Original Article

Comparative Evaluation of Newer Local Anesthetics (Levobupivacaine and Ropivacaine) With Bupivacaine, in Lumbar Epidural Anesthesia for Hip Surgeries: A Randomized Controlled Trial

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Abstract

Background: Hip surgeries are one of most common lower limb surgeries done under regional anesthesia now days. Lumbar epidural anesthesia has earned its reputation among the regional anesthetic techniques due to its advantages of intra and post-operative analgesia, good hemodynamic stability and lesser complications. Newer local anesthetics i.e. Bupivacaine, Levobupivacaine and Ropivacaine are commonly used in epidural anesthesia with variations in their efficacy. **Aim**: To compare newer drugs Levobupivacaine and Ropivacaine with Bupivacaine, in terms of- time required to achieve T10 sensory level and maximum modified Bromage score, time required for 2 segment regression; when used in lumbar epidural anesthesia for hip surgeries. **Methods:** 90 patients of ASA I-II divided in 3 equal randomized groups where all patients were posted for hip surgeries done under lumbar epidural anesthesia using 20 ml of 0.5% Bupivacaine (Group B), 0.5% Levo-Bupivacaine (Group L) or 0.5% Ropivacaine (Group R). **Results:** Time to achieve T10 sensory level was 9.02±2.41 min, 9.36±3.41min and 12.08±1.90 min in group B, Group L and Group R respectively. Modified Bromage score 3 and 4 were higher in patients of Group B and group L. Time for 2 segment regression was 97.86+/-8.01 min in group B,92.06+/-10.20 min in group L & 82.76+/-9.01 min in group R. **Conclusion:** It was concluded Bupivacaine is comparable in terms of efficacy to Levobupivacaine, which is better than Ropivacaine in lumbar epidural anesthesia.

Key words: Bupivacaine, Levobupivacaine, Ropivacaine, Anesthesia, Epidural.

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Introduction

Lumbar epidural block is a form of regional anesthesia involving injection of local anesthetic agent in the lumbar epidural space. Various day care surgeries are being done under lumbar epidural block considering all benefits and risk factors involved and its better outcome over other modalities of anesthesia and analgesia. Some of the most common day care surgeries are lower limb surgeries, in which local anesthetic agents can be used via epidural route for both intra-op and post-op analgesia.[1] An ideal local anesthetic will provide quick onset, sufficient sensory blockade by maintaining hemodynamic stability and minimal systemic side effects. Among the local anesthetics lignocaine, Bupivacaine, Levobupivacaine and Ropivacaine are in current use. Bupivacaine is a long acting amide local anesthetic. The onset of action with Bupivacaine is rapid and anesthesia is long-lasting. The duration of anesthesia is significantly longer with Bupivacaine than with any other commonly used local anesthetic. However Bupivacaine usage is not free from side effects. Toxic blood concentrations depress cardiac conduction and excitability, which may lead to atrio-ventricular block, ventricular arrhythmias and cardiac arrest, sometimes resulting in fatalities. Ropivacaine and Levobupivacaine are two relatively new amide local anesthetic agents that have been produced in order to address the issue of Bupivacaine cardio toxicity.[2] The claimed benefits of both Levobupivacaine and Ropivacaine are reduced cardiac toxicity and more specific effects on sensory rather than motor nerve fibres.[3-6] Ropivacaine, an analogue of Mepivacaine, is one of the long acting amide anesthetic agents similar to Bupivacaine in chemical structure and anesthetic function.[7] It is a first enantiomer-specific compound, which has a reduced risk of cardio toxicity, neuro-toxicity and rapid recovery of motor function. Levobupivacaine is the pure S (−)-enantiomer of Bupivacaine, and in recent year has emerged as a safer alternative for regional anesthesia than its racemic parent.[8] It demonstrated less affinity and strength of depressant effects onto myocardial[9,10] and central nervous[11,12] vital centres in pharmacodynamics studies, and a superior pharmacokinetic profile. Yet, Ropivacaine and Levobupivacaine have not entirely replaced Bupivacaine in clinical practice. With this view in mind, this randomized study was planned to perform the comparative evaluation of Bupivacaine,

Levobupivacaine and Ropivacaine in lumber epidural anesthesia.

Materials and Methods

After Institutional Ethics Committee approval and written informed consent, a prospective, randomized, double-blinded study was carried out on 90 ASA Grade I and II patients of either sex, aged 18-60 years, undergoing various hip surgeries under lumbar epidural anesthesia. The study was conducted on following three groups of 30 patients each and the randomization was done by generating random numbers in Microsoft excel spreadsheet(Microsoft corporation, Washington). Statistical analysis was performed by SPSS Statistics for Windows (version 21.0) statistical package. The results were presented in number, percentage, mean and standard deviation as appropriately. Comparison between three groups was done by ANOVA and two groups by unpaired t-test. A p-value of <0.05 was considered significant. The three study groups are:

Group B -20 ml volume of 0.5% isobaric Bupivacaine
Group L -20 ml volume of 0.5% isobaric Levobupivacaine
Group R - 20 ml volume of 0.5% isobaric Ropivacaine.
Exclusion criteria included the following: Patients refusal for epidural Anaesthesia, ASA Grade III & IV, Age <18 years & > 60 years, History of head injury & psychiatric diseases, Known allergy to any test drugs, Major hepatic, renal or cardiovascular system dysfunction, Body weight >100 kg. or height <145 cm., Patients having cardiac rhythm abnormality - especially bundle branch block, Contraindications to epidural anesthesia (Coagulation defects, infection at site, deformities of spinal column, raised ICP, Pre-existing neurological deficits in lower extremities, fixed cardiac output states), Any patient who has received any analgesic drugs within the past 24 hours.
After thorough pre-anesthetic evaluation, all patients were cannulated in the preoperative room. In operating room they were preloaded with lactated Ringer's solution at 15 ml/kg and standard monitors such as noninvasive blood pressure (NIBP), Pulse oximeter (SPO2), Electrocardiogram (ECG) were attached to all patients. Patient was kept in sitting position, a 18 G epidural catheter with multiple lateral orifices was inserted in a cephalad direction at L2-L4 space via a Touhy needle. The epidural space was identified by loss of resistance to air. After negative aspiration for CSF and blood, a 3 ml test dose of 2% lignocaine with adrenaline was injected over 15 sec through catheter. If there were no untoward effects after 3 min, the main dose of 20 ml of study was injected over 4 min. The onset of sensory block was considered to be the time to achieve T10 level. The surgery was commenced after the maximum motor blockade was achieved. The anesthesiologist performing the block was blinded to the study drug and intraoperative data was recorded. The level of sensory block was checked by loss of pinprick sensation by 23 G hypodermic needle and dermatomal levels was tested every 2 minutes until the highest required level was stabilised for four consecutive tests. Testing was then conducted every 10 minutes until the point of two segment regression of block.
Simultaneously motor block by Bromage Scale was evaluated as follows:

Bromage 0 - The patient is able to move the hip, knee and ankle.
Bromage 1- The patient is unable to move the hip, but is able to move the knee and ankle.
Bromage 2-The patient is unable to move the hip, and knee, but is able to move the ankle.
Bromage 3- The patient is unable to move the hip, knee, and ankle.

Strict hemodynamic monitoring was done. Any fall in BP below 90 mm Hg or more than 20% of base line was treated with administration of oxygen, fast IV fluids and vasopressor. Any fall in heart rate less than 60 beats or more than 20% of base line was treated with injection atropine 0.6 mg IV. Data regarding the time to achieve T10 level, maximum sensory level and maximum motor blockade achieved, time to achieve maximum motor block and time to 2 segment sensory regression. All durations were calculated from the time of injection of local anesthetics through epidural catheter.

Results

All the groups of patients had comparable demographic variables in terms of age, weight and height (p-value >0.05). In sex distribution, study group had predominantly male patients with number of male patients were 20,18 and 22 in Group B, Group L and Group R and number of female patients were 10,12 and 8 in Group B, Group L and Group R respectively [Table 1].
After the administration of 20 ml of the study drugs , Onset of sensory block i.e. time to achieve T10 level was 9.02±2.41 min in Group B and 9.36±3.41 min in Group L which are significantly earlier than 12.08±1.90 min in group R (p value <0.05) [Table 2], which was confirmed by post hoc test. Also the time of 2 segment regression was 97.86+/-8.01 min in Group B, 93.86+/-10.20 min in Group L and 82.76+/-9.01 min in Group R (p-value<0.05) [Table 2], shown that Ropivacaine had significantly earlier regression than the other two drugs as per the post test. Maximum sensory level achieved was T7 in both groups B and L while it was T8 in group R [Table 2].
The duration of maximum motor block achieved was 36.02±2.57 min in Group B, 37.77±4.45 min in Group L and 42.02±3.63 min in Group R [Table 3]

with significant difference between Bupivacaine and Levobupivacaine with Ropivacaine. Intensity of motor blockade was analyzed by help of Bromage Score. Number of patients achieving Maximum Bromage score of 3 in Group B, Group L and Group R were 16, 8, 4; patients with score 2 were 12, 12, 10; patients with score 1 were 2, 10, 14 and patients with score 0 were 0, 0, 2 respectively [Table 4]. On comparing the motor block , mean Bromage score was 2.46 in group B, 1.93 in Group L and 1.53 in Group R respectively and on comparison, it was significantly earlier in Bupivacaine and Levobupivacaine group but more intense in Bupivacaine group (p-value<0.05).

Table 1: Demographic Data.

Parameters	Group B	Group L	Group R	p-Value
Age (years)	40.05± 12.01	40.27± 11.35	40.35± 12.46	0.993
Weight (Kg)	59.92± 10.14	60.6± 9.86	59.32± 9.10	0.840
Height (cms)	161.12 ±9.21	162.47 ±8.02	161.87 ±7.44	0.765
Sex (M/F)	20/10	18/12	22/8	-

Data values are presented as Mean ± SD.

Table 2: Parameters for Sensory Block.

Parameters	Group B	Group L	Group R	p-Value
Onset of Sensory Block (T10) (min)	9.02±2 .41	9.36±3. 41	12.08± 1.90	0.005
Time for 2 segment regression (min)	97.86+ /-8.01	93.86+/ -10.20	82.76+/ -9.01	0.0001
Maximum Sensory level achieved	T7	T7	T8*	-

Data values are presented as Mean ± SD. *T=Thoracic dermatome.

Table 3: Onset of maximum Motor block.

Parameters	Group B	Group L	Group R	p-Value
Time of maximum Motor Block (min)	36.02± 2.57	37.77± 4.45	42.02± 3.63	0.0001

Data values are presented as Mean ± SD.

Table 4: Different Bromage scores among groups.

Parameters	Group B (n=30)	Group L (n=30)	Group R (n=30)
Bromage 3	16	8	4
Bromage 2	12	12	10
Bromage 1	2	10	14
Bromage 0	0	0	2

Discussion

Epidural anesthesia has the potential to provide excellent operating conditions and prolonged post-operative pain relief. It is particularly effective at providing dynamic analgesia, allowing the patient to mobilize and resume normal activities free from pain.

Levobupivacaine, the single enantiomer version of Bupivacaine, offers a new long acting local anesthetic, clinically equivalent in anesthetic potency to Bupivacaine, but with a reduced toxicity profile.[13]

Small unmyelinated C fibres and small myelinated A fibres are responsible for pain transmission while large A fibres transmits motor impulse. Most local anesthetics block C fibres at approximately same rate while rate of A fibre block depends on physicochemical properties of individual drug. High pKa and low lipid solubility favours blockade of C fibres before A fibres.

Ropivacaine blocks Aδ and C fibres to a greater degree than Aβ fibres which is responsible for differential block.[14] In-vitro study demonstrated that in equal doses, the depressant effect of Bupivacaine on A-fibres was 16% greater than that of, Ropivacaine, but only 3% greater on C-fibers.[15] Zaric et al[16] observed that onset of motor blockade measured by the quantitative method was significantly slower with 0.5% Ropivacaine than with the higher concentrations of Ropivacaine. In our study onset of analgesia was 9.02±2.41 min in group B, 9.36±3.41 min in Group L and 12.08±1.90 min in Group R and also regression of block by 2 segments was significantly earlier in R group i.e.82.76±9.01 min as compared to 97.86+/-8.01 min in B group and 93.86+/-10.20 min in L group [Table 2]. Onset and 2 segment regression times are comparable in B group and L group similar to what was observed by Kopacz et al[17] who compared 0.75% Levobupivacaine and Bupivacaine for epidural anesthesia in lower abdominal surgery and observed similar onset times, but a significantly longer duration of sensory blockade was seen with Levobupivacaine. Cox et al[18] reported that 0.5% Levobupivacaine compared with Bupivacaine for supraclavicular plexus blocks generally resulted in longer-lasting sensory (1039 versus 896 minutes) and motor (1050 versus 933 minutes) blocks, the analgesic potencies as such being similar. Finally, Bay-Nielsen et al[19] observed similar analgesic potencies of 0.25% Levobupivacaine and Bupivacaine for infiltration analgesia in inguinal hernia repair.

Similarly in motor blockade, less intense of motor blockade in Ropivacaine might be due to use of 0.5% Ropivacaine in a dose of 15ml. Our results were same as that was observed by Brockway et al[20], who also noted less intense motor blockade with 0.5% Ropivacaine compared with 0.5% Bupivacaine. In our study also, onset of motor blockade is significantly delayed in Ropivacaine (42.02±3.63 min) as compared to Bupivacaine (36.02±2.57 min) and levobupivacaine group (37.77±4.45 min) [Table 3]. Li Y et al[21] observed intense motor block and a higher upper level of analgesia in patients older than 61 years than in patients of 18–40 years with the use of 20 ml Ropivacaine. The result did not match with our study which might be due to use of 15ml Ropivacaine. An increase in concentration resulted in a profound motor blockade. When 0.5% concentration was used, less than 50 % individuals

showed combined Bromage score of 3 and 4 as compared to group B and group L. Casati et al[22] compared efficacy of 0.5% Ropivacaine, Bupivacaine and Levobupivacaine used for epidural anesthesia and found that in 40% patients in Ropivacaine group had motor block less than grade II (Bromage scale) while no patient from Bupivacaine group had motor block less than grade II (Bromage scale). Thus study suggests that Ropivacaine provides satisfactory sensory anesthesia with minimal motor blockade at a concentration of 0.5%. Also, Olfosen et al[23] noted that Ropivacaine had lower speed of onset and offset than Levobupivacaine. This may be due to lower lipid solubility of Ropivacaine. With this study it is also illustrated that Ropivacaine can show comparable efficacy to Bupivacaine and Levobupivacaine if used in higher concentration.

Conclusion

It was concluded Bupivacaine and Levobupivacaine, are comparable in terms of efficacy when used in lumber epidural anesthesia for hip surgeries. Ropivacaine has longer onset time and lesser duration of anesthesia compared to both Bupivacaine and Levobupivacaine.

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