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Juxtaposition of Ropivacaine with Bupivacine Hyperbaric Solutions for Spinal Anaesthesia in Elective Surgeries: A Prospective Randomized Double Blind Study

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Abstract

Background: Baricity is the density of a substance compared to the density of human cerebrospinal fluid which used in anaesthesia to determine the manner in which a particular drug will spread in the intrathecal space and produce shorter duration of onset, greater level of blockade and fast recovery. *Aim:* To compare the clinical efficacy of hyperbaric Ropivacaine and Bupivacaine under spinal anaesthesia in terms of duration of onset, blockade and recovery. *Settings and Design:* Prospective, comparative and randomized double blind study. *Methods and Material:* About 80 patients from K S Hedge Medical College Hospital, NITTE University, Mangaluru, Karnataka, India were enrolled between January 2015 to August 2016 by random sampling method and divided into two groups as A and B. Group A received 3ml of 0.5% hyperbaric Bupivacaine and Group B received 3ml of 0.5% hyperbaric Ropivacaine. Subarachnoid block in L3-L4 space was performed by considering following parameters such as Onset and duration of block and recovery following injection. *Statistical Analysis:* Unpaired t test and Chi square test. $P<0.05$ was considered as statistically significant. *Results:* The duration of onset of sensory block to T10 with 0.5% hyperbaric Bupivacaine was 5.9±0.955 min when compared to 0.5% hyperbaric Ropivacaine which was 5.50±1.219 min with p value of 0.107. *Conclusions:* Hyperbaric Ropivacaine has showed more favourable profile than hyperbaric Bupivacaine in terms of shorter duration of onset, with higher level of sensory blockade and faster recovery.

Keywords: Bupivacaine; Double Blind; Hyperbaric Solutions; Prospective; Randomized Ropivacaine.

Introduction

Pain is one of the most noxious stimuli which are perceived by the human race and it is well documented that the most painful moments which are unforgertable by the patients are those related to surgical procedure [1].

With the advances in the field of anaesthesia various techniques are being used to alleviate pain in the peri-operative period. Spinal anaesthesia is the most commonly used technique used worldwide in providing a fast onset and effective sensory and motor blockade, also this is the most widely accepted anaesthetic technique for day care surgery [2].

Intrathecal anaesthesia has replaced general as the first-line method to provide anaesthesia for lower abdominal and lower limb surgeries as it is very economical and easy to administer [3].

Since the introduction of spinal anaesthesia by August Bier, it has been extensively used due to its simplicity of equipments, low cost, profound analgesia and minimal metabolic alterations [4, 5].

Bupivacaine has been in clinical use for more than 30 years. It is widely used due to its long duration of action and the differential effect of sensory to motor blockade. However it is associated with number of

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side effects like urinary retention, cardiovascular and central nervous system toxicity [6].

Bupivacaine is the most commonly used drug for spinal anaesthesia and is available as a racemic mixture of its enantiomers, dextrobupivacaine and levobupivacaine [6].

One disadvantage with spinal anaesthesia using hyperbaric bupivacaine alone is relatively shorter duration of action which means that early analgesic intervention is needed in the postoperative period [7].

Ropivacaine is a recently introduced amino-amide local anaesthetic agent similar to Bupivacaine in chemical structure [8]. The reason for introducing Ropivacaine was the need for a local anaesthetic that is less cardiotoxic than Bupivacaine and less neurotoxic than intrathecal lignocaine [9]. Hyperbaric Ropivacaine produces more predictable and reliable sensory and motor blockade, with faster onset than a plain solution [10].

The present study was designed to compare the clinical efficacy of hyperbaric solution of 0.5% Ropivacaine with that of commercially available preparation of 0.5% hyperbaric Bupivacaine.

Materials and Methods

This study was initiated after obtaining ethical clearance from Institutional Ethics Committee (IEC), K S Hedge Medical Academy, NITTE University, Mangaluru, Karnataka, India (Ref. No. INST.EC/EC/089/2014-15 dated 17/09/2014). Informed written consent was obtained from the participating patients who met a pre-defined inclusion and exclusion criteria.

Study Population

The subjects for the study was recruited from those who are posted for elective surgery under spinal anaesthesia

Sample Size

The sample size is determined using the formula,

$$\frac{Z[1-\alpha]^2 X\ 2(\mu)^2}{d^2}$$

Where N is sample size. μ = Standard deviation with a value of 2.2. d = Precision with a value of 1. Here $Z[1-\alpha]^2$ is a constant with value of 1.96.

$$\frac{[1.96]^2 X\ 2\ (2.2)^2}{1^2}$$

=37.186688.

Thus the sample size derived was 38 in each group. Considering a failure rate of 5%, the sample size increased to 40 in each group.

Sample Selection

The sample selection was done by a predefined inclusion and exclusion criteria

Inclusion Criteria

1. ASA I and II.
2. Age group 18 to 65years
3. Elective surgeries involving lower abdomen, genitourinary, perineal and lower limb procedures.

Exclusion Criteria

1. ASA III patients.
2. Psychiatric and neurologic disorders
3. Known allergy to drugs used in the study.
4. Any contraindication to spinal anaesthesia.
5. Coagulopathies
6. Block failure

Methodology

Pre anaesthetic evaluation was done for all patients. After the pre anaesthetic evaluation, patient was informed about the nature of the study and anaesthetic technique. Basic lab investigations like haemoglobin (Hb) %, fasting blood sugar (FBS) or random blood sugar (RBS), blood urea, serum creatinine and electrocardiogram (ECG) was done routinely in all patients. Chest X-ray was done when indicated. The entire procedure explained to the patient. Patients was kept nil per oral as per the standard guidelines. Patients were premedicated with Ranitidine 150mg and Diazepam (if weight of the patient <50kg, 5mg is given and if >50kg, 10mg) at 10pm the day before the surgery and 7am on the day of surgery. Anaesthesia machine, circuits, emergency drugs and equipment's and monitors were checked before starting the case. The monitors used were electrocardiogram (ECG), pulse oxymetry, non-invasive blood pressure (NIBP), fraction of inspired

oxygen (FiO2), end tidal carbon dioxide (EtCO2), temperature, tidal volume and airway pressure. Invasive vascular access was secured depending on the need. IV line was secured using 18 gauge cannula and ringer lactate infusion was started during procedure.

Hyperbaric Solutions

Under strict aseptic precautions hyperbaric Ropivacaine was prepared by adding 1ml of 25% dextrose to 2ml of 0.75% commercially available isobaric Ropivacaine. Hyperbaric Bupivacaine is readily available commercially which was used in this study. The specific gravity of both the drugs was determined by urinometer. After transferring the patient to the operation theatre, patient was connected to ECG, NIBP, pulse oxymetry, and baseline values were noted. Preloading was done with Ringer Lactate infusion 20ml/kg. A senior anaesthesiologist prepared the drug who was not involved in the study and observations were noted by a senior postgraduate who was unaware (blinded) of the nature of the study.

In this study, even patient was blinded from the drug. Each patient was advised to lie in lateral position and with all aseptic precautions a skin wheal was raised in L3-L4 interspace with 2ml of 2% Lignocaine. Sub arachnoid block in L3-L4 space was performed under aseptic precautions by senior postgraduate. A 25 guage Quincke Babcock needle was used for all the cases in the study. Immediately after completion of the block, patients were positioned as per requirement of surgery. Oxygen was administrated through a face mask. Patients were monitored for following parameters. Onset, duration of block and recovery. Following block, observation were continued at 30 minutes intervals until the motor block regresses completely as defined by modified Bromage score.

Parameters Evaluated

- Duration of onset of sensory block:
- Duration of onset of motor block:
- Haemodynamic parameters
- The end of study period was defined as the time at which the Modified Bromage score becomes 0.
- The segmental level of sensory block was assessed on both sides. The surgery was allowed to start once sensory block reached at T10 dermatome.

Statistical Analysis

Statistical analysis of data was done by using SPSS software version 20.0. The collected information was summarized as Mean Standard deviation. Unpaired t test. Chi square test for non-parametric data is presented as percentage and frequency. $P<0.05$ was considered as statistically significant.

Results

Table 1: Modified Bromage score

Modified Bromage Score	Criterion
0	Subject is able to move the hip, knee and ankle and is able to lift his leg against gravity.
1	Subject is unable to lift his leg against gravity but is able to flex his knee and ankle
2	Subject is unable to flex his hip and knee, but is able to flex his ankle.
3	Subject is unable to flex his hip, knee and ankle, but is able to move his toes.
4	Complete paralysis.

Table 2: Age distribution between Group-A and Group-B

Demo Graph	Group	N	Mean	Standard Deviation	T	DF	P value
Age	Group A	40	47.48	11.015	3.23	78	**0.002**
	Group B	40	39.38	11.412			

Table 3: Gender distribution between Groups-A and Group-B

Crosstab					
			Group		
			Group A	Group B	
Gender	Female	Count	7	9	16
		% within GROUP	17.5%	22.5%	20.0%
	Male	Count	33	31	64
		% within GROUP	82.5%	77.5%	80.0%
	Total	Count	40	40	80
		% within GROUP	100.0%	100.0%	100.0%

The mean age in group A were (47.48 ± 11.015) and in group B was (39.38 ± 11.412). In both groups the minimum age was 18 years and the maximum age was 60 respectively (p = 0.002) (Table 2).

There was significant male predominance among the patients of both groups (Table 3).

The mean time of onset of sensory blockade in Group-B is 5.50 ±1.219 mins and in Group-A is 5.9 ± 0.955 mins with a P value of 0.107. The comparison of the onset time of motor block between the two groups it shows that it is higher in Group B group with a t value of -8.355 and is statistically significant with a P value of <0.001. The comparison of the time of maximum level attained between the two groups shows that the mean time to reach the maximum level in mins is higher in GROUP B group with a t value of -0.969 and is statistically non-significant with a P value of 0.335. The mean no. of cases that reached the respective maximum levels of block. In both groups the mean level reached was at T6 but in group B had the maximum no of cases that reached the maximum level of T4 with a P value of 0.008 which was significant. Thus in our study groups, group B had cases which reached in higher levels, level up to T4 (Table 4-9).

Table 4: Chi-Square Test

	Value	**P value(Significant if <0.05)**
Pearson Chi-Square	0.313	0.576
N of Valid Cases	80	
Computed only for a 2x2 table		

Table 5: Mean time for onset of sensory block (min)

Groups	**N**	**Mean**	**Std. Deviation**	**95% Confidence Interval for Mean**		**t value**	**P**
				Lower Bound	Upper Bound		
Group A	40	5.90	.955	5.59	6.21	1.63	.107 NS
Group B	40	5.50	1.219	5.11	5.89		
Total	80	5.70	1.107	5.45	5.95		

Table 6: Onset of sensory blockade

Onset of sensory block	**Group A**	**Group B**
	5.9 min	5.5 min

Table 7: Onset of motor blockade

Onset of Motor Block	Group A	40	8.4	1.21529	-8.355	45.996	<0.001
	Group B	40	13.975	4.04137			

Table 8: Mean time for maximum level block attained (Minutes)

	Groups	**N**	**Mean**	**Std Deviation**	**T value**	**DF**	**P Value**
Time of Max Level in Minutes	Group A	40	15.75	2.13337	-0.969	78	0.335
	Group B	40	16.25	2.46774			

Table 9: Showing no. of cases reached maximum level of block in each group

Maximum levels reached in each group Cross-tabulation.					
			Groups		**Total**
			Group A	**Group B**	
Levels	T4	Count	0	5	5
		% within Group	0.0%	12.5%	6.2%
	T5	Count	4	12	16
		% within Group	10.0%	30.0%	20.0%
	T6	Count	28	18	46
		% within Group	70.0%	45.0%	57.5%
	T7	Count	40	40	80
		% within Group	100.0%	100.0%	100.0%

Chi-Square Tests			
	Value	**DF**	**Asymp. Sig. (2- sided)**
Pearson Chi-Square	11.866	3	.008
N of Valid Cases	80		

Discussion

The greatest gift God has given to mankind is not in happiness, but in relief of pain. In pursuit of relief of pain, particularly pain during and after surgery, many attempts have been made since time immemorial. The unmatchable reliability and simplicity of subarachnoid block has made spinal anaesthesia a very useful, successful and popularly employed anaesthetic technique in managing all surgical cases involving lower abdomen, genitourinary, perineal and lower limb procedures.

Bupivacaine is used routinely for perineal surgeries because of its high potency and minimal neurological symptoms. The quality of sensory blockade, motor blockade, hemodynamic changes, duration of blockade and side effect profile are some considerations in selecting a drug for spinal anaesthesia [11].

Ropivacaine, an S-enantiomer of Bupivacaine is being increasingly used for spinal anaesthesia in caesarean section, lower abdominal and perineal surgeries including lower limb surgeries.

Advantages claimed with Ropivacaine are shorter duration of motor block with similar sensory block properties compared to Bupivacaine (Mc Donald SB).Thus it minimizes the psychological discomfort of being immobile for long time [12,13]. Also its major advantage is being lesser cardiotoxic as compared to Bupivacaine [14].

In our study, we noted that there was no statistical significant difference in duration of onset of sensory block to T10 when we used 0.5% hyperbaric Bupivacaine in Group A (5.9 ± 0.955 min) compared to 0.5% hyperbaric Ropivacaine in group B (5.50 ±1.219 min) (P = 0.107). However, Ropivacaine had a faster onset of sensory block than Bupivacaine, which when related with previous studies showed that Ropivacaine has a lesser duration of onset of sensory block compared to Bupivacaine.

J. F. Luck et al in their study found that there was no statistically significant differences observed between the three groups with respect to times [in min; median (range)] to onset of analgesia to pinprick at T10 [Bupivacaine 5 (2–5), Levobupivacaine 5 (2–15), and Ropivacaine 5 (2–15)] when they used 3ml each of 0.5% concentration of each solutions in patients undergoing elective lower abdominal, perineal, or lower-limb surgery under spinal anaesthesia [15].

In our study we found that a modified Bromage score of 4 was achieved in both group A and group B was 100%. But in group B, the duration of reaching modified Bromage score 4 was higher when compared with the group A.

Whiteside et al found that degree of motor blockade assessed with Bromage score of 3 was achieved in 100% of hyperbaric Bupivacaine while only 70% in hyperbaric Ropivacaine [16].

In our study the median maximum level of sensory block was achieved at T6 for both groups. But variation of levels from (T5 – T7) was seen in group A with 3ml of 0.5% hyperbaric Bupivacaine and from (T4 – T7) in group B with 3ml of 0.5% hyperbaric Ropivacaine with a P value of 0.008 which was significant. Hence Ropivacaine provides a higher level of sensory blockade than Bupivacaine.

Bigat et.al, in their study found that the median maximal sensory block level was at T9 (T4–T10) with 7.5mg of 0.5% hyperbaric Bupivacaine and T8 (T5–T11) with 10mg of 0.66% hyperbaric Ropivacaine. In unilateral spinal anaesthesia, Ropivacaine gave a desirable, predictive and a fast recovery [17].

In our study, we also found a statistically significant difference in time for regression of motor blockade to modified Bromage score 0 with group B (210.75 ± 24.95 min) as compared with group A (237.0 ± 23.33 min) (P < 0.001). Hence Ropivacaine provides lesser duration of motor block than Bupivacine.

U Srivastava et al found that the time for regression of motor blockade as determined as assessed with Bromage score 0 was significantly less with hyperbaric Ropivacaine 127±20.42 min as compared with hyperbaric Bupivacaine 182±30.83min [18].

Ropivacaine even though is slow in onset of the motor blockade, but provided a comparable degree of block as that of Bupivacaine in our study. However it regressed faster than the Bupivacaine in our study. Usually, Ropivacaine gives predictively high level of blockade as that of Bupivacaine, but in our study, Ropivacaine had a higher level (T4 in 5 pts) than Bupivacaine (T5 in 4 pts) in an average no. of cases. Hence, Bupivacaine gives a better degree of motor blockade than Ropivacaine.

The limitations of the study were as follows

1. The sample size being small in comparison to the number of surgical procedures done under spinal anaesthesia.
2. The preparation of hyperbaric Ropivacaine was difficult and the temperature and dilution of the preparation could not be accurately followed.
3. A long term follow up for any complications was not done in the study.

Conclusion

Hyperbaric Ropivacaine has got a more favourable profile than hyperbaric Bupivacaine in terms of shorter duration of onset, produces a higher level of blockade and faster recovery. However the onset of motor blockade with Ropivacaine was longer when compared to Bupivacaine, but the degree of blockade was comparable with Bupivacaine and so can be used for spinal anaesthesia in elective surgeries involving lower abdomen, genitourinary, perineal and lower limb procedures with early mobilisation. Ropivacaine is a recent local anaesthetic, with a baricity which is made equal to that of Bupivacaine which provides a better safety margin than Bupivacaine and Lignocaine. Hence to maintain this advantage and improve the quality of anaesthesia, Ropivacaine can be an alternative.

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