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Research Article

A comparative study of Bupivacaine 0.5% versus Ropivacaine 0.5% for supraclavicular brachial plexus block (subclavian perivascular approach only) in ASA II,III Patients

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Abstract

Introduction: Peripheral nerve blocks have become important in clinical practice because of their role in post-operative pain relief, shortening of patient recovery time & avoiding risks and adverse effects of general anaesthesia. Bupivacaine is a long acting local anaesthetic. Due to its long duration of action and combined with its high quality sensory blockade compared to motor blockade it has been the most commonly used local anaesthetic for peripheral nerve blocks. Ropivacaine is a newer, long acting local anaesthetic whose neuronal blocking potential used in peripheral nerve blockade seems to be equal or superior to bupivacaine.

Method of collection of data: Sixty patients aged between 18 years and 60 years, of physical status ASA grade 2 and ASA grade 3 undergoing elective upper limb surgeries lasting more than 30 minutes were included in the study after getting ethical clearance. Each patient was randomly allocated to one of the two groups of 30 patients each. The patients were explained about the procedure and premedicated with tab alprazolam 0.5mg, and tab ranitidine 150 mg. The anesthetic technique employed was supraclavicular brachial plexus block using 30 ml of either 0.5% bupivacaine or 0.5% ropivacaine.

Results: In our study, we observed that onset time of sensory block was earlier in bupivacaine group in comparison with ropivacaine group. Onset time of motor block was earlier in bupivacaine group in comparison with ropivacaine group having a mean value of 22.90±1.88 minutes which is statistically significant. Duration of sensory block was 362.00±47.66 minutes with bupivacaine group and 322.00±42.38 minutes with ropivacaine group. The duration of sensory block was longer in bupivaine group compared with ropivacaine group. The duration of motor block was 399.00±41.05 minutes with bupivacaine group and 366.00±37.29 minutes with ropivacaine group. The duration of motor block was longer in bupivaine group compared with ropivacaine group. The duration of analgesia was 402.00±42.86 minutes with bupivacaine group (Group B) and 371.00±36.52 minutes with ropivacaine group (Group R) in our study.

Conclusion: On the basis of our study, we can draw the conclusion that at equal volumes bupivacaine 0.5% has an advantage over ropivacaine 0.5% for supraclavicular brachial plexus block in terms of early onset of sensory blockade, early onset of motor blockade, prolonged duration of sensory blockade, prolonged duration of motor blockade, prolonged duration of analgesia.

Keywords: Supraclavicular brachial plexus block, Subclavian perivascular approach, bupivacaine, ropivacaine.

1. Introduction

Peripheral nerve blocks have become important in clinical practice because of their role in post-operative pain relief, shortening of patient recovery time & avoiding risks and adverse effects of general anaesthesia. Hence, peripheral nerve blockade is now a well-accepted concept for comprehensive anaesthetic care.

Regional nerve blocks are based on the concept that pain is conveyed by nerve fibers, which can be interrupted anywhere along their pathway. For upper limb surgeries, brachial plexus block is the preferred regional anaesthesia technique [1]. Brachial plexus block [2] at the supraclavicular level provides anaesthesia for the upper limb surgeries by blocking

the middle & lower plexus [3] (Median, Radial and Ulnar N).

Local anaesthetics administered as regional nerve blocks provide post-operative pain relief by blocking signal transmission to dorsal horn [4]. Bupivacaine is a long acting local anaesthetic [5]. Due to its long duration of action and combined with its high quality sensory blockade compared to motor blockade it has been the most commonly used local anaesthetic for peripheral nerve blocks.

Ropivacaine is a newer, long acting local anaesthetic whose neuronal blocking potential used in peripheral nerve blockade seems to be equal or superior to bupivacaine.[6] Studies shows that it has significantly greater safety margin over bupivacaine because of lower CNS and Cardiac toxicity[7] and hence can be used in higher concentrations. One of the drawbacks of ropivacaine mentioned is its less intense motor blockade compared to bupivacaine.[8]

Hence here is an attempt through the study to compare bupivacaine with ropivacaine in supraclavicular brachial plexus block (subclavian perivascular approach only) [9]. This study is designed to compare 30 ml of bupivacaine 0.5 % and 30 ml of ropivacaine 0.5 % for supraclavicular brachial plexus block by perivascular approach.

1.1 Aims and objectives of the study

The present study was a prospective study at Rajah Muthiah Medical College And Hospital, Chidambaram in the Department of Anaesthesiology with the objective to compare the effect of bupivacaine 0.5% & ropivacaine 0.5% used for supraclavicular approach to brachial plexus block (subclavian perivascular approach only) with respect to:

- Onset time of Sensory blockade.
- Onset time of Motor blockade.
- Duration of Sensory blockade.
- Duration of Motor blockade.
- Duration of Analgesia.
- Side effects/ Complications.

2. Materials and Methods

2.1 Source of data

Present study entitled “A comparative study of bupivacaine 0.5% and ropivacaine 0.5% for supraclavicular brachial plexus block (subclavian perivascular approach only) in ASA 2&3 patients was carried out in the department of Anaesthesiology, Rajah Muthiah Medical College And Hospital, Chidambaram from January 2016 to July 2016

2.2 Study Design

Comparative randomized study

2.3 Sample Size

Two groups of 30 each.

2.4 Sampling Method:

Simple random sampling.

2.5 Statistical Analysis:

Student’s t-test.

2.6 Method of collection of data

Sixty patients aged between 18 years and 60 years, of physical status ASA grade 2 and ASA grade 3 undergoing elective upper limb surgeries lasting more than 30 minutes were included in the study after getting ethical clearance from the college ethical committee.

Each patient was visited pre-operatively and the procedure explained and written and informed consent was obtained. Complete blood count, Blood grouping, Blood sugars, Bleeding time, Clotting time, Blood urea, Serum Creatinine, serum electrolytes (sodium, potassium, chloride) chest x-ray, ECG were done. All the patients were pre-medicated with tablet alprazolam 0.5mg and tablet raniditine 150mg overnight and the morning of surgery.

2.7 Inclusion Criteria

Patients aged between 18 years to 60 years under physical status ASA grade 2 and 3 of scheduled for elective upper limb surgeries after obtaining written informed consent from patient/ patient attenders.

2.8 Exclusion Criteria

Known allergy to local anaesthetics, Patient’s refusal, History of cardiovascular disorders, neuromuscular disorders, bleeding disorders or patient on anticoagulant therapy, hepatic failure, renal failure, pregnancy, brachial plexus injury, local infections.

Each patient was randomly allocated to one of the two groups of 30 patients each: Group B – i.e., Bupivacaine group receives 30 ml Bupivacaine 0.5% (5 mg/ml). Group R – i.e., Ropivacaine group receives 30 ml Ropivacaine 0.5% (5 mg/ml).

All the necessary equipment and drugs needed for administration of general anaesthesia were kept ready in order to manage failure of block.

2.9 Procedure

Intravenous access obtained in the limb opposite to that undergoing surgery with a large bore i.v. cannula. Standard multi parameter monitors ECG, Pulse oximeter, Noninvasive blood pressure were connected and monitored in all the patients and recorded at interval of 5 minute in the first 30 minutes and every 30 minutes thereafter. Patient was placed in supine position with the head turned away from the side to be blocked. Arm to be anaesthetized adducted and extended towards the ipsilateral knee as far as possible. Supraclavicular area aseptically prepared and draped. An intradermal wheal raised about 1 cm above the mid-clavicular point.

Sub-clavian artery palpable in supraclavicular fossa (subclavian perivascular approach only) was used as landmark. A 23gauge

needle inserted behind the artery in backward-inward-downward direction till paresthesia in the forearm elicited. After negative aspiration for blood, 30 ml of respective drug was injected depending on whether patient is allotted to either of group B or R.

2.10 Assessment of sensory block

Sensory block was assessed by pin prick with 23g hypodermic needle in skin dermatomes c4-t2 once in every minute for initial 30 minutes and then after every 30 minutes till patient regained normal sensations and graded according to Visual analogue scale (VAS) as:

0-No Pain.
2-Annoying (Mild pain).
4-Uncomfortable (Moderate pain).
6-Dreadful (Severe pain).
8-Horrible (Very severe pain).
10-Agonizing (Worst possible pain).

2.11 ASSESSMENT OF MOTOR BLOCK:

Quality of motor block was assessed at the same intervals and graded according to Modified Lovett's Scoring as:

Grade 6- Normal.
Grade 5 –slightly reduced muscular force.
Grade 4 – pronounced reduction. Grade 3 – slightly impaired mobility.
Grade 2 – pronounced mobility impairment. Grade 1 – Almost complete paralysis.
Grade 0 – Complete paralysis.

2.12 The effect on the following parameters were Observed:

Onset time of Motor blockade- taken from the completion of injection of study drug till the patient develops motor blockade.(Lovett"s Grade 1)

Onset time of Sensory blockade- taken from the completion of injection of study drug till the patient does not feel the pin prick.(Visual analogue scale score -0)

Duration of Motor blockade- taken from the Onset of Motor blockade till complete recovery of motor power. (Lovett's grade 6)

Duration of Sensory blockade– taken from the Onset of Sensory blockade till the patient feels pin prick. (visual analogue scale of 2)

Duration of Analgesia- taken as the time between the onset of sensory action and onset of pain, was the time when patient received first dose of analgesic. Supplemental analgesia was given when visual analogue scale score was more than 4.

Patients were watched for Bradycardia, Convulsions, Restlessness, Disorientation, Drowsiness, Nausea, Vomiting & any other complications.

All the values were expressed as Mean, Standard deviation; statistical comparison was performed by student's t-test & chi-square test.

A two tailed p value of >0.05 was considered to be statistically not significant, a p value of <0.05 as statistically significant, a p value of <0.01 as statistically highly significant & a p value of <0.001 as statistically very highly significant.

3. Results

The present study was conducted on 60 consenting patients aged between 18-60 years. Group B received 30ml of 0.5% Bupivacaine. Group R received 30ml of 0.5% Ropivacaine for Brachial plexus block by supraclavicular approach.

3.1 Demographic Data:

Table 1: Age distribution of patients studied

Age in years	Group B		Group R	
	No	%	No	%
21-30	7	23.3	7	23.3
31-40	10	33.3	9	30.0
41-50	10	33.3	12	40.0
51-60	3	10.0	2	6.7
Total	**30**	**100.0**	**30**	**100.0**
Mean ± SD	39.47±9.12		39.23±9.09	

Samples are age matched with P=0.921.

Table 2: Gender distribution of patients studied

Gender	Group B		Group R	
	No	%	No	%
Male	23	76.7	21	70.0
Female	7	23.3	9	30.0
Total	**30**	**100.0**	**30**	**100.0**

Samples are gender matched with P=0.559.

As shown in table1, both the groups, Group B (Bupivacaine) and Group R (Ropivacaine) are age matched. As shown in table 2, both the groups, Group B (Bupivacaine) and Group R (Ropivacaine) are gender matched.

Table 3: Distribution of patients according to height (cms)

Height (cm)	Group B		Group R	
	No	%	No	%
<160	6	20.0	5	16.7
160-170	17	56.7	20	66.7
>170	7	23.3	5	16.7
Total	**30**	**100.0**	**30**	**100.0**

As shown in table 3, both the groups are matched with respect to the Height of the patient.

Table 4: Distribution of patients according to weight (Kg)

Weight (kg)	Group B		Group R	
	No	%	No	%
<60	7	23.3	8	26.7
60-70	13	43.3	15	50.0
70-80	10	33.3	7	23.3
Total	**30**	**100.0**	**30**	**100.0**

As shown in table 4, both the groups, group B and group R, are matched with respect to weight of the patients.

Table 5: Comparison of heart rate in two groups studied

HR	Group B	Group R	P value
0 min	86.63±6.99	84.03±7.98	0.185
5 min	86.27±6.49	82.80±7.21	0.055
10 min	84.67±5.88	81.80±6.65	0.082
15 min	82.07±4.86	79.53±7.23	0.117
20 min	80.13±5.20	77.87±6.17	0.129
25 min	76.67±4.62	76.53±5.61	0.920
30 min	74.67±4.34	74.73±4.74	0.955

As shown in table 5, Heart rate variation between the groups, group B and group R, at every 5 minute interval from 0-30 min, is not statistically significant (p>0.05).

Table 6: Comparison of systolic blood pressure (mm hg) in two groups studied

SBP (mm Hg)	Group B	Group R	P value
0 min	126.53±8.22	124.47±7.53	0.314
5 min	126.33±6.69	125.13±6.05	0.469
10 min	123.80±5.81	122.93±6.21	0.579
15 min	121.87±5.68	120.07±6.23	0.247
20 min	117.80±5.57	117.60±5.74	0.892
25 min	116.00±5.38	116.20±5.37	0.886
30 min	114.00±4.90	114.80±4.44	0.510

As shown in table 6, systolic blood pressure (mm hg) variation between the groups, group B and group R, at every 5 min interval from 0-30 minutes, is not statistically significant (p>0.05).

Table 7: Comparison of diastolic blood pressure (mm hg) in two groups studied

DBP (mm Hg)	Group B	Group R	P value
0 min	79.87±5.43	81.60±6.40	0.263
5 min	79.73±2.27	80.73±5.45	0.357
10 min	79.47±3.52	79.27±5.77	0.872
15 min	79.47±1.96	78.13±4.95	0.176
20 min	76.93±4.63	77.67±4.24	0.525
25 min	76.13±4.81	76.73±5.77	0.663
30 min	75.60±4.74	76.20±4.44	0.615

As shown in table 7, Diastolic blood pressure (mm hg) variation between the groups, Group B and Group R, at every 5 min interval from 0-30 minutes, is not statistically significant (p>0.05).

Table 8: Comparison of mean arterial pressure (mm hg) in two groups studied

MAP (mm Hg)	Group B	Group R	P value
0 min	95.42±5.75	95.89±5.79	0.755
5 min	95.27±3.24	95.53±5.06	0.809
10 min	94.24±3.42	93.82±4.65	0.690
15 min	93.60±2.72	92.11±4.74	0.141
20 min	90.56±4.48	90.98±4.18	0.707
25 min	89.42±4.63	89.89±4.46	0.692
30 min	88.40±4.37	89.07±3.87	0.534

As shown in table 8, Mean blood pressure (mm hg) variation between the groups, Group B and Group R, at every 5 min interval from 0-30 minutes, is not statistically significant (p>0.05).

Table 9: Comparison of duration of surgery (DOS) in two groups studied

Study variables	Group B	Group R	P value
DOS	123.50±31.87	114.67±25.43	0.240

As seen in table 9, There is no statistically significant difference found between the two groups with respect to the duration of surgery (p>0.05).

Table 10: Comparison of group b and group r on the basis of onset time of sensory and motor blockade

Study variables	Group B	Group R	P value
Sensory onset time	15.70±2.35	20.13±3.05	<0.001
Motor onset time	20.43±2.22	22.90±1.88	<0.001

Onset time of Sensory and Motor blockade was earlier in Group B when compared with Group R. The p value was < 0.001 which is statistically very highly significant.

Table 11: Comparison of group b and group r on the basis of duration of sensory and motor blockade

Study variables	Group B	Group R	P value
Duration of sensory blockade	362.00± 47.66	322.00± 42.38	0.001
Duration of motor blockade	399.00± 41.05	366.00± 37.29	0.002

Duration of Sensory and Motor blockade was prolonged in Group B when compared with Group R. The p value was 0.001 and 0.002 respectively which is statistically very highly significant.

Table 12: Comparison of group b and group r on the basis of duration of analgesia

Study variables	Group B	Group R	P value
Duration of analgesia	402.00± 42.86	371.00± 36.52	0.004

Duration of Analgesia was prolonged in Group B when compared with Group R. The p value was 0.004 which is statistically very highly significant.

Table 13: Complications/ side effects

Complication	Group B		Group R	
	No	%	No	%
Nil	30	100.0	30	100.0
Vomiting	0	0	0	0.0
Total	**30**	**100.0**	**30**	**100.0**

As shown in table 13, the side effects/ complication rate are negligible if right dose is used and properly deposited.

4. Discussion

Brachial plexus blockade for upper limb surgeries is the most common major peripheral nerve block technique. The supraclavicular approach to brachial block is carried at the level of trunks of brachial plexus. It provides most effective blockade since plexus is blocked at the middle of Brachial plexus, resulting in homogenous spread of anaesthetic drug throughout the plexus.

A significant difference exists between various local anaesthetics like lignocaine, mepivacaine, bupivacaine in terms of onset times, total duration and safety profile when used in brachial blocks. Ropivacaine is a newer long acting amide local anaesthetic found to be equally efficacious to bupivacaine, but with a better safety profile when used in brachial block.

Sixty ASA 1 and ASA 2 patients undergoing elective upper limb surgeries lasting more than 30 minutes were included in the study. Patients were divided into 2 groups of 30 each (Group B and Group R). Group B received supraclavicular Brachial plexus block with 30 ml of 0.5% Bupivacaine. Group R received supraclavicular Brachial plexus block with 30 ml of 0.5% Ropivacaine. Parameters observed included Onset time of sensory block, Onset time of Motor block, Duration of Sensory block, Duration of Motor block, Duration of Analgesia and Side effects.

4.1 Patient characteristics across the Groups:

The patients in our study groups did not vary much with respect to Age, Sex, Height or Weight. The type of surgeries performed was almost identical in both the groups. The study groups did not vary much with respect to Duration of surgery (Statistically not significant).

4.2 Changes in the perioperative cardiovascular Parameters

There was no significant difference between the study groups with respect to pattern of changes in Heart rate, Systolic blood pressure, Diastolic blood pressure, Mean arterial pressure peri operatively.

4.3 Onset time of Sensory and Motor block

In our study, we observed that onset time of sensory block was earlier in bupivacaine group (Group B) having a mean value of 15.70±2.35 minutes in comparison with ropivacaine group (Group R) having a mean value of 20.13±3.05 minutes, which is statistically significant.

In our study, we observed that onset time of motor block was earlier in bupivacaine group (Group B) having a mean value of 20.43±2.22 minutes in comparison with ropivacaine group (Group R) having a mean value of 22.90±1.88 minutes which is statistically significant.

Hence, we conclude that bupivacaine 0.5 % has an advantage of early onset of sensory and motor blockade when compared to ropivacaine 0.5% for supraclavicular brachial plexus block (subclavian perivascular approach only) at equal volume.

4.4 Duration of Sensory block and Motor block:

In our study the Duration of sensory block was 362.00±47.66 minutes with bupivacaine group and 3022.00±42.38 minutes with ropivacaine group. The duration of sensory block was longer in bupivaine group compared with ropivacaine group, which is statistically significant.

The duration of motor block was 399.00±41.05 minutes with bupivacaine group and 366.00±37.29 minutes with ropivacaine group. The duration of motor block was longer in bupivaine group compared with ropivacaine group, which is statistically significant.

Hence, we conclude that Bupivacaine 0.5 % has an advantage of prolonged duration of sensory and motor blockade when compared to ropivacaine 0.5% for supraclavicular brachial plexus block (subclavian perivascular approach only) at equal volume.

4.5 Duration of Analgesia

The mean time from onset of block to request of Analgesics was taken as total Duration of Analgesia. The Duration of Analgesia was 402.00±42.86 minutes with bupivacaine group (Group B) and 371.00±36.52 minutes with ropivacaine group (Group R) in our study. The duration of analgesia was longer in bupivaine group compared with ropivacaine group, which is statistically significant.

4.6 Adverse Effects/ Complications

No patient in our study developed any significant Side effects.. This signifies that adverse effects were not significant in both the groups.

5. Summary and Conclusion

The study was a prospective, randomized study carried out in Rajah Muthiah Medical College And Hospital, Chidambaram.. Sixty ASA 2 and ASA 3 patients undergoing elective upper limb surgeries lasting more than 30 minutes were included in the study.

Patients were divided into 2 groups of 30 each. (Group B and Group R). Group B received supraclavicular brachial plexus block with 30 ml of 0.5% bupivacaine. Group R received supraclavicular brachial plexus block with 30 ml of 0.5% ropivacaine. Parameters observed included onset time of sensory block, onset time of Motor block, duration of Sensory block, duration of Motor block and duration of analgesia, side effects.

Under all asepsis, all the patients were administered supraclavicular brachial plexus block (subclavian perivascular approach only). All necessary equipment's and drugs needed for administration of general anaesthesia were kept ready in order to manage failure of the block.

The patients in our study groups did not vary much with respect to Age, Sex, Height or Weight. The type of surgeries performed was almost identical in both the groups. The study groups did not vary much with respect to Duration of surgery (Statistically not significant). There was no significant difference between the study groups with respect to pattern of changes in heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure perioperatively.

Onset of sensory blockade was faster in Group B (Bupivacaine) i.e., 15.70±2.35 minutes compared to Group R (Ropivacaine) i.e., 20.13±3.05 minutes which was statistically significant. Duration of sensory blockade was also longer in Group B (Bupivacaine) i.e., 362.00±47.66 minutes compared to Group R (Ropivacaine) i.e., 322.00±42.38 minutes and was statistically significant. Onset of Motor blockade was faster in Group B (Bupivacaine) i.e., 20.43±2.22 minutes compared to Group R (Ropivacaine) i.e., 22.90±1.88 minutes which were statistically significant.

Duration of Motor blockade was also longer in Group B (Bupivacaine) i.e., 399.00±41.05 minutes compared to Group R (Ropivacaine) i.e., 366.00±37.29 minutes and was statistically significant. Also, the time for demand of analgesics was prolonged in Group B (Bupivacaine) i.e., 402.00±42.86 minutes compared to Group R (Ropivacaine) i.e., 371.00±36.52 minutes and this difference was statistically significant.

With the present study we can summarize that bupivacaine 0.5 % has early onset of sensory blockade, early onset of motor blockade, Prolonged duration of sensory blockade, Prolonged duration of motor blockade, Prolonged duration of analgesia when compared to ropivacaine 0.5 % at equal volumes. Both the drugs maintain stable hemodynamic profile peri operatively and are devoid of any side effects at the concentration and volumes used for the study.

On the basis of our study, we can draw the conclusion that at equal volumes bupivacaine 0.5% has an advantage over ropivacaine 0.5% for supraclavicular brachial Plexus block (subclavian perivascular approach only) in terms of

- Early onset of Sensory blockade.
- Early onset of Motor blockade.
- Prolonged Duration of Sensory blockade.
- Prolonged Duration of Motor blockade.
- Prolonged Duration of Analgesia.

References

[1] Hirschel G (1911-07-18). "Die anästhesierung des plexus brachialis fuer die operation en an der oberen extremitat" [Anesthesia of the brachial plexus for operations on the upper extremity]. 58: 1555–6.

[2] Kulenkampff, D (1911). "Zur anästhesierung des plexus brachialis" [On anesthesia of brachial plexus]. 38: 1337–40.

[3] Partridge BL, Katj J, Benirschke K. Functional Anatomy of the brachial plexus sheath: Implications for Anaesthesia. Anaesthesiology 1987; 66: 743.

[4] Charles BB, Gary RS. Local anaesthetics. Miller's Anaesthesia 5th edition. New York; Churchill livingstone.2000; 491-517.

[5] Singelyn F J. Clinical application of Bupivacaine for upper extremity. *Current topics in Medicinal Chemistry*, 2001; 1(3): 219-225.

[6] Lew D, Jerry D, V Loka *et al*. Ropivacaine for peripheral nerve blocks: Are there advantages. *Techniques of Regional Anaesthesia and pain management* 2001; 5 (2): 56-59.

[7] Singelyn F J, clinical application of Ropivacaine for upper extremity. Current topics in medicinal chemistry, 2001; volume 1 number 3: 219-225.

[8] Feldman HS, Arthur GR, Covino BG. Comparitive systemic toxicity of convulsant and supraconvulsant doses of intravenous ropivacaine, Bupivacaine and Lidocaine in the conscious dog. *Anaesthesia Analgesia* 1989; 69:794-801.

[9] Tripathi D, Shah K, Shah C, S Shah, E Das. Supraclavicalar Brachial Plexus Block for Upper Limb Orthopedic Surgery: A Randomized, Double Blinded Comparison Between Ropivacaine and Bupivacaine. *The Internet Journal of Anesthesiology*. 2012; 30 (4).