ORIGINAL RESEARCH

A Comparative Study of Relative Potencies For Motor Block of 0.5% Isobaric Bupivacaine, 0.5% Isobaric Levobupivacaine and 0.5% Isobaric Ropivacaine In Ambulatory Surgery

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ABSTRACT

Introduction: Regional Anaesthesia has been increasing in popularity for ambulatory surgery as both primary anaesthetic as an adjunct to improve post operative analgesia.Aim of the studywas to study was conductedto compare the anaesthetic efficacy ofintrathecal 0.5% isobaric ropivacaine, 0.5% isobaricbupivacaine and 0.5% isobariclevobupivacaine for motor block in lower abdominal and lower limb surgeries.

Materials and methods: 150 ASA grade I and II patients of both sexes in the age group of 19-65 years undergoing day caresurgeries were selected and randomly divided into 3 groups of 50 patients each and were given intrathecal0.5% isobaric ropivacaine, 0.5% isobaric bupivacaine and 0.5% isobaric levobupivacaine.The baseline pulse rate and mean arterial pressure were recorded. Patients in all 3groups received 3ml of respective drugintrathecally and assessed for sensory and motor blockade.

Results: On comparison of data we have found that intrathecal 0.5% isobaric ropivacaine produces delayed onset of both sensory and motor block but of shorter duration which is statistically significant when compared with that of 0.5% isobaric bupivacaine and 0.5% isobaric levobupivacaine. There is no significant inter-group difference between bupivacaine and levobupivacaine except for the mean duration of sensory block, which is more in levobupivacaine group. The quality of motor block was assessed by Bromage scale, shows relatively lesser degree of motor block for ropivacaine group, when compared with that of bupivacaine and levobupivacaine groups. The incidence of hypotension and bradycardia is more in bupivacaine group. The height of block (peak sensory level-T4+T6) on percentage basis is higher for bupivacaine group 50% followed by levobupivacaine48% and ropivacaine44% respectively.

Conclusion: Ropivacaine produces adequate spinal blockade of shorter duration with early ambulation and faster home discharge when compared with 0.5% isobaric0.5% levobupivacaine and bupivacaine, hence considered as drug of choice for ambulatory anaesthesia

Keywords: Ambulatory surgery, Ropivacaine,bupivacaine,Levo-bupivacaine, Subarachnoid block.

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INTRODUCTION

Escalating healthcare costs have been a concern in developing countries. The cost-effectiveness of day-care surgery is well recognized and recent advances in anaesthetic and surgical techniques, have resulted in an ever-increasing number of surgical procedures being performed on a day-care basis world-wide. Ambulatory surgery demands good surgical anaesthesia and increases the need for a local anaesthetic with faster onset and rapid recovery from sensory and motor block.[1]

German surgeon August Bier (1861–1949)performed first surgery under spinal anesthesia.[1-3] Although Bier deserves credit for the introduction of spinal anesthesia into clinical practice, it was Corning who created the experimental conditions that ultimately led to the development of both spinal and epidural anesthesia.[3] Spinal anaesthesia has the definitive advantage of producing profound nerve block by relatively simple injection of a small amount of local anestheticintrathecally. The greatest challenge of this technique is to control the spread of localanaesthetic through CSF (both extent and degree) without producing unnecessarily extensive spread and increasingrisk of complications.The great interpatient variability in spread was observed and described as 'lauenhaft' (waywardness) by August Bier.Bupivacaine is the first long acting amide local anaesthetic synthesized in 1957 and introduced in the market in 1965. Its advantage, when compared to lignocaine is its longer duration of actiondue to increased lipid solubility and protein binding but has lower therapeutic index with respect to cardiovascular toxicity.

Increase in demand for day care surgery has generated a need for a local anaesthetic which allows early ambulation. More-

over, the major concern about cardiotoxicity of bupivacaine has led to the identification of optically active isomers of mepivacaine family -ropivacaine, a pure S-(-) enantiomer, whose toxicology was selectively and extensively studied before its introduction on the market in 1996.Ropivacaine has an isopropyl group bound to piperidine nitrogen in place of mepivacaine's methyl group and bupivacaine's butyl group. It is manufactured as pure s-enantiomer rather than a racemic mixture. During the rapid and extensive use of ropivacaine in the clinic, unwanted side-effects have been found to be very limited.[4]

The major clinical advantage of isobaric anaestheticsolutions is that the patient's position during and afterintrathecal injection have no effect on the spread of local anaesthetic in CSF. It is useful when lower thoracic dermatomal sensory block is desired and when degree of sympathetic blockade needs to be minimized. Ambulatory surgery demands good surgical anaesthesia with rapid recovery from sensory and motor block, allowing more patients to be discharged in less time with high satisfaction.

MATERIALS AND METHODS

A comparative randomized study was carried out in the department of Anaesthesiology,OsmaniaMedical College / Hospital, Hyderabad, from December 2012 to September 2013. After approval by Institutional Ethical Committee, study was undertaken in 150 patients of both sexes who are undergoing elective lower limb and abdominal surgeries under Subarachnoid analgesia on day care basis.

Inclusion criteria

ASA physical status I-II patients,age of the patients ranged between 19-55yrs weighing 35- 65kgs and height ranging between 150-168 cms.

Exclusion criteria

Patients havingLocal infection**,** Coagulopathy and bleeding disorders**,** ASA physical status grade >III.

Patients were randomly allocated into three groups of 50 each named as Group B - 0.5% Isobaric Bupivacaine, Group LB- 0.5% Isobaric Levo-bupivacaineand Group R - 0.5% Isobaric Ropivacaine and were given3ml of selected local anaestheticintrathecally.

Study is to compare the anesthetic efficacy of intrathecal 0.5% isobaric bupivacaine, 0.5% isobaric levobupivacaine and 0.5% isobaric ropivacaine, in day care lower limb and lower abdominal surgeries with respect to onset and duration of sensory and motor block and Quality of motor blockade.

Informed written consent was obtained from each patient and procedure was explained to patients. In the assessment room, vital parameters-Heart rate,Blood pressure and Respiratory rate were recorded. Thorough systemic examination and airway assessment were done and blood investigations reviewed.

In the operating room, airway equipment and drugs for emergency were kept ready before instituting spinal block, a peripheral venous cannula was secured on left hand dorsum and 500ml of Ringer's lactatesolution was given at the rate just to keep the cannulapatent. Using an aseptic technique, with patient in right lateral position a 26G Quincke short beveled needle was introduced in midline at L3-4 interspinousspace.Once a free flow of CSF was obtained, 3ml of selectedlocal anaestheticsolution was injected within 10 seconds. The anaesthetic solution was injected without aspiration or barbotage at the beginning or end of the injection. Assessment of motor block was started immediately after placing the patient in supine position and continued every minute till Bromage score of 3 was reached. The level of sensory anaesthesia was defined as loss of sharp sensation to pinprick and was recorded bilaterally in mid-clavicular line and regression of sensory and motor block was compared.

Bromage score

Grade	Criteria	Degree of block
I	Free movement of legs and feet	Nil (0%)
II	Just able to flex knees with free movement of feet	Partial (33%)
III	Unable to flex knees, but with free movement of feet	Almost complete (66%)
IV	Unable to move legs or feet	Complete (100%)

The Onset of Motor Block was defined as time to achieve Bromage score of 3.Duration of Motor Block was taken as time from subarachnoid injection to return of Bromage score to 0.Heart rate and MAP, systolic blood pressure were measured at 2minute interval for the first 10 minutes and at 5 minute intervals thereafter by an automated oscillotonometer. SpO_2monitored continuously by pulse oximetry. Hypotension was defined as a decrease in mean arterial blood pressure more than 20% from baseline or systolic blood pressure less than 90mm Hg. Hypotension was managed by incremental doses of 6mg i.v.ephedrine. Bradycardia- HR< 50/min was managed by incremental doses of 0.5mg intravenous atropine. Respiratory depression was said to be present if respiratory rate was < 8/ min and SpO_2< 90%. Vomiting managed with ondansetron 4mg i.v.Urinary retention was monitored postoperatively and catheterization was planned in patients with urinary retention for more than 6 hours. Patients were shifted to recovery room after completion of surgery. Statistical analysis was done using Microsoft Excel 2010 and Analysis Tool Pak in excel 2010. The results were expressed as mean and standard deviation for quantitative variables like Age, Pulse rate and onset of sensory and motor block, duration of sensory and motor block. The comparison between the means of three groups was done using one way analysis of variance (ANOVA). The intra-group and inter-group analysis of variance is expressed as Mean Squares (MS). F test statistic is calculated at $\alpha = 0.05$. A p value < 0.05 is considered statistically significant suggesting that there is significant difference of means in at least two groups.

Then, Bonferroni Post-Hoc Testis used to perform multiple comparisions and identify the groups among which there is a significant difference, when the F test statistics is significant.

RESULTS

This study includes 150 patients posted for lower limb and lower abdominal surgeries, divided into three groups of 50 each. All the patients received respective drug intrathecally. Group B- 0.5%Isobaric Bupivacaine, Group LB - 0.5% IsobaricLevobupivacaine and Group R-0.5%Isobaric Ropivacaine;. The anaesthetic efficacy of the above three drugs were contrasted, and the results are as follows.

Mean age group in Group B is 43.9 yrs Group LB is 43.16 yrs and Group-R is 39.8 yrs,

Males and females are Group-R are 35, 15, Group B are 36,14 and Group LB are 32, 18 patients are distributed in present study. Demographically there is no significant difference found with respect to age and sex factors.

The average duration of surgery, in all the three groups is not statistically significant. The 'p' value is 0.535.

In this table 2, the maximum distribution of upper extent of

Group R		Group B		Group LB		ANOVA			Post Hoc 't' test		
Mean	S.D	Mean	S.D	Mean	S.D	MS b/w groups (df=2)	MS Within_groups (df=147)	F	R B	R LB	B LB
94.2	20.85	97.4	12.95	98.8	26.95	278	442.91	0.63			
MS = Mean Squares; df = degrees of freedom; * = P<0.05 (0.535)- not significantDifference significant between groups by Post hoc Bonferroni 't' test:- Ropivacaine and Bupivacaine = R-B; Ropivacaine and Levobupivacaine = R-LB; Bupivacaine and Levobupivacaine = B-LB											

Table-1: Duration of Surgery (In Minutes)

Peak Sensory Level	Group R		Group B		Group LB	
	No.	%	No.	%	No.	%
T2	-	-	-	-	-	-
T4	0	0%	4	8%	2	4%
T6	5	10%	18	36%	22	44%
T8	42	84%	28	56%	24	48%
T10	3	6%	0	0%	2	4%
T12	0	0%	0	0%	0	0%
Total	50	100	50	100	50	100

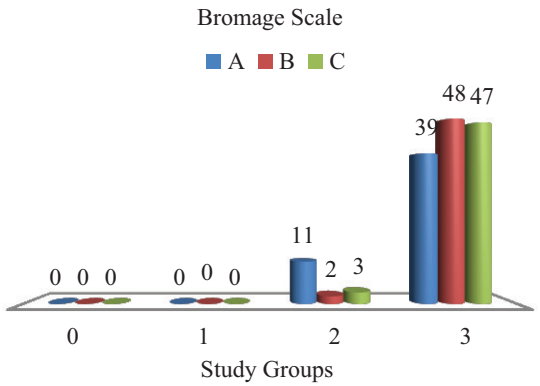
Table-2: Peak Sensory Level

Group R		Group B		Group LB		ANOVA			Post Hoc 't' test		
Mean	S.D	Mean	S.D	Mean	S.D	MS Between groups (df=2)	MS Within groups (df=72)	F	R B	R LB	B LB
Sensory block											
Mean Onset Time											
5.4	1.05	4.42	1.80	4.4	1.51	16.34	2.22	7.36		*	
Mean Duration											
145.3	32.95	176.2	48.17	189.8	42.68	26000.17	1742.49	14.92		*	
Motor Block											
Mean Onset Time											
6.48	1.15	5.76	1.93	5.48	1.7	13.31	2.65	5.02		*	
Mean Duration											
130.2	30.64	168.6	46.11	172.6	39.06	27402.67	1530.35	17.9		*	
MS = Mean Squares; df = degrees of freedom; * = P<0.05 (0.000895617)-significantDifference significant between groups by Post hoc Bonferroni 't' test:- Ropivacaine and Bupivacaine = RB; Ropivacaine and Levobupivacaine = R-LB; Bupivacaine and Levobupivacaine = B-LB;											

Table-3: Mean Onset Time and Duration of Sensory Block and Motor block(In Minutes)

Parameter	Group R		Group B		Group LB		'p'(ANOVA)
	Mean	S.D.	Mean	S.D.	Mean	S.D.	
Pulse rate	85.74	17.03	83.84	14.13	84.88	16.19	0.8349 Not significant
Respiratory rate	13.36	1.68	13.16	1.29	13.58	1.13	0.322 Not significant
Mean Arterial Pressure	87.3	17.5	91.32	18.13	89.44	18.08	0.534 Not significant
The study showed stable hemodynamic status with decreased incidence of hypotension and insignificant 'p' value.							

Table-4: Baseline Hemodynamics



A -Ropivacaine, B - Bupivacaine and C - Levobupivacaine

Figure-1: Quality of Motor Block (Bromage Scale)

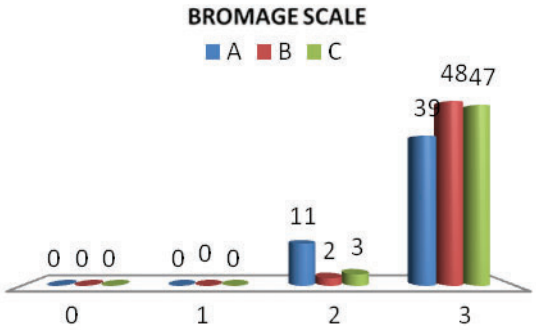


Figure-2: Adverse Effects in Three Groups

sensory block in group R is at T8
(84%). In Group B, it is 56% at T8 and 36% at T6 and in group LB, levels are distributed almost equally between T8 (48%) and T6 (44%).

The average time taken for onset of sensory block is 4.42 minutes in group **B** (Bupivacaine), 4.4minutes in group **LB** (Levobupivacaine) and 5.4 minutes in group **R** (Ropivacaine). The p value is 0.00089 which is significant between groups. By using post- hoc't' test the p value between group R and group B, group R and group LB is significant as P=0.001,P= 0.0002, The p value between group B and group LB is not significant(p=0.952). It implies the descending order of onset of sensory block is **R>B~LB**.

In mean duration of sensory block in Group R is 145.3 minutes, in Group B is 176.2 minutes and in Group LB is 189.8 mins. The 'p' value is $1.26x10^{-06}$ which is significant. The't' test is significant when we compared group R with both group B(P=0.0003) and group LB (P=0.008), whereas it is not significant between group B and group LB(P=0.13). from this test we find that the duration of sensory blockade in group LB> group B> group R.

The mean onset of motor block in all the three groups is tabulated. The p value is 0.0078, which is significant. The mean onset of motor block in group R, when compared with that of group B and group LB was significant(P=0.0008), which was determined by't' test. The mean onset of motor block is not significant(P=0.44) between group Rand group LB. The 'p' value is not significant. The order of mean onset of motor block in descending order is, R>LB>B groups.

The total duration of motor block in all the three groups are tabulated. Group R- (Ropivacaine) has a mean duration of 130.2 ± 30.64min followed by group B (Bupivacaine) and group LB (Levobupivacaine), with significant p value of $1.1x10^{-07}$ determined by ANOVA. The 't' test proves significant difference between group R, group B and LB, and no significant difference between Group B and Group LB.

Study Groups A-Ropivacaine, B-Bupivacaine and C-Levobupivacaine

The study shows that the percentage of cases not achieving Bromage scale 3 is higher in group R (22%) i.e., Ropivacaine group than the other two groups B and LB which is 4% and 6% respectively.

The study showed stable hemodynamic status with decreased incidence of hypotension and insignificant 'p' value.

The incidence of hypotension, Shivering and Bradycardia is 8%, 4% and 6% in Group B.

DISCUSSION

This is a study done on 150 patients, divided into three groups of 50 each. These groups, namely R, B&LB received equal concentration (5mg ml^{-1}) and volume (3ml) of isobaric Bupivacaine,Isobaric Levobupivacaine and Isobaric Ropivacaine respectively. Our study shows a slower onset of sensory block in the ropivacaine group than the bupivacaine group, which is comparable with a study in patients undergoing elective surgery conducted by J. B. Whiteside, D. Burke and J. A. W. Whitesmit.[5] The lesser lipid solubility of ropivacaine may cause the drug to penetrate the large myelinated A fibers less than more lipid soluble Bupivacaine. This was shown by Rosenberg PH, Kytta J, Alila A, in a study: "Absorption of bupivacaine, etidocaine, lignocaine and ropivacaine into N-heptane, rat sciatic nerve and human extradural and subcutaneous fat.[6] But, other studies conducted by M Mantouvalou et al[7], DAMcNamee, McClelland et.al[8] and Andrea Casati, Elena Moizo, Chiara Marchetiet. al[9] have shown no significant differences in the onset of sensory block in the three groups. The intergroup difference between bupivacaine and levobupivacaine was insignificantin our study, which was supported by a study conducted by Christian Glaser, Peter Marhofer, Gabriela Zimpfer, Marie T. Heinz, et al.; Levobupivacaine versus Racemic Bupivacaine for Spinal Anesthesia.[10] no difference in the onset of sensory block between bupivacaine and levobupivacaine.[11]

A study conducted by A Mehta, V Gupta, R Wakhloo, N Gupta, A Gupta, R Bakshi, B Kapoor, S Gupta[12] found that the mean onset of sensory block in ropivacaine, bupivacaine and levobupivacaine was 5.4 minutes, 4.4min, and 4.38min respectively, the mean onset of motor block with Ropivacaine, Bupivacaine and Levobupivacaine was 6.46 minutes, 5.67min, and 5.46min respectively, which is comparable with results of our study.[12] The onset of motor block was slower in Ropivacaine group, when compared with that of Bupivacaine and Levobupivacaine group in our study. This

is consistent with the findings in a study conducted by M Mantouvalou et.al.[7]

Another study conducted by Coppejans HC et.al[13] titled, "In a low dose combined spinal epidural anaesthesia for caesarean delivery" also supports this finding.P. Gautier, M. Dekock L. Huberty T Demir[14] also confirms slower onset of block with ropivacaineincomparision to both bupivacaine and levobupivacaine.

In a study by F Fattorini and Z Ricci et.al[15] there was no significant difference in the onset of motor block between bupivacaine and levobupivacaine group which coincides with the findings of our study.In a randomized double blinded study conducted in patients undergoing elective hip replacement by Glaser C, Mahofer P et.al: Levobupivacaine versus racemic Bupivacaine for spinal anaesthesia, there was no significant difference in the onset of both sensory and motor block.[10]

The duration of sensory block in our study was maximum in the Levobupivacaine group, followed by Bupivacaine and the least in Ropivacaine group with mean duration of sensory block more in levobupivacaine group which might be attributable to the greater intrinsic vasoconstrictor property of Levobupivacaine.[16] Findings of our study were consistent with the study by M Mantouvalou et.al[7]

Delfino et.al[17-19] compared equal doses of isobaric Ropivacaine and Bupivacaine i.e., 0.5% 3ml solution in orthopaedic surgery and found that duration of sensory block in Ropivacaine wasshorter than Bupivacaine group and quality of motor block was lesser in ropivacaine group. Van Kleef, etal, found that the intensity of motor block was lower with 15mg group of ropivacaine when compared with 22.5mg group of ropivacaine.[20]

The relative motor block potency of Rop: Bup was 0.66 after epidural administration[21] and for Rop: Lev was 0.83 after intrathecal administration[22] which means that there is lesser trend for motor blockade in ropivacaine group than in levobupivacaine and bupivacaine groups which is consistent with other study conducted by Mantouvalou[7] Malinovsky J.M., Charles F, Kick O.[18] The height of sensory block is higher for bupivacaine group i.e., T4+T6 is more than the other two groups (5% for ropivacaine, 48% for bupivacaine and 44% for levobupivacaine group). The incidence of hypotension and bradycardia is more in bupivacaine group, when compared with the two other drugs.

CONCLUSION

We conclude from this study, that the intrathecal administration of 3ml of 0.5% isobaric ropivacaine when compared to 3ml of 0.5% isobaric bupivacaine and 0.5% isobaric levobupivacaine produces delayed onsets of both sensory and motor block and early recovery.Ropivacaine scores above the other two drugs as a choice of drug for regional anaesthesia in ambulatory surgery. Ropivacaine produces adequate spinal blockade of shorter duration with early ambulation and faster home discharge when compared with Levobupivacaine and Bupivacaine. Hence, Isobaric Ropivacaine is considered as drug of choice for subarachnoid block in ambulatory anaesthesia.

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