

A Comparative Study between Ropivacaine with Clonidine and Bupivacaine with Clonidine in Brachial Plexus Blocks in Upper Limb Surgeries

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Abstract: Introduction: Pain is one of mankind's oldest and most dreaded maladies. Despite increased knowledge and scientific advances, the diagnosis and effective treatment of pain remains one of the most formidable challenges with many difficulties and pitfalls.

Materials and Methods: The present study titled "A comparative study of Ropivacaine and Clonidine with Bupivacaine and Clonidine in supraclavicular brachial plexus block" was carried out at District headquarters Hospital, Nalgonda. It was a prospective and randomized study. Sixty patients of age group between 18 and 70 years admitted between December 2013 and July 2015 were selected for the study. These patients were undergoing elective operative procedures for upper limb surgeries (i.e. elbow, forearm and hand surgeries). Exclusion criteria included patient's refusal, history of bleeding disorders or patients on anticoagulant therapy, peripheral neuropathy, local infection, respiratory disease, or known allergy to local anaesthetic drugs.

Results: The present study was conducted on 60 consenting patients aged between 18-70 years. Group RC received 30ml of 0.75% Ropivacaine + 1.5 mcg/kg Clonidine. Group BC received 30 ml of 0.5% Bupivacaine + 1.5 mcg/kg Clonidine for brachial plexus block by supraclavicular approach. Table-1 shows age distribution of the patients in both the groups. The minimum age in both groups was 18 years. The maximum age in both groups was 60 years and 65 years respectively. The mean age in group BC were 31.20 ± 12.59 and RC were 32.00 ± 13.17 respectively. There was no significant difference in the age of patients between the Group BC and Group RC. Both groups were similar with respect to age distribution ($p > 0.05$).

Conclusion: Ropivacaine and Clonidine can be used in supraclavicular brachial plexus block in view of its faster onset of action and similar duration of action compared with Bupivacaine and Clonidine, and similar quality of block. Ropivacaine, being less cardiotoxic is a good alternative to Bupivacaine. Clonidine is a good adjuvant in brachial plexus block as it hastens the onset of block and prolongs the duration of block, reduces patient anxiety and improves patient comfort level intra operatively as well as post operatively.

Key Words: Pain, Ropivacaine, Clonidine, supraclavicular brachial plexus block, Bupivacaine

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I. Introduction

Pain is one of mankind's oldest and most dreaded maladies. Despite increased knowledge and scientific advances, the diagnosis and effective treatment of pain remains one of the most formidable challenges with many difficulties and pitfalls.

Regional nerve blocks are based on the concept that the pain is conveyed by nerve fibres which are amenable to interruption anywhere along their pathway.

The idea that pain is conducted and modulated in the nervous system, originated with the specific theory of Johannes P Muller, described in 1826. This was followed by the alternate intensity theory of Erb in 1874; an idea that later culminated in the gate control theory of pain by Melzack and Wall in 1965.

In 1855, Rynd described the idea of introducing a solution of morphine hypodermically around a peripheral nerve.

Wood, in 1855 was the first person to perform a subcutaneous injection with a graduated glass syringe and a hollow needle, a device developed initially by Pravaz for injection of ferric chloride into an aneurysm to produce coagulation¹.

Trephination was practiced by Incas, and their tradition holds that the 'Shaman', performing the procedure chewed Cocoa Leaves and Spat into the wound producing local anaesthetic effect².

In 1881, Carl Koller demonstrated ocular surface anaesthesia with cocaine³. Ester local anaesthetics which were developed later lost their value due to short duration of action, allergic reaction and systemic toxicity. Later, amide anaesthetics were synthesized. In the recent years peripheral nerve blocks are gaining importance for their longer duration of action, quality of block and post-operative analgesic effect. It also avoids the side effects of general anaesthesia.

Bupivacaine is commonly used in brachial plexus blocks because of its longer duration of action compared to Lignocaine⁴. Concerns have been raised about the cardiotoxic effects of Bupivacaine after accidental IV injection. Bupivacaine cardiotoxicity was more resistant to resuscitation compared to other local anaesthetics^{4,5,6}.

Studies have found out that commercial Bupivacaine is a racemic mixture of (R) - and (S) - stereoisomers⁷. The cardiac toxic effects were attributed to the dextro (R) isomer while its pharmacologic effects were achieved by its levo (S) isomer. In response to the problem of cardiovascular toxicity as a result of accidental intravascular injection of Bupivacaine, single enantiomers like Ropivacaine⁸ and Levo-(S)-bupivacaine⁹ were developed. These have less cardiotoxicity on milligram to milligram basis in animal studies^{4,10,11}, and data in human studies have also shown that the potential of Ropivacaine to produce central nervous system and cardiotoxicity is less^{12,13}. The cardiotoxicity of Ropivacaine and Levobupivacaine was more amenable for resuscitation compared to Bupivacaine^{4,5}. Ropivacaine provides a better differential block between sensory and motor block when given epidurally. It has a shorter duration of action and is less potent than Bupivacaine¹⁴.

To prolong the duration of the major nerve blocks, several adjuvants have been used such as epinephrine, bicarbonate, opioids, clonidine and neostigmine¹⁵. Clonidine has been shown to be a valuable adjuvant to major nerve blocks. It is an alpha – 2 receptor agonist and has been shown to reduce the time of onset to the block and provide better quality of anaesthesia^{16,17}.

We made an attempt to compare the clinical characteristics of Ropivacaine with Clonidine and Bupivacaine with Clonidine used while giving brachial blocks.

II. Materials AND METHODS

The present study titled “A comparative study of Ropivacaine and Clonidine with Bupivacaine and Clonidine in supraclavicular brachial plexus block” was carried out at District Headquarters Hospital, Nalgonda. It was a prospective and randomized study.

Sixty patients of age group between 18 and 70 years admitted between December 2013 and July 2015 were selected for the study. These patients were undergoing elective operative procedures for upper limb surgeries (i.e. elbow, forearm and hand surgeries).

Exclusion criteria included patient's refusal, history of bleeding disorders or patients on anticoagulant therapy, peripheral neuropathy, local infection, respiratory disease, or known allergy to local anaesthetic drugs.

Each patient was visited pre operatively and the procedure was explained and informed written consent was obtained. Investigations like complete blood count, blood grouping, urine examination for albumin, sugar and microscopy, random blood sugar, blood urea, serum creatinine, bleeding time, clotting time, chest x-ray, ECG were done.

Each patient was randomly assigned to one of the two groups of 30 patients each, group BC or group RC by a computerized randomization.

Group – BC i.e., Bupivacaine group received 0.5% Bupivacaine according to body weight + 1.5 mcg/kg Clonidine

Group – RC i.e., Ropivacaine group received 0.75% Ropivacaine according to body weight + 1.5 mcg/kg Clonidine

Each patient was made to lie supine without a pillow, arms at the side, head turned slightly to the opposite side with the shoulders depressed posteriorly and downward by moulding the shoulders over a roll placed between the scapulae. The supraclavicular area was aseptically prepared and draped. The anaesthesiologist stands on the side of the patient to be blocked.

An intradermal wheal was raised with local anaesthetic approximately 1cm above the midclavicular point. The subclavian artery palpable in supraclavicular fossa was used as landmark. The tip of index finger was rested in supraclavicular fossa directly over the arterial pulsation. A filled 10ml syringe with a 23 gauge, 32mm needle attached was held in right hand and connected to the nerve stimulator. The nerve stimulator needle was inserted through skin and advanced slowly downward (caudal) rolled slightly inward (medially) and slightly backward (posteriorly).

As soon as muscle twitches were elicited at 0.5 mA, the needle was fixed in position and after confirming negative aspiration of blood, the respective drug was injected depending on whether the patient as allotted to either of group BC or RC.

Time of onset of sensory block was recorded using pinprick in skin dermatomes C4-T2 once in every 1 minute until onset of the block for a maximum of 30 minutes after injection and thereafter every 30 minutes till patient regained normal sensations. The same observer assessed the motor block at same time intervals.

Onset of sensory block was from the time of injection of drug to time of loss of pain on pinprick. Onset of motor block was from the time of injection to time of complete loss of movement.

Sensory block was assessed by pinprick with a short beveled 23G needle as

Grade 0 – Sharp pin prick felt

Grade 1 – Analgesia, dull sensation felt

Grade 2 – Anaesthesia, no sensation felt.

Motor block was graded according to the modified Bromage scale.

Grade 0 – Normal motor function with full extension and flexion of elbow, wrist, and fingers.

Grade 1 – Decreased motor strength, with ability to move only fingers.

Grade 2 – Complete motor block with inability to move elbow, wrist, and fingers.

Duration of sensory blockade was the time in minutes from the onset of analgesia to the recurrence of pain to pin prick. Duration of motor blockade was the time in minutes from the onset of paresis to the recurrence of motor movements.

The quality of the block was graded according to whether opioids were used during intra operative period (grade II) or if adjuvants of any kind were not used throughout the surgery (grade I). For the patients who were anxious and perturbed by the sensation of touch on the operating limb, Inj. Fentanyl 50 mcg IV was administered. The blocks that required conversion to general anesthesia were excluded from the study.

The heart rate, oxygen saturation, respiratory rate and blood pressure were recorded at intervals of 5 minutes. Patients were watched for complications such as bradycardia, convulsions, restlessness, disorientation or drowsiness.

All the values were expressed as mean \pm standard deviation. Statistical comparison was performed by student's 't' test and Chi-Square test.

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

III. Results

The present study was conducted on 60 consenting patients aged between 18-70 years. Group RC received 30ml of 0.75% Ropivacaine + 1.5 mcg/kg Clonidine. Group BC received 30 ml of 0.5% Bupivacaine + 1.5 mcg/kg Clonidine for brachial plexus block by supraclavicular approach.

Table -1: Age distribution of patients

Age in Years	Group-BC (Bupivacaine+ Clonidine)		Group-RC (Ropivacaine+Clonidine)	
	Number of Patients	Percent	Number of Patients	Percent
18-24	12	40	10	33.33
25-31	6	20	10	33.33
32-38	5	16.67	3	10.00
39-45	2	6.67	2	6.67
46-52	1	3.33	2	6.67
53-59	2	6.67	1	3.33
60-66	2	6.67	2	6.67
Total	30	100.00	30	100.00
Mean \pm SD	31.20 \pm 12.59		32.00 \pm 13.17	
Minimum	18		18	
Maximum	60		65	
$\chi^2=2.348$, p= 0.8850				

Table-1 shows age distribution of the patients in both the groups. The minimum age in both groups was 18 years. The maximum age in both groups was 60 years and 65 years respectively. The mean age in group BC were 31.20 \pm 12.59 and RC were 32.00 \pm 13.17 respectively. There was no significant difference in the age of patients between the Group BC and Group RC. Both groups were similar with respect to age distribution (p>0.05).

Figure 1: Bar graph showing age distribution of patients

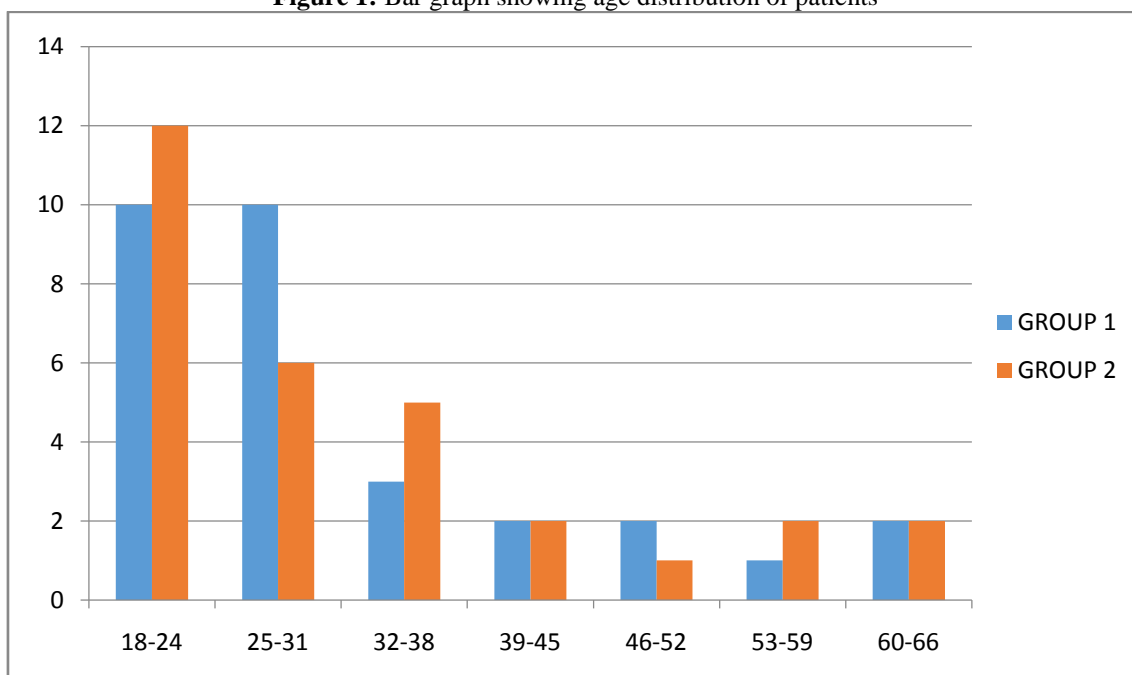


Table -2: Distribution of patients according their sex

Sex	Group BC		Group RC	
	Number of Patients	Percent	Number of Patients	Percent
Male	21	70.00%	22	73.30%
Female	9	30.00%	8	26.70%
Total	30	100.00%	30	100.00%
$\chi^2 = 0.08208, p = 0.7745$				

No significant difference was observed in sex distribution of the cases between two groups ($P > 0.05$).

Figure 2: Showing the sex distribution of patients in each group

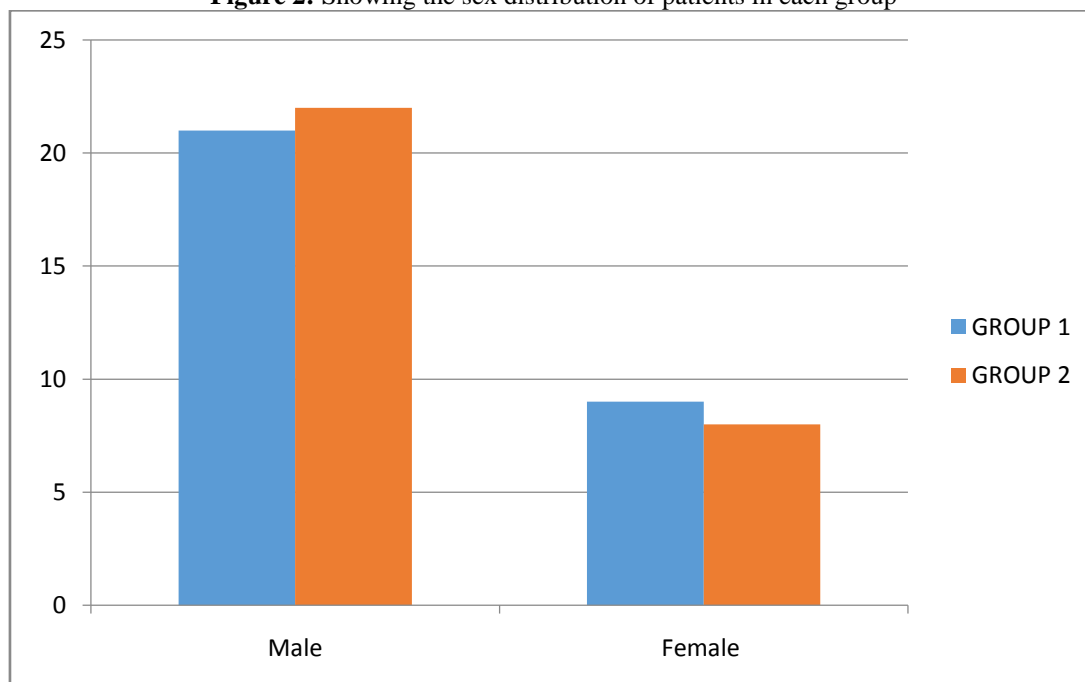


Table 3: Showing the weight distribution in each group

Weight	Group BC		Group RC	
	Number of Patients	Percent	Number of Patients	Percent
40-49	12	40	9	30
50-59	11	36.67	15	50
60-69	7	23.33	6	20
Total	30	100	30	100
Mean± SD	52.93± 6.52		53.73± 5.45	
Minimum	40		42	
Maximum	68		62	
$\chi^2= 1.121, p=0.5710$				

The two groups are compared according to their weight. This was statistically not significant ($p>0.05$)

Figure 3: Bar graph showing patients according their weight

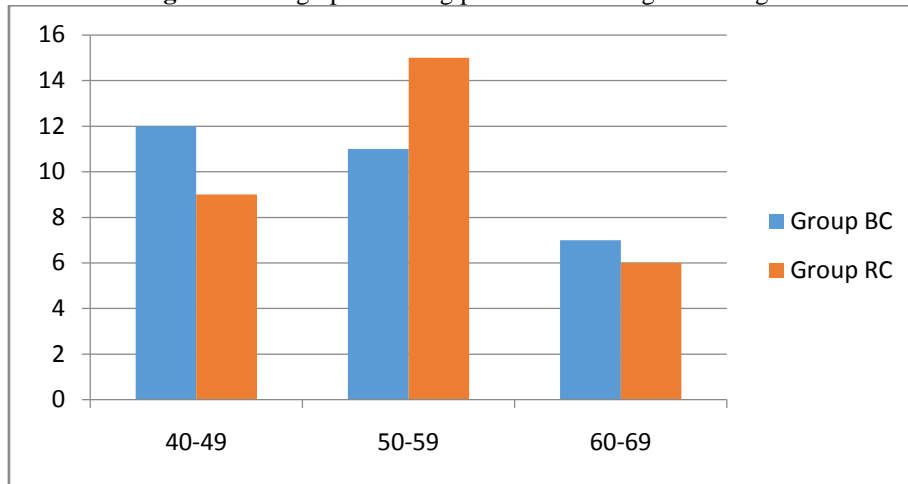


Table 4: Comparison of onset of sensory and motor blockade

Onset of Block (min)	Group BC				Group RC				
	Min	Max	Mean	S.D.	Min	Max	Mean	S.D.	
Motor	8	15	12.57	1.9205	7	13	8.07	1.5447	p= 0.001
Sensory	6	12	10.37	1.5313	5	12	6.93	1.8557	p= 0.001

In group BC the mean onset time of sensory blockade was 10.37 minutes and motor blockade was 12.57 minutes whereas in group RC, the mean onset time of sensory blockade was 6.93 minutes and motor blockade was 8.07 minutes.

Onset of sensory and motor blockade was earlier in case of Group RC (Ropivacaine group) when compared with group BC (Bupivacaine group). The p value was < 0.001 which is statistically significant.

Figure 4: Bar graph showing comparison of mean onset of sensory and motor blockade between the two groups

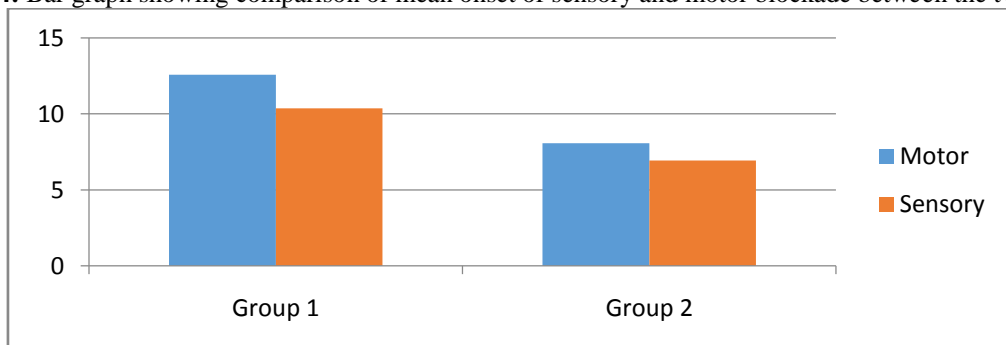


Table 5: Duration of blockade (min)

Duration of Block	Group BC				Group RC				
	Min	Max	Mean	S.D	Min	Max	Mean	S.D	
Motor	370	480	431.33	32.56	340	480	415.33	36.11	p=0.07
Sensory	390	520	480.33	20.13	380	500	469.67	25.15	P=0.07

In group BC the mean duration of sensory blockade was 480.33 minutes and motor blockade was 431.33 minutes when compared to group RC, where sensory blockade duration was 469.67 minutes and duration of motor blockade 415.33 minutes.

The duration of sensory and motor blockade was similar in Group BC when compared to Group RC. There was no statistical difference between the two (p>0.05).

Figure 5: Bar graph showing duration of blockade (min)

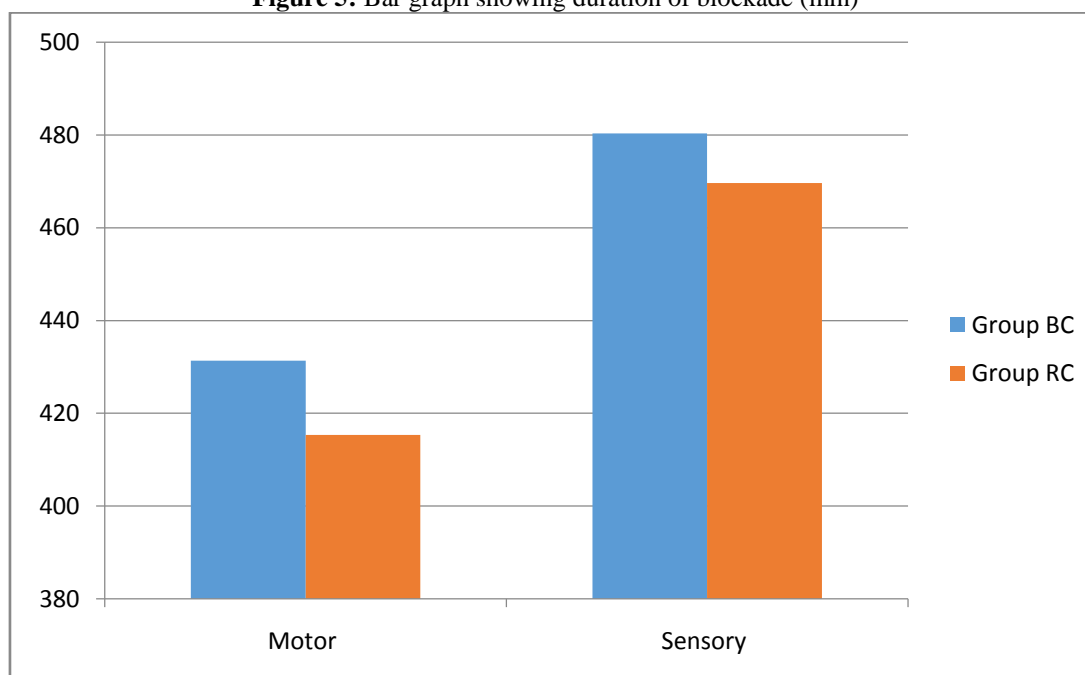


Table 6: Quality of blockade

Class	Group BC	Group RC
1	20	22
2	10	8
Total	30	30

$X^2 = 0.31, P = 0.57$

In Class I 20 patients needed no additional drug like opioids (Inj. Fentanyl 50 mcg IV) when compared with Class II where 22 patients didn't need any adjuvant. Adjuvants were used in 10 patients in group I whereas 8 patients needed adjuvants in Group II.

This is statistically not significant (p > 0.05).

Figure 6

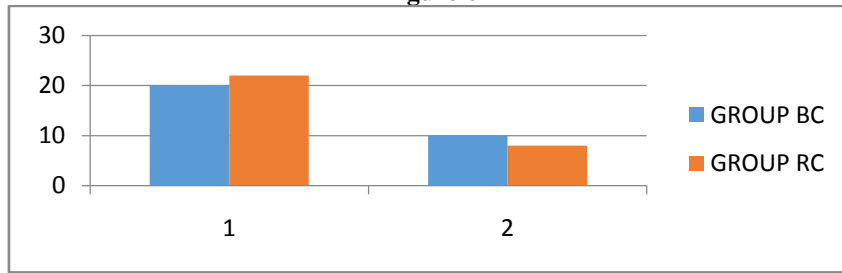


Table 7: Distribution of patients according to the diagnosis

Diagnosis	Group BC	Group RC
Crush injury	7	7
Fracture both bones forearm	8	8
Fracture radius	9	11
Fracture ulna	1	1
Others	5	3
Total	30	30

Figure 7: Bar graph showing distribution of patients according to the diagnosis

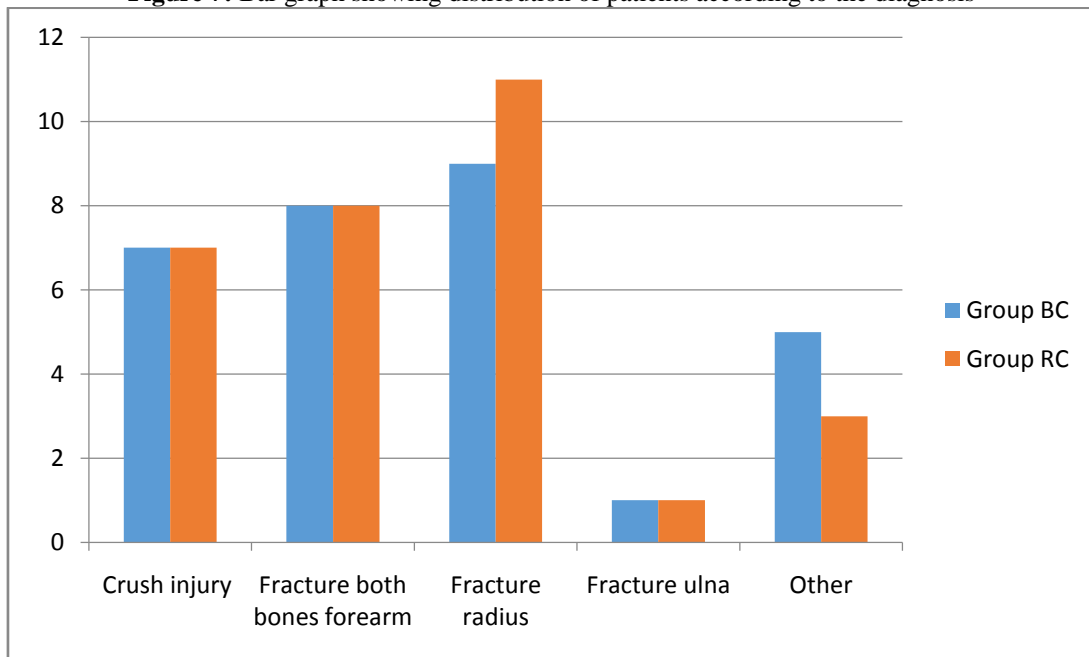
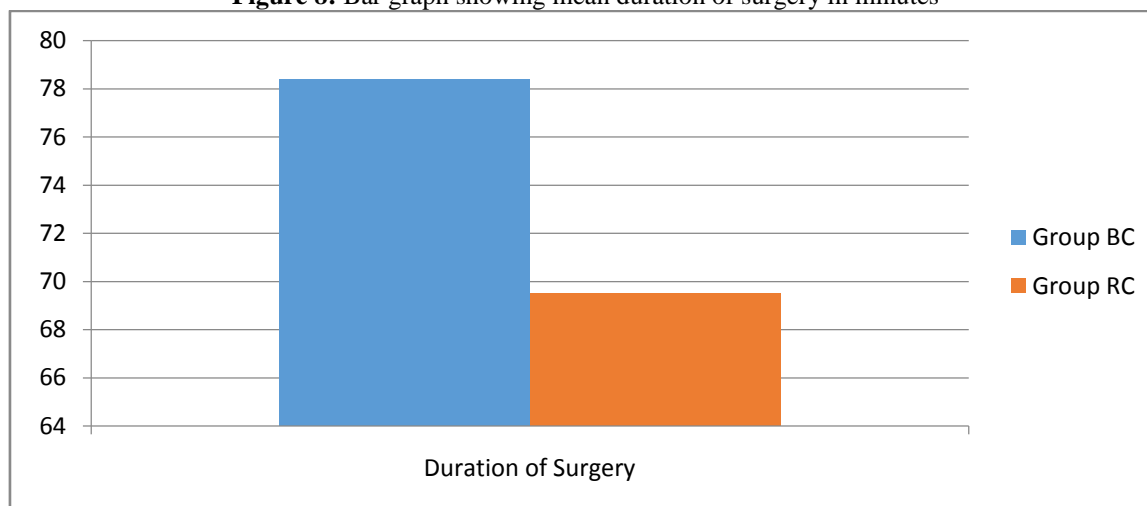


Table 8: Mean duration of surgery in minutes

Duration of Surgery	Group BC				Group RC			
	Min	Max	Mean	S.D.	Min	Max	Mean	S.D.
	50	130	78.41	21.10	50	130	69.5	19.3
	p=0.15							

In group BC, the mean duration of surgery was 78.41 ± 21.10 minutes whereas in group RC the mean duration of surgery was 69.5 ± 19.3 minutes. The mean duration of surgery in group BC was similar compared to group RC. The p value (0.15) was also not statistically significant.

Figure 8: Bar graph showing mean duration of surgery in minutes



IV. Discussion

Regional anaesthetic techniques are used for both operative anesthesia and for postoperative analgesia. They are becoming more popular as a result of advances in drugs, equipment, and improved techniques of anatomical localization, including nerve stimulator and ultrasonic location.

Regional anaesthetic techniques may be used alone or in combination with sedation or general anesthesia depending on individual circumstances. The advantages of regional techniques include:

- Avoidance of the adverse effects of general anesthesia:
- Postoperative analgesia
- Preservation of consciousness during surgery:
- Sympathetic blockade and attenuation of the stress response to surgery
- Improved gastrointestinal motility and reduced nausea and vomiting.
- Simplicity of administration
- Rapid mobilization of patient and early discharge
- More economical for the patient

The net effect of these features lead to a reduction in the incidence of major postoperative respiratory complication.

The upper limb is well suited to regional anaesthetic techniques and these remain among the most useful and commonly practiced peripheral regional techniques. Supraclavicular block offers dense anesthesia of brachial plexus for surgical procedures at or distal to the elbow. This approach provides perhaps the best overall efficacy of complete arm block from a single injection as the trunks/divisions of the brachial plexus are closely related at this point.

The choice of local anaesthetic to be used in a brachial block was Bupivacaine, a long acting amide local anaesthetic. However, concerns about its high lipid solubility and high cardiotoxicity limited its use. With the advent of newer and safer long acting amide local anaesthetics such as Ropivacaine and Levobupivacaine, Bupivacaine has largely been replaced. Ropivacaine has lower lipid solubility and produces less central nervous toxicity and cardiotoxicity than Bupivacaine. It has been shown that Ropivacaine interferes with mitochondrial respiration and ATP synthesis less than both racemic bupivacaine and Levobupivacaine. Ropivacaine is thus gaining popularity over Bupivacaine for peripheral nerve blocks.

There has been a search for an ideal adjuvant to local anaesthetics for regional nerve block that prolongs the analgesia with lesser side effects. Several adjuncts have been described to decrease the time of

onset to the block and to prolong the duration of the block. Drugs such as opioids, dexamethasone, tramadol, clonidine, neostigmine, epinephrine and bicarbonate have been used as adjuncts to brachial plexus blocks.

Evidence regarding the analgesic benefit of opioid adjuncts remains equivocal. There appears to be no advantage for reduced adverse effects by the peripheral administration of opioid analgesics. Nausea, vomiting and pruritis occurred even with the peripheral administration of opioids.

Sufficient data is not available to allow the recommendation of tramadol and neostigmine as adjuncts to local anaesthetics in brachial plexus block¹⁵.

The analgesic properties of Clonidine, an alpha 2 agonist, when administered intrathecally or epidurally as an adjuvant have been well demonstrated. Several authors have found that Clonidine, when added to local anaesthetic in brachial plexus block in doses up to 150 mcg, hastens the onset, prolongs the motor and sensory block and analgesia without an increased incidence of side effects. Hence, Clonidine has been used in the present study as an adjuvant to the brachial plexus blocks administered.

The present study is undertaken to compare the onset, duration of sensory and motor block and the quality of block achieved by Bupivacaine with Clonidine and Ropivacaine with Clonidine. Supraclavicular brachial plexus block was administered in 60 patients selected randomly for elective and emergency surgeries. 0.5% Bupivacaine was administered with 1.5 mcg/kg of Clonidine to 30 patients selected randomly and 0.75% Ropivacaine was administered with 1.5 mcg/kg Clonidine to 30 patients selected randomly.

This study was conducted at District Headquarters Hospital, Nalgonda between December 2013 to June 2015. Both the groups were comparable with regards to mean age, sex, and weight.

V. Conclusion

On the basis of this study we can conclude that:

- Ropivacaine 0.75% with Clonidine 1.5 mcg/kg has faster onset of sensory and motor blockade compared to Bupivacaine 0.5% with Clonidine 1.5 mcg/kg in supraclavicular plexus block
- Ropivacaine 0.75% with Clonidine 1.5 mcg/kg has similar duration of motor and sensory blockade compared to 0.5% Bupivacaine with Clonidine 1.5 mcg/kg in supraclavicular brachial plexus block
- Ropivacaine 0.75% with Clonidine 1.5 mcg/kg has similar quality of block compared to 0.5% Bupivacaine with Clonidine 1.5 mcg/kg in supraclavicular brachial plexus block
- The addition of Clonidine hastens the onset of the block and prolongs the duration of block when added to Bupivacaine and Ropivacaine in a dose up to 150 mcg.

Ropivacaine and Clonidine can be used in supraclavicular brachial plexus block in view of its faster onset of action and similar duration of action compared with Bupivacaine and Clonidine, and similar quality of block. Ropivacaine, being less cardiotoxic is a good alternative to Bupivacaine. Clonidine is a good adjuvant in brachial plexus block as it hastens the onset of block and prolongs the duration of block, reduces patient anxiety and improves patient comfort level intra operatively as well as post operatively.

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