords: Bupivacaine, Ropivacaine, hemodynamic, local anaesthesia drugs, lower extremities

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Introduction

Spinal block more generally called Intrathecal Block is a type of anaesthesia during which conduction block is achieved by giving a small dose of local anesthetic (L/A) in intrathecal space¹. In comparison, it is an easy method that provides a reduced stress response and improved post operative pain relief. Ropivacaine produces less hemody-

namic instability and neurological toxicity. The criteria which lead to the selection of local anaesthetic drug for spinal anesthesia is dependent on the expected time required for surgery and the time duration for early discharge of the patient. On a conventional basis, ester and amide-linked local anaesthetic drugs such as bupivacaine, lignocaine, cinchocaine and tetracaine are used for spinal anaesthesia². Due to adverse effects such as toxicity to cardiovascular and central nervous system, the search for a safer alternative is desirable. For this purpose, a newer alternative such as Ropivacaine, which is a new amide local anaesthetic drug, is developed ropivacaine is known to possess less toxicity to the simultaneous period of block in sensation and motor function along with maintenance of C-

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VS status and less toxicity³. Therefore, ropivacaine is commonly used as an alternative to bupivacaine. Both drugs belong to the same pipercolonylidide group. The main difference is the occurrence of the propyl group on the amine moiety (pipercolonylidide) in ropivacaine whereas, in bupivacaine, the butyl-1 group is attached to the amine portion of pipercolonylidide. Ropivacaine is the first long-acting, commercially available local anaesthetic. It is a pure *ä*-enantiomer⁴. The safety and effectiveness of intrathecal injection of hyperbaric and plain forms of Ropivacaine were conducted in various surgical operations such as urologic and orthopaedic surgeries^{5,6}. The pK_a values of ropivacaine are high while it possesses low lipophilicity. Ropivacaine also blocks C and A α (ache fibers) more than A β (motor fibers) which leads to decreased post-operative motor blockade which in turn leads to the achievement of early ambulation of patients. But the lesser duration of motor and sensory blocks can have a negative impact when dealing with longer duration surgeries or the quality of motor blockade is insufficient. To nullify these problems, the addition of adjuvants is done to ropivacaine⁷. One of the recent studies equating the anaesthetic effect of hyperbaric bupivacaine with isobaric ropivacaine given intrathecally for elective lower limb surgery reported that in ropivacaine group the sensory, motor onset, peak sensory time, and peak motor time were significantly delayed as compared to the bupivacaine group ($p < 0.001$)⁸. As compared to bupivacaine in ropivacaine group the two dermatomes' sensory segment regression and duration of motor blockade were significantly prolonged ($p < 0.001$)⁹. Another study showed that there were significant differences in mean time to onset of sensory block and mean duration of sensory block at T_{10} ($p = 0.001$) between bupivacaine and ropivacaine, given intrathecally for elective lower limb surgeries. Patients receiving ropivacaine mobilized sooner ($p = 0.002$). Evidence from the literature suggested that two studies reported that ropivacaine has no advantages except a shorter duration of action¹⁰. As no reports are indicating the efficacy and safety of these two drugs in the

Pakistani population, so this study was conducted to assess these parameters while comparing the drugs. The main goal of this study was to evaluate the mean systolic BP, mean heart rate and side effects of hyperbaric bupivacaine (0.5%) and isobaric ropivacaine (0.5%).

Patients and Methods

Before conducting this study, the patients were elaborated on the entire procedure of this study. This study was designed on randomized, controlled, and double-blinded protocols. The response of the participants was kept anonymous during the study duration. The principal investigator of the study was only aware of the findings. The guidelines provided by Pakistan Medical and Research Council and the Helsinki declaration were used to carry out the study. The time duration for the collection of data was 6 months from July 7, 2020 to January 8, 2021, at the orthopedic department, Operation Theatre of Abbasi Shaheed Hospital. The research was initiated, and data were collected after approval from the Ethical and Scientific review committee, Karachi Medical & Dental College. Written informed consent was obtained from all the study participants prior to enrollment in the study. The purpose of research, intervention given, and process involved in data collection and potential risks and benefits of the research to all the study participants.

The research was conducted on 100 elective lower limb surgeries under spinal anaesthesia. American Society of Anesthesiologists (ASA) was used to put physical status type '1 and 11 patients¹¹. The age of the participants ranged from 18-60 years weighing 60-80 kg. Pre-operative examination of the patients was conducted. Informed consent was obtained after explaining the entire procedure in their native language. A complete acknowledgement of one's privacy was maintained. The height and weight of the patients were recorded. For 6 hours, the patients were not given anything to eat orally before the operation. Vitals of the patients including pulse rate, blood pressure, respiratory rate, oxygen saturation (SPO_2) and ECG fluctuations were monitored in the pre-opera

tion room.(0.4%) HES was administered 15 minutes before subarachnoid block in the concentration of 6 mL/kg of body weight. 26 G Quincke needle was used to give anaesthesia to the patient who was in a sitting/lateral position. Similar volumes (3 mL) and in a concentration (0.5%) of both the tested drugs (bupivacaine and ropivacaine) were administered. The patients that were administered ropivacaine were allocated as group 'R' while those who received bupivacaine were named as Group 'B'. For 5 minutes, monitoring of the patient's vitals such as oxygen saturation, BP and arterial pulse was carried out. After half an hour, these readings were recorded again. After 30 minutes, the vitals were recorded with the duration of 10 minutes.

Pinprick test was used to assess the sensory blockage when it reaches from T₅ dermatomal to the level of T₆. The extent of motor blockade was monitored as per divisions of the Bromage scale (modified) which relates to the extent of motor blockade with the failure in antigravity movements of the legs. The modified Bromage scale corresponds to no weakness (Score 0), inability to raise extended leg antigravity in the supine position (Score 1), unable for knee flexion (Score 2) and to cause movement of the joints present in the legs (Score 3). The sampling technique used to analyse the data collected in this study was the non-probability consecutive sampling technique.

A certain set of rules were set to enroll the participants for this study. The criteria are mentioned as under:

Inclusion criteria were the American Society of Anaesthesiologists (ASA) Type I (a normal and a healthy individual) and Type II criteria (a person having a milder form of any systemic illness). The age of the patient must be 18-60 years and weight fall in the range of 60-80 kgs and he/she must be indicated an elective lower limb surgery.

Excluding criteria were ASA Type III (an individual having a severe form of any systemic illness that is not fatal), Type IV (an individual with a severe form of systemic illness that is a continuous risk to life) and Type V (a dilapidated patient who isn't relied upon to survive without the surgery),less

less than 18 year of age or more than 60 years, having a pre-existing disease of CNS, CVS, spinal deformity or arthritis. Regional Anaesthesia i.e., Sub-Arachnoid block should not be given to patients with drug allergy, high ICP, abnormality in bleeding and infection at the site, lipid disorder, failure to co-operate/psychosis of the patient, emergency surgeries of lower extremities, history of alcoholism, addiction of medicine, showing unwillingness for participation in this study, and pregnancy. Confounding variables that may hinder the validation of the results include an obligation of the inclusion and exclusion criteria, non-performance of the required investigation like Activated Partial Thromboplastin Clotting Time (APTT)PT, Prothrombin time, International Normalized ratio (INR) that accounts for coagulation profile, improper cannulation at least at two proper sites, improper preload before anaesthesia, failure to follow standard protocol of monitoring were strictly kept in mind and were excluded to have a better understanding of the variables.

OpenEpi sample size software was used to analyse the sample size of this study. The primary outcome was considered as the time limit of sensory blockage. In the 'R' and 'B' groups, the two dermatomes in the sensory portion regression were 117.200 ± 12.5 minutes and 108.5 ± 10.61 minutes. Ninety percent was used as a level to assess the difference between the two groups with a type 1 error test of 5% for each group comprising 50 clinical participants. Oximeter, hemodynamic parameter, oxygen saturation and ECG of all the patients were recorded. Time required for motor and sensory block, onset, and T₀ which corresponds to the time at which the drug was administered were noted down on a structured proforma. With the administration of fluids, intra-operative losses were balanced. Catheterization of the bladder was performed when indicated by surgical the procedure. When the sensory block has reached the S₂ level, the patients were encouraged to move. The data on ill effects for instance bradycardia, hypotension, nausea, and vomiting were also obtained.

The overall management aim is to maintain a Minimum Mean Arterial Pressure (MAP) that will ensure adequate tissue perfusion. Most cases require fluid as first-line management to restore an adequate circulating volume. If the hypotension persists after restoring adequate circulating volume, the appropriate drug treatment is required for example inotropic support-vasopressors.

Data were recorded on a pre-designed structured performa which was analysed by using 20.0 IBM SPSS Statistics. Before analysis of the data collection, Performa was weighted at least twice against the database by the investigator for accuracy. Any error found was corrected before the actual analysis. Descriptive statistics were performed. Categorical data (i.e., ASA categories etc.) was presented as frequency & percentage. Quantitative variables were presented as mean \pm SD. ASA categories (Class 1 and 2) were compared between bupivacaine and ropivacaine groups by using Chi-square test statistics. P-value less than 0.05 was considered significant.

Results

On a random basis, 100 clinical participants were allocated for elective lower limb surgery in groups i.e., 'B' Group and 'R' Group. In table 1, while considering demographic parameters and the time required for surgery, there was no significant difference between the study groups. There were 44% and 56% females and males respectively. The baseline hemodynamic parameters showed no statistical significance between the study groups. After administration of both the drugs, mean systolic blood pressure dropped in both the study groups which is shown in Figure 1. The drop prevailed until 20 minutes in Group 'R' while this reduction was more in 'B' group. These levels elevated after 20 minutes and 60 minutes, a peak was observed in the mean systolic BP ($P \leq 0.05$). Comparatively lower values for all the tested parameters in the group 'B' were observed as compared to group 'R' during the trial. A decrease in mean heart rate was observed between the 'B' and 'R' groups as shown in Figure 2. A rise in both groups was observed at 20 minutes of the adminis-

tration of the drugs. However, the levels further decreased below the baseline at 60 minutes of the administration of the drugs. Contrary to data of mean systolic BP, the values of mean heart rate were lesser in Group 'R' as this drug is less lipophilic than bupivacaine so is associated with a lower potential for CNS and CVS toxicity. The levels returned to baseline during 20 minutes of the study. The rate of hypotension was found to be more in Group 'B'. Ephedrine was given to the patients of Group B in the ratio of 13 (26%) to lower the systolic BP. On the other hand, only 5 (10%) participants of 'R' group at ($p=0.037$). Similarly, side effects such as nausea, vomiting, and headache were studied, and they were found to be statistically non-significant (Table 1). Group B also showed a higher rate of shivering in the patients at ($p=0.01$). However, symptoms such as backache and bradycardia were absent in both the studied groups.

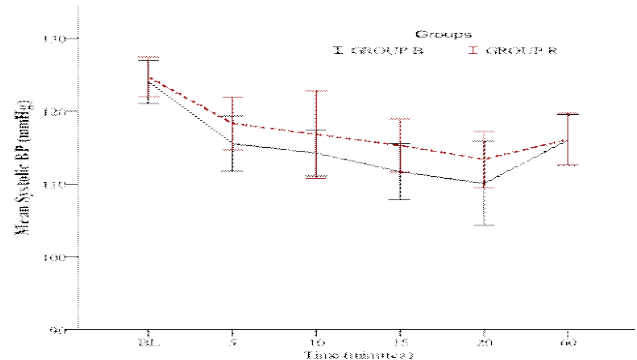


Fig 1. Mean systolic blood pressure between study groups vs time (100 individuals) ^a

Group B and R corresponds to Bupivacaine and Ropivacaine respectively.

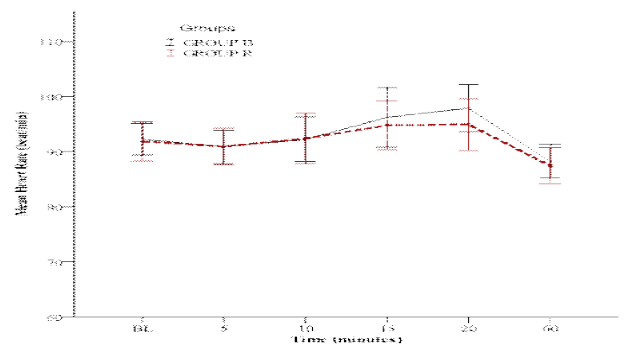


Fig 2. Mean heart rate (beats/min) on the duration of time basis between Ropivacaine and Bupivacaine administered (100 patients) ^a

Group B and R corresponds to Bupivacaine and Ropivacaine respectively.

Table 1. Side effects observed after the administration of Ropivacaine (R) and bupivacaine (B)^a

Adverse effects of drug	Group R (50 patients)	Group B (50 patients)	Pvalues
Drop in BP	5 (10%)	13 (26.0%)	0.037
Headache	2 (4%)	3 (6%)	0.98
Vomiting	5 (10%)	6 (12%)	0.74
Nausea	9 (18%)	4 (8%)	0.13
Shivering	13 (26%)	1 (2%)	0.01

Fisher exact and Chi-square test were applied. Group R and B corresponds to Ropivacaine and Bupivacaine respectively.

Discussion

Ropivacaine and Bupivacaine were studied for their effects on the cardiovascular system and possible side effects. Due to the severity of the side effects, the accidental intravascular administration of anaesthetics especially local ones are a bothersome issue. Due to the duration and nature of the blockade, ropivacaine has been considered an advancement in regional blockade^{12,13,14}. The current study deals with the comparison of intrathecal administration of bupivacaine with the drug ropivacaine during elective lower limb surgery. Any notable significant differences were not found between the effects on the levels of hemodynamic attributes in both tested drugs; however, changes caused by both the drugs were transitory and eventually returned closer to baseline levels. The levels have transitioned after 20 minutes of the administration of the drugs. However, these levels showed a transition between 20-60 minutes of the study. A rise in mean heart rate while a drop in mean systolic BP was observed during the first 40 minutes of the trial. Settlement of the level of the anaesthesia i.e., dermatomes level occurred up to 25-30 minutes after giving spinal anaesthesia. It is merely the vasodilator effect of the local anesthetic drug. Both effects i.e., direct, and indirect ones on the heart are primary factors affecting the CVS by the local anaesthetic with conduction blockade and negative inotropes¹⁵. Administration of the higher than recommended doses of ropivacaine to achieve greater motor blockade or increased duration of sensory blockade may result in severe cardiac depression.

The mode of action of bupivacaine includes a reduction in the levels of Ca^{+2} in the protein synthesizing organelle i.e., Endoplasmic Reticulum (The transportation system of eukaryotic cells), changes the Na^+/Ca^{+2} channels in the outer envelope (membrane), the conversion of energy derived from mitochondria and inhibition of synthesis of Cyclic Adenosine Monophosphate¹⁶. The conductivity is manipulated by the blockage of Na^+ , Ca^{+2} and K^+ channels, causing arrhythmias. The other indirect consequence includes blockade of autonomous intervention and mediation of the central nervous system. In Vivo studies showed that the lowering of activity of voltage-dependent sodium gates in membranes of the nervous system is carried out by local anaesthetics, delayed induction of cardiac impulse, increased and narrowing voltage of the QRS complex, increase in the duration of the PR interval and AV block simultaneously resulting ventricular arrhythmias¹⁷. Lesser and more transient inhibition of Na^+ potential is demonstrated by Ropivacaine than

Different protocols have been used such as Minimum Local Analgesic Dose (MLAD), which employs epidural injection of 20 ml of L/A for providing appropriate analgesic effects during the first stage of labour. Some studies have shown equal potency of both the drugs to relieve pain, side effects, fewer consequences for the newborn and type of delivery²⁴. Other methods that are used to determine the quality of sensory blockade in clinical anaesthesia suggested that Ropivacaine is a better alternative than Bupivacaine²⁵.

If no adequate use of the pre-load before giving the spinal anaesthesia. The type of the fluid is important as colloids are better fluid than lactated ringer's solution. Gradual patient positioning after giving spinal anaesthesia is required more negative effects if suddenly change the patient. Standard monitoring is required; inadequate monitoring could not pick immediate changes in the hemodynamic system. The local anaesthetic drug is used with caution in a patient with hypotension, hypovolemia, and heart block.

Conclusion

Based on the results obtained from present study, it was concluded that isobaric ropivacaine at 0.5% concentration is comparatively a better alternative than 0.5% hyperbaric bupivacaine. The study recommends that 0.5% isobaric ropivacaine was associated with decreased rate of hypotension and heart rate. Percentage of side effects of bupivacaine were more on contrary to ropivacaine.

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