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Comparison Of Epidural Bupivacaine (0.5%) And Ropivacaine(0.75%) In Patients Posted For Abdominal And Lower Limb Surgeries

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Abstract

Background: For abdominal and lower limb surgeries, Epidural Anesthesia is one of the most useful and versatile techniques than General Anesthesia and Spinal Anesthesia in that it allows the practitioner to simultaneously offer anesthesia, analgesia, and chronic pain management. Epidural blockade facilitates faster recovery and improved postoperative pain control. Bupivacaine is a long acting amide local anesthetic and it is a very important step in the evolution of Regional Anesthesia. The recognition of acute life threatening cardiotoxicity of Bupivacaine led to the search for a better anesthetic agent comparable with Bupivacaine but with lower cardiotoxicity. This resulted in to the development of a relatively new amide named, Ropivacaine, which got registered for clinical use in 1996. Ropivacaine is a new long acting amino amide local anesthetic which is chemically homologous with Bupivacaine and Mepivacaine. Ropivacaine exhibits lesser cardiotoxicity and CNS toxicity.

Materials and Methods: 60 patients between age group 18 to 60 years scheduled for elective surgery of abdomen and lower limbs were enrolled in the study and equally and randomly divided into Bupivacaine Group and Ropivacaine Group. The study was prospective randomized double blind study to compare 20 ml of 0.5% Bupivacaine and 20ml of 0.75% Ropivacaine administered to the two groups.

Results: There were no significant differences in parameters monitored but Ropivacaine 0.75% was associated with relatively faster postoperative recovery and longer duration of postoperative analgesia.

Conclusion: Ropivacaine 0.75% can be used as a safe alternative to Bupivacaine 0.5% for Epidural Anesthesia in abdominal and lower limb surgeries.

Keywords: Epidural Anesthesia, Bupivacaine, Ropivacaine, Abdominal Surgeries, Lower Limb Surgeries

Introduction

In 1921, the Spanish Fidel Pages described the injection of anesthetics into the Epidural Space in the lumbar and thoracic regions and this markedly increased the possibilities of the Epidural Block. The subsequent improvements in needles and catheters, new drugs, and a better understanding of physiology and pharmacology contributed to the development of the Epidural Block, which is nowadays an essential technique in anesthesiology. [1]

Central Neuraxial Blockade in the form of Epidural Anesthesia avoids the disadvantages of General Anesthesia (GA) as GA is associated with airway manipulation, poly pharmacy and other untoward effects like postoperative nausea, vomiting, need for supplemental intravenous analgesics etc. Epidural Anesthesia is simple, safe and effective and is

therefore very popular for lower abdominal and lower limb surgeries. Epidural Anesthesia is also more versatile than Spinal Anesthesia, giving the clinician the opportunity to simultaneously provide anesthesia and analgesia to enable more rapid recovery from surgery, better postoperative analgesia control and chronic pain management.

Epidural Anesthesia involves the use of local anesthetics injected into the epidural space to produce a reversible loss of sensation and motor function. Epidural Anesthesia requires larger amounts of local anesthetics when compared to its usage in Spinal Anesthesia. Epidural Anesthesia is versatile and can be administered by a single injection or through a catheter. The use of a catheter allows the anaesthetist to add local anesthetics as surgery progresses, extending duration beyond the original dose. Epidural Anesthesia provides excellent conditions for surgical procedures below the umbilicus. Epidural Anesthesia is also an excellent option for the elderly patients who may not tolerate a general anesthetic.

Recent studies suggest that advances in anesthesia and postoperative analgesia can affect postoperative outcome. Epidural anesthesia and analgesia have the potential to reduce or eliminate the perioperative physiologic stress responses to surgery and thereby decrease surgical complications and improve outcomes. Anesthesia with an effective block, having least onset time and which can be prolonged with least complications is therefore one of the challenges being faced by the anaesthesiologist.

Bupivacaine: Bupivacaine is a long acting amino amide local anesthetic. It is chemically known as I-Butyl-N-(2.6-dimethylphenyl)-2-piperdinecarboxamide. Mechanism of action of Bupivacaine is similar to that of any other local anesthetic. The primary action of local anesthetics is on the cell membrane of the axon, on which it produces electrical stabilization. The large transient increase in permeability to sodium ion, necessary for propagation of impulse is prevented. Thus the resting membrane potential is maintained and depolarization in response to stimulation is inhibited. Bupivacaine dosage is 0.5% concentration @ 2 mg/kg, and limited up to 150 mg in 4 hours. Bupivacaine has been in use since 40 years but search for better anesthetic continues especially due to its high cardiotoxicity and Central Nervous System (CNS) toxicity. [2]

Ropivacaine: Ropivacaine is a relatively newer amino amide local anesthetic. It is chemically known as (S)-N-(2,6-dimethylphenyl)-I-propylpiperidine-2-carboxamide. It is a Na+ channel blocker. The Na+ channel has an activation gate (A) near its extracellular mouth and an inactivation gate at the intracellular mouth. Na+ channel exist in activated open, inactivated closed and rested closed states during various phases of the action potential. The local anesthetic (LA) receptor is located within the channel in its intracellular half. The LA transverses the membrane in its lipophilic form (B), reionises in the axoplasm and approaches the LA receptor through the intracellular mouth of the channel. Ropivacaine dosage is 0.75% concentration @ 2 mg/kg, and limited up to 150 mg in 4 hours. Ropivacaine exhibits lesser cardiotoxicity and CNS toxicity therefore it is being compared to Bupivacaine in this study. [3 5 6]

Ropivacaine with its efficacy, lower propensity for motor block and reduced potential for Central Nervous System (CNS) and lesser cardiac toxicity appears to be an important viable option for Regional Anesthesia and for management of postoperative pain. [4 7]

This prospective randomised double blind study is hypothesised to study and compare effects of 20 ml of 0.75% Ropivacaine against 20 ml of 0.5% Bupivacaine for Epidural Anesthesia in the abdominal and lower limb surgeries in adults aged 18 to 60 years, The study parameters are:-

1. Demographic Parameters Age, Weight and Height.
2. Onset of Sensory Block.
3. Onset of Motor Block.
4. Intensity of Motor Blockade.
5. Duration of Anesthesia.
6. Intraoperative Hemodynamic Changes.
7. Postoperative Analgesia.
8. Adverse Effects.

Materials And Methods

After obtaining approval from the hospital academic and ethics committee and written informed valid consent, 60 patients between age group 18 to 60 years scheduled for elective surgery of abdomen and lower limbs were enrolled in the study.

Volume 5, Issue 1; January-February 2022; Page No 1228-1234

Study Design: The study was prospective randomized double blind study.

Inclusion Criteria:

1. Age Group 18 to 60 years.
2. ASA physical status I and II.
3. Abdominal and lower limb surgery (elective).

Exclusion Criteria:

1. Consent not given.
2. ASA Physical status III and IV.
3. Comorbid diseases namely Cardiac, Pulmonary, Diabetes, Raised Intracranial pressure, Severe Hypovolemia, Any bleeding coagulopathy, Local infection at the injection site, Allergy to the drug to be used, Pregnancy, Patients posted for Emergency surgeries, and Patients with morbid obesity.

Method: 60 Patients were randomly allocated to one of the two groups of 30 each as stated below, using a standard randomization code:

1. **Bupivacaine Group (Group B):** Patients in Group B were administered 20 ml of 0.5% Bupivacaine by epidural route after uneventful epidural test dose with 3cc of injection 2% adrenalized lignocaine.
2. **Ropivacaine Group (Group R):** Patients in Group R were administered 20 ml of 0.75% Ropivacaine by epidural route after uneventful epidural test dose with 3cc of injection 2% adrenalized lignocaine.

Drug Solution Used and Dosage: Drug solution used are 0.5% Bupivacaine and 0.75% Ropivacaine. Total volume of solution taken in both groups was 20 ml.

Equipment Used: The following equipment was used for monitoring purpose:

1. Standard monitors.
2. Pulse Oximetry for saturation (SPO2).
3. Cardioscope for rate and rhythm.
4. Non-invasive Pulse Rate and Blood Pressure monitoring.

Procedure: A wide bore intravenous line was taken and preloading was done with 500 ml of Ringer's solution just about 15 minutes before the intended time of drug administration. Vitals parameters were observed throughout the procedure.

Study Parameters Monitored: (a) Demographic Parameters (b) Mean Time for onset of Sensory Block (SB), (c) Mean Time for onset of Motor Block (MB), (d) Mean duration of Sensory Block (SB), (e) Mean duration of Motor Block (MB), (f) Mean Time to Rescue Analgesia, (g) Pulse Rate and (h) Systolic Blood Pressure (SBP).

Calculations: In our study, we compare the means of two groups. The unpaired T test compares one parameter between the two different groups. The decision has to be taken between the two hypotheses:-

Step 1: Define Null Hypothesis H_0 and Alternative Hypothesis H_1

H_o: $\mu_1 = \mu_2$ and that there is no difference between the means of Group 1 and Group 2, and differences found if any is merely due to chance.

H_1: $\mu_1 \neq \mu_2$ Mean in the two groups is SIGNIFICANTLY different.

Step 2: Collect Data

The defined parameters data was recorded for 60 patients for Bupivacaine Group n_1=30, and Ropivacaine Group n_2=30. The degrees of freedom v = df = n1 – n2 – 2 = 58.

Step 3: Obtain value of μ_d, σ_d, $T_{calculated} = T_{calc}$, P value ($T_{calc}$ for v=58) from T Test calculator @ GraphPad website.

The mean (μ), standard deviation (σ), mean difference ($\mu_d = \mu_1 - \mu_2$), and standard error of difference σ_d, ($\sigma_d = \{(\sigma_1^2/n_1) + (\sigma_2^2/n_2)\}^{1/2}$ are calculated. These values are used to obtain T calculated = T_{calc} ($T_{calc} = \mu_d / \sigma_d$). The P value for ($T_{calc}$ for v = 58) is obtained from T Test Calculator @GraphPad website.

Step 4: Compare P values and take decision to accept or reject null hypothesis.

If P value (T_{calc} @ v = 58) > 0.05, then the null hypothesis is accepted $\mu_1 = \mu_2$ and any difference is merely due to chance. Therefore it can be concluded that the performance parameter of both drugs is same or "INSIGNIFICANT".

Volume 5, Issue 1; January-February 2022; Page No 1228-1234

If P value (T_{calc} @ v = 58) ≤ 0.05, then the null hypothesis is rejected i.e alternative hypothesis is accepted $\mu_1 \neq \mu_2$. Therefore it can be concluded that the difference between the two drugs is "SIGNIFICANT".

Results

The table below indicates calculations for the demographic parameters data for Bupivacaine Group (Group 1 or Group B) and Ropivacaine Group (Group 2 or Group R):-

Table 1: Data Analysis on Demographic Parameters for Bupivacaine and Ropivacaine groups. Given v=58 and $P_{0.95}$=0.05

Demographic Parameters	Bupivacaine Group		Ropivacaine Group		T_{calc}	P_{calc}	Significance
	μ_1	σ_1	μ_2	σ_2			
Age in Years	46.8	11.57	46.06	9.93	0.2658	0.7913	$P_{calc} > 0.05$. Not Significant
Height in cms	160.23	3.919	158.53	5.55	1.37	0.1758	Not Significant
Weight in Kgs	58.567	4.883	60.333	5.101	1.3698	0.1760	Not Significant

There were no significant differences in any of the demographic parameters for both the groups.

In our study, the block parameters data were recorded, T_{calc} and P_{calc} were obtained. The significance levels are indicated in the Table 2 below:

Table 2: Data Analysis on Study Parameters for Bupivacaine and Ropivacaine groups.

Study Parameters	Bupivacaine Group		Ropivacaine Group		T_{calc}	P_{calc}	Significance
Mean Time for onset of SB	6.59	2.842	6.92	3.048	0.4337	0.6661	Not Significant
Mean Time for onset of MB	10.19	2.94	10.35	3.38	0.1956	0.8456	Not Significant
Mean duration of Sensory Block	251.16	13.246	250.100	16.033	0.2810	0.7797	Not Significant
*Pulse Rate at 0 Hrs (Induction Time)	87.467	6.745	88.733	8.634	0.6329	0.5293	Not Significant
*Pulse Rate @12 Hrs	85.867	6.010	87.533	5.084	1.1592	0.2511	Not Significant
*Systolic Blood Pressure at 0 Hrs	129.133	9.947	128.267	9.45	0.3457	0.7308	Not Significant
*Systolic Blood Pressure @12 Hrs	129.033	8.834	129.00	8.626	0.0146	0.9884	Not Significant
Mean duration of Motor Block	276.8	14.5	265.23	15.16	3.02	0.0037	**Significant (P_{calc}<0.05)**

Volume 5, Issue 1; January-February 2022; Page No 1228-1234

Mean duration to Rescue Analgesia	369.27	25.99	390.63	26.18	3.1714	0.0024	**Significant (P_{calc}<0.05)**

*Pulse Rate and Systolic Blood Pressure were measured @ every 5 minutes interval from Induction Time to 12 Hours. P_{calc} @ every 5 minutes interval was found Not Significant.

There were significant differences in only two of the block parameters in both the groups, namely the "Mean Duration of Motor Block" and "Mean Duration to Rescue Analgesia".

In the present study, the following two parameters were significant:-

1. "Mean Duration of Motor Block" is shorter in Ropivacaine Group as compared to Bupivacaine group.
2. In the present study, another parameter "Mean Time to Rescue Analgesia" is longer in Ropivacaine Group as compared to Bupivacaine Group.

Thus Ropivacaine 0.75% was associated with faster post op recovery and relatively longer duration of postoperative analgesia.

Hence Ropivacaine 0.75% can be used as a safe, efficient, and effective alternative to Bupivacaine 0.5% for Epidural Anesthesia in abdominal and lower limb surgeries.

Discussion

Anesthesia with an effective block, having least onset time, adequate period of block up to surgery, and flexibility to prolong anesthesia with least complications till completion of surgery is one of the biggest challenges faced by an anaesthesiologist. Here Regional Anesthesia (RA) suits best and is noted for its simplicity, safety and effectiveness as compared to General Anesthesia (GA) and Spinal Anesthesia (SA). [8 9]

Orthopaedic surgeries are usually associated with perioperative pain which is a potent trigger for the stress response and autonomic system which is thought to be an indirect cause of various adverse effects like myocardial ischaemia, infarction, thromboembolic phenomena, impaired pulmonary function, ileus, fatigue, muscle catabolism, postoperative infection and postoperative confusional states. Type of anesthesia to be administered and the anesthetic selection is the key to attenuate the stress response and eliminate the adverse effects.

Among different types of RA, Epidural Anesthesia is considered by many as the gold standard technique for major surgeries. Epidural Anesthesia is one of the most common regional anesthesia techniques for abdominal, lower limbs, pelvic and vascular surgeries. Epidural Anesthesia is a safe, inexpensive, and effective technique at providing dynamic anesthesia and analgesia, prolonging postoperative pain relief, thus allowing the patient to mobilize and resume normal activities unlimited by pain. It also improves the postoperative outcome and attenuates the physiological response to surgeries, in particular, there is significant reduction in pulmonary infections, pulmonary embolism, ileus, acute renal failure and blood loss. It also reduces incidences of hemodynamic changes as a result of sympathetic blockade as it produces segmental anesthesia unlike subarachnoid block anesthesia. The benefit of good quality epidural includes improved respiratory functions, decreased postoperative cardiac complications, earlier mobilization and less chances of deep vein thrombosis with shorter hospital stay. [10]

Though spinal anesthesia provides an efficient block, it has disadvantages such as height of block cannot be controlled, duration of block is constant and cannot be prolonged and it is associated with complications such as Post Dural Puncture Headache (PDPH), Neurological Sequelae etc. The advantage of Epidural Anesthesia over Spinal Anesthesia is the ability to maintain continuous anesthesia after placement of an epidural catheter thus making it suitable for a prolonged duration procedure as well as for postoperative analgesia.

The Epidural space contains fat, the dural sac, spinal nerves, blood vessels, and connective tissue. In Epidural Anesthesia, majority of the local anesthetic administered is absorbed systematically by the rich venous plexus found within the epidural space. Local anesthetics administered in the Epidural Space move in a horizontal and longitudinal direction. Theoretically if enough local anesthetic is injected, it

Volume 5, Issue 1; January-February 2022; Page No 1228-1234

could spread up to the foramen magnum and down to the sacral foramina. Clinically, the extent of longitudinal spread is volume dependant and cephalad spread is limited.

It has been found the an epidural will spread only 4 additional dermatomes when increasing the volume of local anesthetics from 10 ml to 30 ml. Horizontal spread occurs through intervertebral foramina, entering the dural cuff. [10]

Different local anesthetics are used for Epidural Anesthesia, most popular in India being Lignocaine and Bupivacaine. The drawback of Lignocaine is its intermediate duration of action, while Bupivacaine exhibits cardiotoxicity and CNS toxicity.

Ropivacaine is a long acting amide local anesthetic agent and first produced as a pure enantiomer. It produces effects similar to other anesthetics via reversible inhibition of sodium ion influx in nerve fibres. Ropivacaine is less lipophilic than Bupivacaine and is less likely to penetrate large myelinated motor fibres, resulting in a relatively reduced motor blockade. Thus Ropivacaine has a greater degree of motor sensory differentiation which could be useful when motor blockade is undesirable. The reduced lipophilicity is also associated with decreased potential for central nervous system toxicity and cardiotoxicity. Ropivacaine displays a linear dose proportional pharmacokinetics when administered intravenously up to 80 mg. It is metabolised extensively in the liver and excreted in urine. [1 3 11 12]

The aim of this study was to compare the effects of 0.75% Ropivacaine with 0.5% Bupivacaine for Epidural Anesthesia in the abdominal and lower limb surgeries. Our study consisted of 60 patients aged between 18 to 60 years, ASA Physical Status I and II undergoing Epidural Anesthesia for abdominal and lower limb surgeries. The 60 patients were randomly divided into two groups, Bupivacaine Group (B Group) and Ropivacaine Group (R Group). B Group received 20 ml 0.5% Bupivacaine while R Group received 20 ml 0.75% Ropivacaine, both through Epidural route.

Demographic parameters like age, height, weight in both the groups did not vary much as indicated in Table 1 above. The primary block parameters studied were Mean Time for Onset of Sensory Block, Mean Time for Onset of Motor Block, Mean Duration of Sensory Block, Mean Duration of Motor Block, and the Mean Duration of Analgesia. The Heart Rate and Systolic Blood Pressure were noted every five minutes from 0 hours at induction up to 12 hours of postop surgery, for all the 60 patients. These results are summarised in Table 2 above.

Among the primary block parameters, the differences in Duration of Motor Block and the Duration of Analgesia among both the study groups were found to be statistically significant for $p < 0.05$. The duration of Motor Block was assessed from the time of administration of the drug to complete motor recovery (Bromage Scale-0). In our study the Mean Duration of Motor Block in Bupivacaine was 276.8±14.50 minutes whereas in Ropivacaine it was 265.8±15.16 minutes. Thus it was found that the motor function was earlier with Ropivacaine when compared to Bupivacaine. Also, Mean Duration of Postoperative Analgesia was 369±25.99 minutes with Bupivacaine Group while it was 390.63±28.18 minutes with Ropivacaine Group.

Thus patients in the Ropivacaine group needed rescue analgesia after a much longer period of time as compared to patients in the Bupivacaine Group.

In our study, the two study groups did not differ significantly with respect to heart rate and systolic blood pressure at any time interval between inductions to 12 hours postop surgery. There were no episodes of bradycardia in either group. The changes in the systolic blood pressure during the 12 hour time interval were also statistically and clinically found insignificant between the two study groups. Also, there were no episodes of postoperative sequelae like headache, backache, nausea and vomiting for the next 24 hours among the 60 patients under study.

None of our patients experienced any respiratory depression and the mean respiratory rate between the study groups was statistically insignificant. From the studies of the two groups it can be inferred that Ropivacaine produces almost similar changes in haemodynamic parameters as that of Bupivacaine. Thus no adverse effects were noted in both groups intraoperatively and postoperatively.

Conclusion

Patients administered with 0.75% Ropivacaine had a shorter duration of motor block and longer period of

Volume 5, Issue 1; January-February 2022; Page No 1228-1234

rescue analgesia when compared with 0.5% Bupivacaine. Based on this present clinical comparative study, we conclude that 0.75% Ropivacaine, when administered through epidural route, provides better anesthesia and analgesia for abdominal and lower limb surgeries.

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Volume 5, Issue 1; January-February 2022; Page No 1228-1234