



Comparison of Epidural Ropivacaine and Ropivacaine Clonidine Combination for Elective Caesarean Sections among Two Groups Ropivacaine and Ropivacaine With Clonidine.

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Type of publication: Original Research Paper

Conflicts of Interest: Nil

Abstract

Background and Aim:

The aim is to determine the qualitative and quantitative aspects of epidural block of ropivacaine 0.75 % (20ml) versus ropivacaine 0.75% with clonidine (30mcg) for elective cesarean section.

Settings and Design: A randomized double-blind study was conducted among 60 healthy parturients, scheduled for elective cesarean section, at JNMC, wardha, India.

Materials and Methods: Epidural block was administered with 20 ml of ropivacaine 0.75% (group R) and ropivacaine 0.75% and clonidine 30 µg (group RC) and anesthetic level was achieved minimum until T6-T7 dermatome. Onset time of analgesia, sensory and motor block levels, maternal heart rate and blood pressure, neonatal Apgar scores, postoperative analgesic dose and adverse events were recorded.

Results: 60 patients were enrolled in this study and were subjected to statistical analysis. Groups were comparable with regard to demographic data, neonatal Apgar scores and incidences of side effects except for the higher incidence of dry mouth in patients of RC group. Onset of analgesia was much shorter in RC group along

with prolonged duration of analgesia. The incidence of bradycardia and hypotension was more in RC group as compared to R group which was statistically significant. The dose requirement for postoperative pain relief was significantly lesser in RC group.

Conclusions: The addition of 30 µg clonidine to isobaric epidural ropivacaine results in longer, complete and effective analgesia with similar block properties and helped to reduce the effective dose of ropivacaine when compared with plain ropivacaine for caesarean delivery.

Keywords: Caesarean section, Ropivacaine, Clonidine, Analgesia, Epidural anesthesia.

Introduction

The word 'caesarean' was derived in Middle Ages from Latin word 'caedere' which means 'to cut'.¹ Caesarean Section is one operation where spinal anaesthesia has become increasingly popular over the years. Obstetric anaesthesia requires special knowledge of the physiological changes in pregnancy and effects of anaesthesia and surgery on mother and foetus.² In order to combat the undesirable side effects of spinal anaesthesia, epidural anaesthesia was introduced by Sicaud³ and Cathelin⁴ in 1901 through sacral hiatus route and later on

through lumbar epidural space. With epidural analgesia there is decrease incidence and severity of hypotension, no risk of post dural puncture headache and by inserting an epidural catheter, level and duration of block may be extended to the desirable level as compared to spinal block.

Bupivacaine has been studied extensively in labor analgesia and anaesthesia. In recent years, ropivacaine has been increasingly replacing bupivacaine for the said purpose because of its similar analgesic properties, lesser motor blockade and decreased propensity of cardiotoxicity.⁵ though a slightly larger dose of ropivacaine is required as compared to bupivacaine to achieve the analgesic and anesthetic effects, the addition of adjuvant can decrease the dose of ropivacaine required thereby eliminating quite a few side effects associated with larger doses of ropivacaine.⁶

Clonidine has been used as an adjuvant in regional anaesthesia in various settings.^{7,8} It is an α -2 adrenergic agonist that produces analgesia via a non-opioid mechanism. The combination of epidural clonidine with bupivacaine for labor analgesia has been extensively studied, and it has been shown to improve analgesia when added to epidural ropivacaine but there is hardly any study which has compared the effects of addition of epidural clonidine with those of ropivacaine alone for caesarean section. The coadministration of clonidine and local anesthetic produced better analgesia than either drug alone.^{9,10} There are a few studies which have shown comparison of bupivacaine and ropivacaine but addition of clonidine as an adjuvant helps in sparing of doses of either drug,

which consequently reduces the incidence of side effects associated with larger doses of these anesthetics.^{11,12}

Material and Methods

After the approval of ethics committee, written informed consent of the patients and their relatives were taken. Sixty healthy pregnant females of American Society of Anaesthesiologist (ASA) physical status II, scheduled for elective caesarean section, were enrolled in this randomized double-blind study. All had full term (>36 and <40 gestation weeks) singleton fetus with an estimated fetal weight of >2300 g and were aged >19 years and less than 34 years with body weights in the range 55-90 kg and were of height >150 cm.

Inclusive Criteria

- ASA grade II patient.
- Age group 20 -34 years
- Posted for Elective LSCS
- Gestation week->36 - <40weeks
- Body weight-55-90kgs
- Height->150cm
- Fetal weight->2300g

Exclusive criteria

- ASA grade III & Above patients
- Maternal cardiac disease
- Maternal hematological disease
- Multiple pregnancies
- Psychiatric diseases
- Gestational diabetes
- H/O drug abuse and allergy to local anesthetics
- Infection at local sites
- Spine abnormalities

All the patients were administered premedication in the form of tablet ranitidine 150 mg a night before and in the morning 2 hours before surgery with a sip of water. In the operation theatre, a good IV access was secured and patients were preloaded with 15mL/kg of lactated ringer's

solution. Monitoring gadgets were attached to monitor ECG, heart rate, Non-Invasive Blood Pressure (NIBP) and SpO₂. Baseline hemodynamic parameters, respiratory rate, ECG and SpO₂ were recorded. Women were randomly assigned in a double-blinded fashion to one of the two groups with the help of a computer-generated code whereby numbered envelopes were assigned to each patient. The syringes used in the study were prepared by an anaesthesia technician who was not a part of the operation theatre team. Women were placed in the sitting position, and local anaesthesia of skin and subcutaneous tissues was performed at lumbar level L3-4 with lignocaine HCl 2% 1-2 mL, the epidural space was localized and confirmed with the loss of resistance to saline technique using an 18-gauge Touhy needle. An epidural catheter was then inserted into the epidural space in a cephalic direction tip was kept at T8 level, then aspirated for detection of cerebrospinal fluid or blood. After the catheter was secured to skin surface, subjects were repositioned with left uterine displacement by keeping a wedge beneath the right half of lower back and a pillow was placed below the head and shoulders. Thereafter, 3 mL of 2% lignocaine HCl with 1 in 2 lakh adrenaline solution was administered as a test dose and any untoward effect was observed for. After 5-7 minutes of institution of the test dose, patients in group R received epidural anaesthesia with 20 mL of 0.75% ropivacaine, whereas patient in group RC received 20 mL of 0.75% ropivacaine and clonidine 30 µg. Surgical procedures were initiated only after the anesthetic level was completely established minimum until T6-T7. The sensory level was checked and confirmed with pin-prick method bilaterally at 5, 10, 15, 20, 25 and 30 minutes. Motor block using a modified Bromage scale⁴⁹ (0 = no block, 1 = inability to raise extended leg, 2 = inability to flex knee and 3 = inability to flex ankle and foot) was also

recorded at the same intervals. The following variables were recorded: time to initial onset of analgesia, highest level of sensory analgesia, the time to complete motor block. Maternal hemodynamic parameters, which included heart rate, ECG, NIBP (systolic, diastolic and MAP), respiratory rate and SpO₂, were monitored continuously. Initial bolus dose timing was assumed to be as baseline time. Recordings were made every 5 minutes until 30 minutes and at 15-minute intervals thereafter for the next hour and finally at 30 minutes. Hypotension (defined as systolic arterial pressure falling more than 20% mmHg) was treated with injection mephenteramine 3-6 mg in bolus doses and heart rate <55 beats/minute was treated with 0.3 mg of injection atropine. Intravenous fluids were given as per the body weight and operative loss requirement with no patient requiring blood transfusion. Patients were given supplementary O₂ with the help of venturi mask. During the surgical procedure, adverse events like anxiety, nausea, vomiting, pruritis, shivering, maternal bradycardia or hypotension were recorded. Nausea and vomiting were treated with 4-6 mg of i.v. ondansetron. Maternal vitals were recorded in the recovery room also at 1, 5, 10, 20 and 30 minute interval. The onset of pain was managed by top-up doses of 8 mL of 0.175% ropivacaine in R group, whereas 20 µg clonidine was added to the same volume of ropivacaine in RC group. Neonatal condition was evaluated by Apgar score after delivery. An Apgar score of less than 7 was considered abnormal in this project⁵⁸. The data were analyzed statistically. The variables (maternal hemodynamic parameters and block characteristics) in the two groups were compared using the chi-square test and P value. Student's t-test was used to compare maternal hemodynamic parameters. For all the statistical analysis, the level of significance was P < 0.05. Neonatal Apgar scores were tested by multiple linear regression analysis.

Observation and Results

Table 1: Distribution of patients according to their age (yrs).

Age Group(yrs)	Group R	Group RC	χ^2 -value	p-value
20-25 yrs	19(63.33%)	18(60%)	1.50	0.47,NS
26-30 yrs	8(26.67%)	11(36.67%)		
31-35 yrs	3(10%)	1(3.33%)		
Total	30(100%)	30(100%)		
Mean±SD	26.06±3.92	24.50±3.36		
Range	20-35 yrs	20-35 yrs		

Graph 1: Distribution of patients according to their age (yrs)

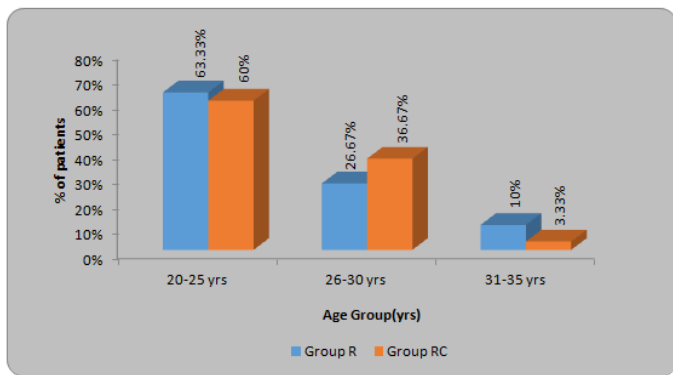


Table 1 and Graph 1 shows age distribution of the patients in both groups. The minimum age in Group R and RC is 20 years. Maximum age in Group R and Group RC are both 35 years. The mean values of age with standard deviations are 26.06±3.92 and 24.50±3.36 for group R and group RC respectively. Both the groups were similar with respect to age distribution and there was no statistical significant difference between the two groups ($p>0.05$, χ^2 – value – 1.50).

Table 2: Distribution of patients according to their weight (kg).

Weight(kg)	Group R	Group RC	χ^2 -value	p-value
55-64 kg	3(10%)	7(23.33%)	6.14	0.10,NS
65-74 kg	17(56.67%)	9(30%)		
75-84 kg	9(30%)	14(46.67%)		
≥85 kg	1(3.33%)	0(0%)		
Total	30(100%)	30(100%)		
Mean±SD	72.44±6.71	72±7.59		
Range	59-85 kg	58-84 kg		

Graph 2: Distribution of patients according to their weight(kg)

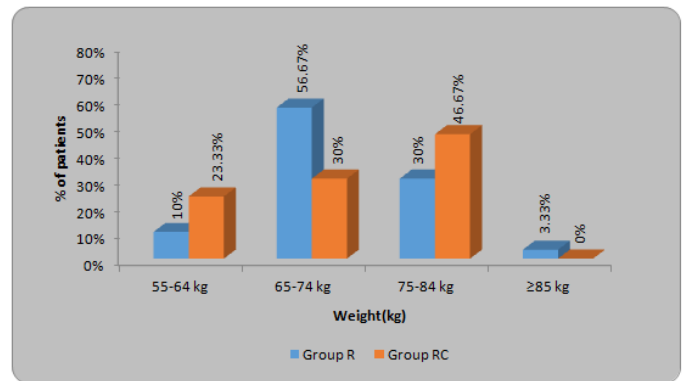


Table 2 and Graph 2 show the weight wise distribution of patients between the two groups.

- In group R and RC, the weight of the patients ranged from 55kg to 87kg with the mean weight being at 72.44±6.71 and 72±7.59 respectively.

With regard to weight, the difference between the two groups was not statistically significant ($p > 0.05$, χ^2 value 6.14)

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

Height(cms)	Group R	Group RC	χ^2 -value	p-value
150-155 cms	15(50%)	14(46.67%)	0.92	0.62,NS
156-160 cms	10(33.33%)	13(43.33%)		
>160 cms	5(16.67%)	3(10%)		
Total	30(100%)	30(100%)		
Mean±SD	154.55±6.71	156.72±7.59		
Range	150-158	152-160		

Graph 3: Distribution of patients according to their height (cms).

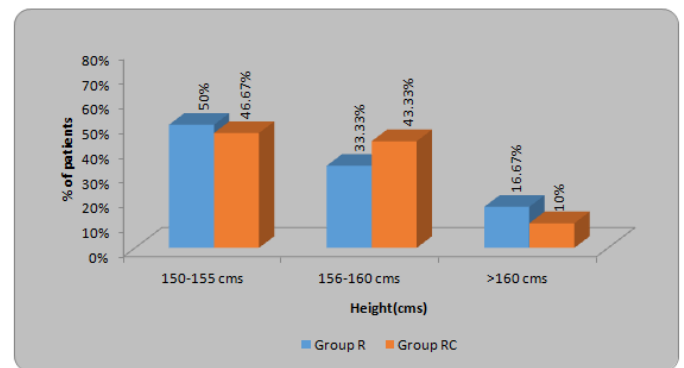


Table 3 and **Graph 3** show the height wise distribution of patients between the two group.

- In group R and RC, the height of the patients ranged from 150cm to 168cm with the mean height being at 154.55±6.71 and 156.72±7.59 respectively.

With regard to height, the difference between the two groups was not statistically significant ($p > 0.05$, χ^2 value 0.92)

Table 4: Comparison of duration of surgery (min) in two groups Student's unpaired t test

	N	Mean	Std. Deviation	Std. Error Mean	t-value	p-value
Group R	30	67.86	8.07	1.47	0.09	0.92,NS
Group RC	30	67.66	8.33	1.52		

Graph 4: Comparison of duration of surgery in two groups.

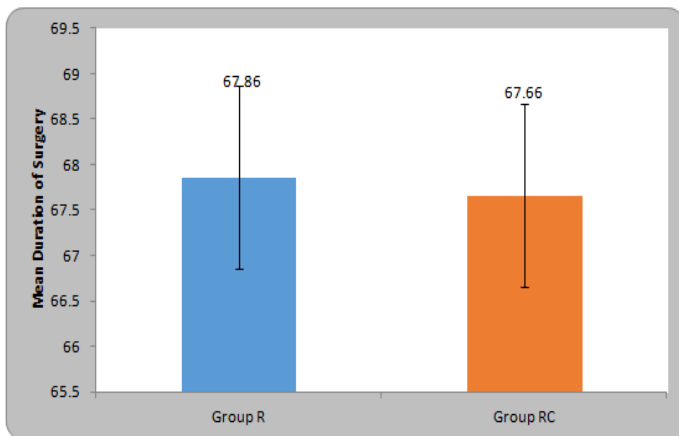


Table 4 and **Graph 4** shows the duration of surgery between the two group.

- In group R and RC, the mean of duration of surgery is 67.86±8.07 min and 67.66 ±8.33min respectively.

With regard to duration of surgery, the difference between the two groups was not statistically significant ($p > 0.05$, t-value 0.09)

Table 5: Comparison of initial block characteristics in two groups Student's unpaired t test.

	Group R		Group RC		t-value	p-value
	Mean	SD	Mean	SD		
Onset time at T10-T11(min)	20.66	1.02	12.63	1.24	27.24	0.0001,S
Time to sensory blockade at T6-T7	20.90	1.12	14.20	0.92	25.20	0.0001,S
Time to complete motor block (minutes)	26.93	0.58	16.73	1.01	47.72	0.0001,S

Graph 5: Comparison of initial block characteristics in two groups.

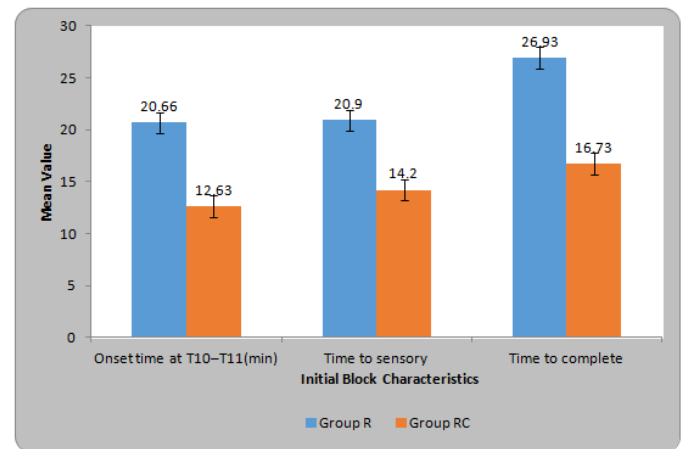


Table 5 **Graph 5** shows Onset of anaesthesia at T10-T11 mean time required for onset in R group was 20.66±1.02 minutes and in RC group 12.63±1.24 minutes and difference was statistically significant ($p < 0.05$), Mean time required to achieve sensory blockade up to level T6-T7 in R group was 20.90±1.12 minutes and 14.20±0.92 minutes in RC group and the difference was statistically significant ($P < 0.05$). Mean time required for complete motor blockade was 26.93 ± 0.58 minutes in R group and 16.73±1.01 minutes in RC group and difference was statistically significant ($P < 0.05$)

Table 6: Comparison of pulse rate in two groups.

	Group R		Group RC		t-value	p-value
	Mean	SD	Mean	SD		
BL	117.6	5.92	116.53	3.98	0.81	0.48,NS
5M	116.6	4.665	116.83	4.58	0.19	0.84,NS
10M	116.2	5.14	115.36	5.67	0.59	0.55,NS
15M	116.96	3.28	105	4.96	11.004	0.0001,S
20M	115.43	3.68	104.2	5.906	8.836	0.0001,S
25M	113.4	2.60	100.2	6.26	10.652	0.0001,S
30M	113.4	4.67	98.56	6.48	10.160	0.0001,S
45M	111.13	4.79	98.73	7.48	7.644	0.0001,S
1H	107.23	5.59	96.4	6.57	6.871	0.0001,S
1H15M	104.73	6.97	92.63	6.55	6.927	0.0001,S
1H30M	104.93	8.78	90.7	6.64	7.078	0.0001,S

Graph 6: Comparison of heart rate in two groups

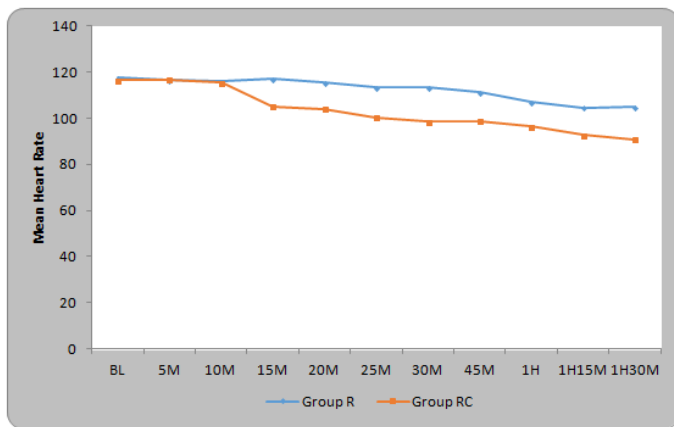


Table 6 Graph 6 shows comparison of heart rate in two groups. Mean baseline pulse rate was 117.6 ± 5.92 in R group and 116.53 ± 3.98 in RC group and difference was not statistically significant. At 5 minutes, mean pulse rate in R group was 116.6 ± 4.668 and in RC group was 116.83 ± 4.58 and difference was not statistically significant. At 10 min, difference in Mean pulse rate in R and RC group was not statistically significant. At 15 minutes, mean pulse in R group was 116.96 ± 3.28 and in RC group 105 ± 4.96 and difference was statistically significant ($P < 0.05$). The decrease in heart rate in RC group after 15 minutes was possibly due to effect of clonidine. There was no incidence of bradycardia in both the groups and no intervention required.

Table 7: Comparison of heart rate in group R with baseline

	Mean	SD	t-value	p-value	% change
BL	117.6	5.92	-	-	
5M	116.6	4.665	2.838	0.008,S	0.85
10M	116.2	5.14	5.037	0.0001,S	1.19
15M	116.96	3.28	0.952	0.349,NS	0.54
20M	115.43	3.68	4.249	0.0001,S	1.85
25M	113.4	2.60	6.332	0.0001,S	3.57
30M	113.4	4.67	10.832	0.0001,S	3.57
45M	111.13	4.79	18.573	0.0001	5.50
1H	107.23	5.59	33.982	0.0001,S	8.82
1H15M	104.73	6.97	32.136	0.0001,S	10.94
1H30M	104.93	8.78	17.920	0.0001,S	10.77

Graph 7: Comparison of heart rate in group R with baseline

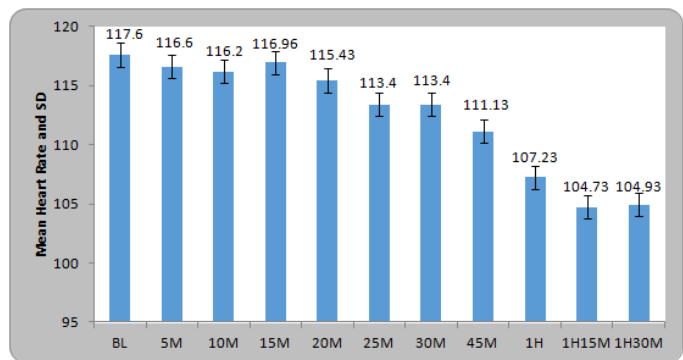


Table 7 Graph 7 shows comparison of heart rate in group R with base line.

Base line heart rate in group R was 117.6 ± 5.92 and at the end of 1 hour and 30 minutes it was 104.93 ± 8.78 . Percentage change in heart rate was 10.77%. So moderate decrease in heart rate was noted in R group.

Table 8: Comparison of heart rate in group RC with baseline

	Mean	SD	t-value	p-value	% change
BL	116.53	3.98	-	-	
5M	116.83	4.58	0.732	0.470,NS	0.26
10M	115.36	5.67	1.002	0.325,NS	1.00
15M	105	4.96	13.070	0.0001,S	9.89
20M	104.2	5.90	12.135	0.0001,S	10.58
25M	100.2	6.26	12.588	0.0001,S	14.01
30M	98.56	6.48	13.387	0.0001,S	1.44
45M	98.73	7.48	12.257	0.0001,S	15.28
1H	96.4	6.57	15.784	0.0001,S	17.27
1H15M	92.63	6.55	18.258	0.0001,S	20.51
1H30M	90.7	6.64	19.699	0.0001,S	22.17

Graph 8: Comparison of heart rate in group RC with baseline.

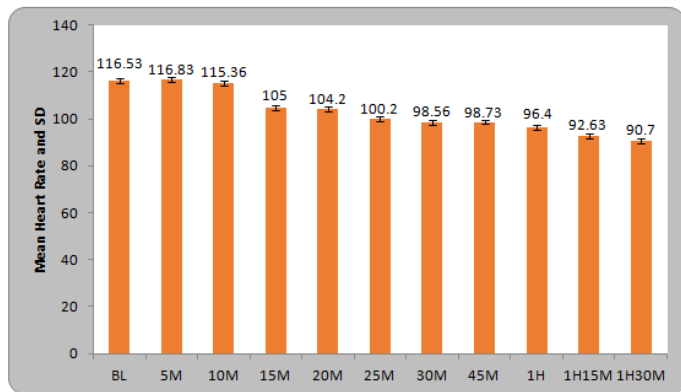


Table 8 Graph 8 shows comparison of heart rate in group RC with base line. Base line heart rate in group RC was 116.53±3.98. Percentage change in heart rate upto 15 minutes was 9.89 .There after there was noticeable decrease in heart rate till 1hour 30 minutes. Percentage decrease in heart rate at the end of 1hour 30 minutes was 22.51% in RC group as compared to R group(10.77%), which might be due to effect of clonidine in RC group.

Table 9: Comparison of SBP in two groups.

	Group R		Group RC		t-value	p-value
	Mean	SD	Mean	SD		
BL	136.73	4.34	138.7	6.06	1.443	0.154,NS
5M	134.8	4.34	135.73	4.38	0.82	0.411,NS
10M	134.03	1.49	130.86	5.13	3.241	0.002,S
15M	134.13	2.67	129.86	7.81	2.830	0.006,S
20M	133	6.23	125.63	8.50	3.827	0.0001,S
25M	128.53	4.77	121.5	8.71	3.876	0.0001,S
30M	126.63	4.57	119.96	5.99	4.841	0.0001,S
45M	122.66	7.91	119.6	7.18	1.571	0.122,NS
1H	125.36	6.53	114.76	6.07	6.508	0.0001,S
1H15M	123.13	7.49	115.33	7.32	4.077	0.0001,S
1H30M	123.2	8.25	110.63	8.04	5.969	0.0001,S

Graph 9: Comparison of SBP in two groups

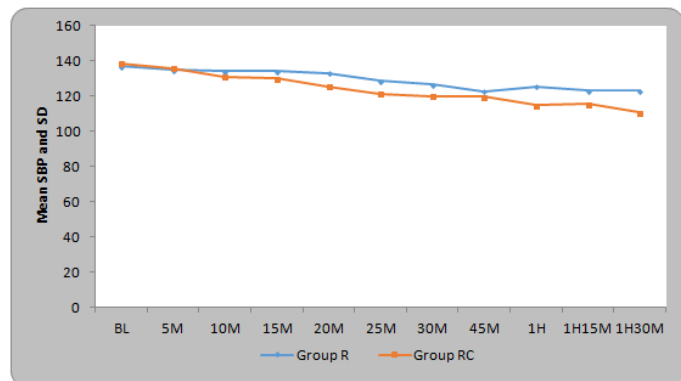


Table 9 graph 9 shows comparison of SBP in two groups

Mean base line SBP was 136.73±4.34 in R group and 138.7±6.06 in RC group and the difference was not statistically significant. Even at 5 minutes, difference in Mean base line SBP in R group and RC group was not statistically significant. At 10 minutes Mean base line SBP was 134.03±1.49 in R group and 130.86±5.13 in RC group and the difference was statistically significant (P<0.05). There after difference in Mean SBP in R group and RC group was statistically significant (P<0.05). The difference might be due to hypotensive action of clonidine in RC group.

Table 10: Comparison of SBP in group R with baseline.

	Mean	SD	t-value	p-value	% change
BL	136.73	4.34	-	-	-
5M	134.8	4.34	41.738	0.0001,S	1.41
10M	134.03	1.49	4.707	0.0001,S	1.97
15M	134.13	2.67	7.208	0.0001,S	1.90
20M	133	6.23	6.606	0.0001,S	2.73
25M	128.53	4.77	19.566	0.0001,S	6.00
30M	126.63	4.57	31.281	0.0001,S	7.39
45M	122.66	7.91	19.873	0.0001,S	10.29
1H	125.36	6.53	26.263	0.0001,S	8.32
1H15M	123.13	7.49	22.109	0.0001,S	9.95
1H30M	123.2	8.25	18.582	0.0001,S	9.90

Graph 10: Comparison of SBP in group R with baseline

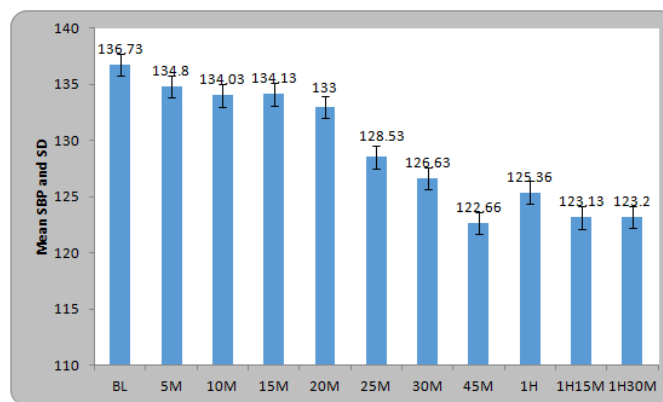


Table 10 Graph 10 shows comparison of SBP in group R with Base line

Base line SBP in group R was 136.73± 4.34 and at the end of 1 hour and 30 minutes it was 123.2±8.25. Percentage change in SBP was 9.9%. So moderate decrease in SBP

was noted in R group which was statistically significant.

(P<0.05)

Table 11: Comparison of SBP in group RC with baseline.

	Mean	SD	t-value	p-value	% change
BL	138.7	6.06	-	-	
5M	135.73	4.38	3.74	0.0001,S	2.14
10M	130.86	5.13	11.521	0.0001,S	5.65
15M	129.86	7.81	7.792	0.0001,S	6.37
20M	125.63	8.50	14.548	0.0001,S	9.42
25M	121.5	8.71	20.595	0.0001,S	12.40
30M	119.96	5.99	34.277	0.0001,S	13.51
45M	119.6	7.18	20.813	0.0001,S	13.77
1H	114.76	6.07	42.198	0.0001,S	17.26
1H15M	115.33	7.32	22.303	0.0001,S	16.85
1H30M	110.63	8.04	26.419	0.0001,S	20.24

Graph 11: Comparison of SBP in group RC with baseline

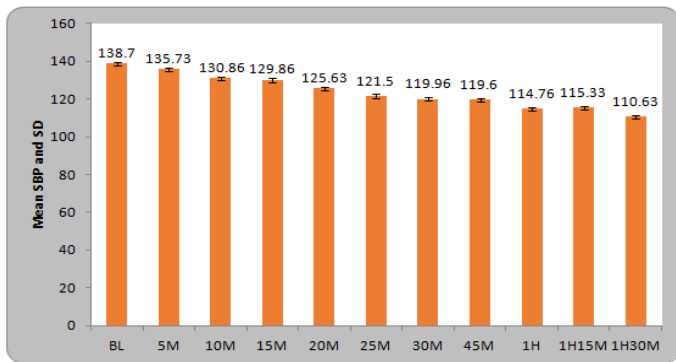


Table 11 Graph 11 shows Comparison of SBP in group RC with base line. Base line SBP in group RC was 138.7± 6.06 and at the end of 1 hour and 30 minutes it was 110.63±8.04. Percentage change in SBP was 20.24%. So significant decrease in SBP was noted in RC group as compared to R group (9.9%), which might be due to hypotensive action of clonidine.

Table 12: Comparison of DBP in two groups.

	Group R		Group RC		t-value	p-value
	Mean	SD	Mean	SD		
BL	90.66	1.42	91.93	3.94	1.65	0.104,NS
5M	87.73	2.61	88.03	1.06	0.58	0.56,NS
10M	87.66	1.58	84	4.29	4.39	0.0001,S
15M	85.96	2.41	82.43	3.947	4.18	0.0001,S
20M	82.56	1.33	80.73	3.273	2.83	0.006,S
25M	80.86	2.01	78.06	2.85	4.39	0.0001,S
30M	81.53	1.001	75.16	2.67	12.18	0.0001,S
45M	79.73	6.09	74.83	4.21	3.62	0.001,S
1H	79.03	2.61	72.9	3.42	7.78	0.0001,S
1H15M	79.16	1.44	73.23	5.131	6.09	0.0001,S
1H30M	78.56	2.86	70.93	6.73	5.71	0.0001,S

Graph 12: Comparison of DBP in two groups

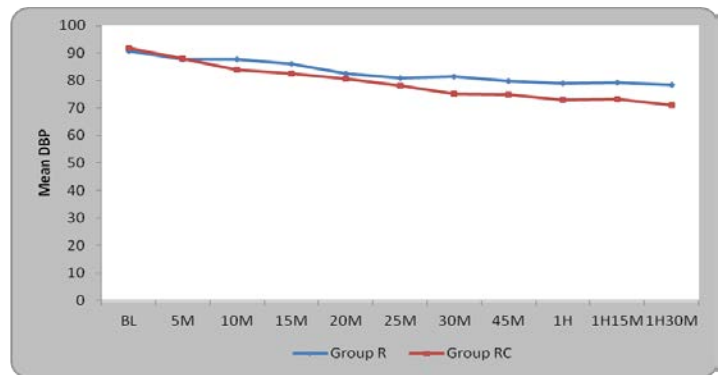


Table 12 Graph 12 shows Comparison of DBP in two groups. Mean base line DBP was 90.66±1.42 in R group and 91.93±3.94 in RC group and the difference was not statistically significant. Even at 5 minutes, difference in Mean base line DBP in R group and RC group was not statistically significant. At 10 minutes Mean base line DBP was 87.66± 1.58 in R group and 84±4.29 in RC group and the difference was statistically significant (P<0.05). There after difference in Mean DBP in R group and RC group was statistically significant (P<0.05). The difference might be due to hypotension action of clonidine in RC group.

Table 13: Comparison of DBP in group R with baseline.

	Mean	SD	t-value	p-value	% change
BL	90.66	1.42	-	-	
5M	87.73	2.61	5.972	0.0001,S	3.23
10M	87.66	1.58	10.286	0.0001,S	3.31
15M	85.96	2.41	11.089	0.0001,S	5.18
20M	82.56	1.33	24.048	0.0001,S	8.93
25M	80.86	2.01	21.380	0.0001,S	10.81
30M	81.53	1.001	27.865	0.0001,S	10.07
45M	79.73	6.09	9.129	0.0001,S	12.06
1H	79.03	2.61	19.458	0.0001,S	12.83
1H15M	79.16	1.44	26.528	0.0001,S	12.68
1H30M	78.56	2.86	18.438	0.0001,S	13.35

Graph 13: Comparison of DBP in group R with baseline

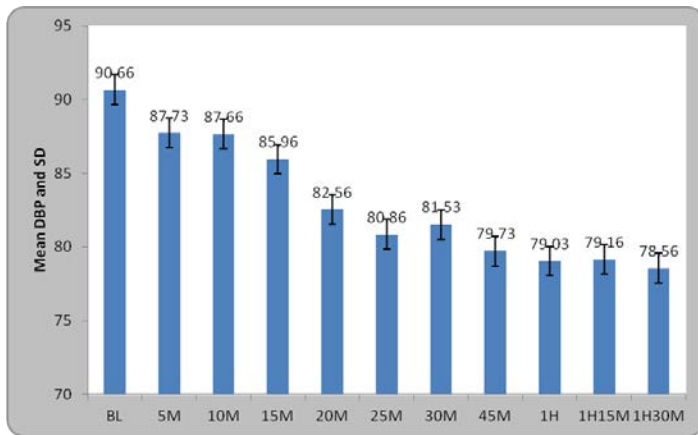


Table 13 Graph 13 shows comparison of DBP in group R with Base line. Base line DBP in group R was 90.66 ± 1.42 and at the end of 1 hour and 30 minutes it was 78.56 ± 2.86 . Percentage change in DBP was 13.35%. So moderate decrease in DBP was noted in R group which was statistically significant. ($P < 0.05$)

Table 14: Comparison of DBP in group RC with baseline.

	Mean	SD	t-value	p-value	% change
BL	91.93	3.94	-	-	-
5M	88.03	1.06	5.20	0.0001,S	4.24
10M	84	4.29	22.325	0.0001,S	8.63
15M	82.43	3.947	16.526	0.0001,S	10.33
20M	80.73	3.273	13.591	0.0001,S	12.18
25M	78.06	2.85	23.714	0.0001,S	15.09
30M	75.16	2.67	29.072	0.0001,S	18.24
45M	74.83	4.21	35.781	0.0001,S	18.60
1H	72.9	3.42	21.609	0.0001,S	20.70
1H15M	73.23	5.131	17.217	0.0001,S	20.34
1H30M	70.93	6.73	13.694	0.0001,S	22.84

Graph 14: Comparison of DBP in group RC with baseline

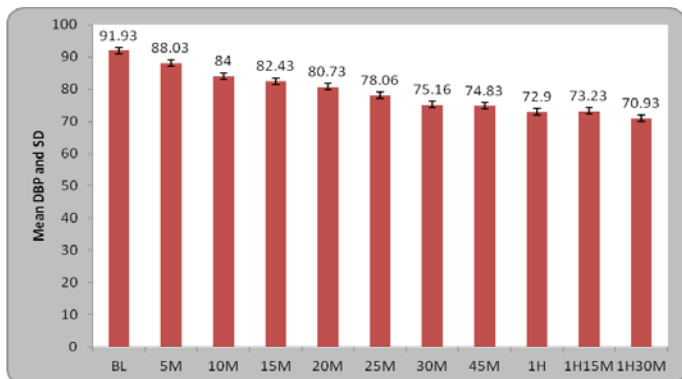


Table 14 Graph 14 shows Comparison of DBP in group RC with base line. Base line DBP in group RC was $91.93 \pm$

3.94 and at the end of 1 hour and 30 minutes it was 70.93 ± 6.73 . Percentage change in DBP was 22.84%.

So significant decrease in DBP was noted in RC group as compared to R group (13.35%), which might be due to hypotensive action of clonidine.

Table 15: Comparison of MAP in two groups.

	Group R		Group RC		t-value	p-value
	Mean	SD	Mean	SD		
BL	106.13	1.67	107.53	3.95	1.785	0.079,NS
5M	103.23	0.85	103.96	1.54	2.27	0.027,S
10M	103.1	0.80	99.70	3.41	5.308	0.0001,S
15M	101.93	1.14	98.1	3.45	5.766	0.0001,S
20M	99.5	2.22	95.6	4.87	3.986	0.0001,S
25M	96.53	1.77	92.46	4.36	4.723	0.0001,S
30M	96.46	2.17	90.06	3.51	8.482	0.0001,S
45M	94.13	6.95	89.8	4.25	2.911	0.005,S
1H	94.56	4.04	86.8	4.13	7.355	0.0001,S
1H15M	93.63	2.94	87.16	5.89	5.380	0.0001,S
1H30M	93.26	4.47	84.1	6.964	6.063	0.0001,S

Graph 15: Comparison of MAP in two groups

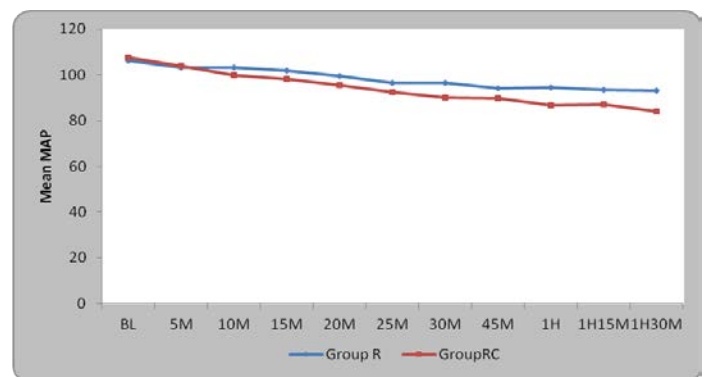


Table 15 Graph 15 shows Comparison of MAP in two groups. Mean base line MAP was 106.13 ± 1.67 in R group and 107.53 ± 3.95 in RC group and the difference was not statistically significant. Even at 5 minutes, difference in Mean base line MAP in R group and RC group was not statistically significant. At 10 minutes Mean base line MAP was 103.1 ± 0.8 in R group and 99.7 ± 3.41 in RC group and the difference was statistically significant ($P < 0.05$). There after difference in Mean MAP in R group and RC group was statistically significant ($P < 0.05$). The difference might be due to hypotension action of clonidine in RC group.

Table 16: Comparison of MAP in group R with baseline.

	Mean	SD	t-value	p-value	% change
BL	106.13	1.67	-	-	
5M	103.23	0.85	7.660	0.0001,S	2.73
10M	103.1	0.80	8.344	0.0001,S	2.85
15M	101.93	1.14	9.370	0.0001,S	3.96
20M	99.5	2.22	21.480	0.0001,S	6.25
25M	96.53	1.77	27.097	0.0001,S	9.05
30M	96.46	2.17	33.918	0.0001,S	9.11
45M	94.13	6.95	11.249	0.0001,S	11.31
1H	94.56	4.04	20.267	0.0001,S	10.90
1H15M	93.63	2.94	28.154	0.0001,S	11.78
1H30M	93.26	4.47	19.691	0.0001,S	12.13

Graph 16: Comparison of MAP in group R with baseline

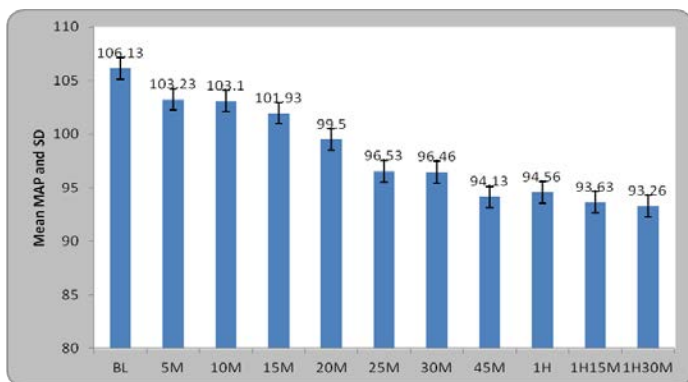


Table 16 Graph 16 shows comparison of MAP in group R with Base line

Base line MAP in group R was 106.13± 1.67 and at the end of 1 hour and 30 minutes it was 93.26± 4.47.

Percentage change in MAP was 12.13%.

So moderate decrease in MAP was noted in R group which was statistically significant. (P<0.05)

Table 17: Comparison of MAP in group RC with baseline.

	Mean	SD	t-value	p-value	% change
BL	107.53	3.95	-	-	
5M	103.96	1.54	5.23	0.0001,S	3.32
10M	99.70	3.41	24.89	0.0001,S	7.28
15M	98.1	3.45	15.149	0.0001,S	8.77
20M	95.6	4.87	14.797	0.0001,S	11.09
25M	92.46	4.36	23.896	0.0001,S	14.01
30M	90.06	3.51	34.619	0.0001,S	16.25
45M	89.8	4.25	33.773	0.0001,S	16.49
1H	86.8	4.13	29.027	0.0001,S	19.28
1H15M	87.16	5.89	19.710	0.0001,S	18.94
1H30M	84.1	6.96	19.131	0.0001,S	21.79

Graph 17: Comparison of MAP in group RC with baseline

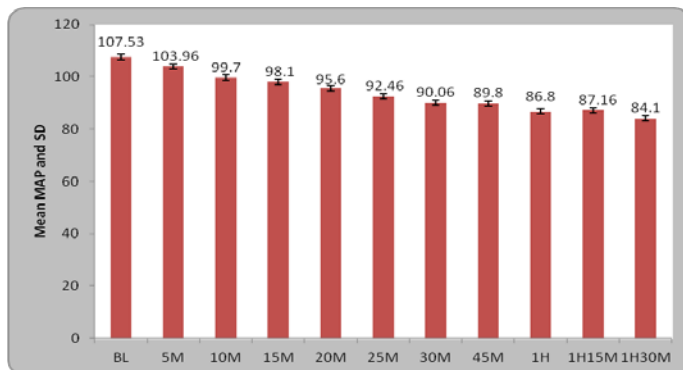


Table 17 Graph 17 shows Comparison of MAP in group RC with base line Base line MAP in group RC was 107.53± 3.95 and at the end of 1 hour and 30 minutes it was 84.1±6.96. Percentage change in MAP was 21.79%. So significant decrease in MAP was noted in RC group as compared to R group (12.13%), which might be due to hypotensive action of clonidine.

Table 18: Comparison of RR in two groups

	Group R		Group RC		t-value	p-value
	Mean	SD	Mean	SD		
BL	23.90	0.40	24.33	1.83	1.270	0.209,NS
5M	22.13	0.43	22.23	1.01	0.500	0.619,NS
10M	22.73	0.78	22.77	1.14	0.132	0.895,NS
15M	20.60	1.04	20.77	1.74	0.451	0.653,NS
20M	21.16	0.91	21.70	1.57	1.66	0.11,NS
25M	21.73	0.98	21.53	1.57	0.592	0.556,NS
30M	20.13	0.90	20.77	1.48	2.005	0.050,NS
45M	21.60	1.04	21.47	1.07	0.489	0.627,NS
1H	20.03	0.72	20.20	1.00	0.743	0.460,NS
1H15M	19.23	1.25	19.53	1.01	1.023	0.311,NS
1H30M	20.30	0.92	20.50	1.38	0.660	0.512,NS

Graph 18: Comparison of RR in two groups

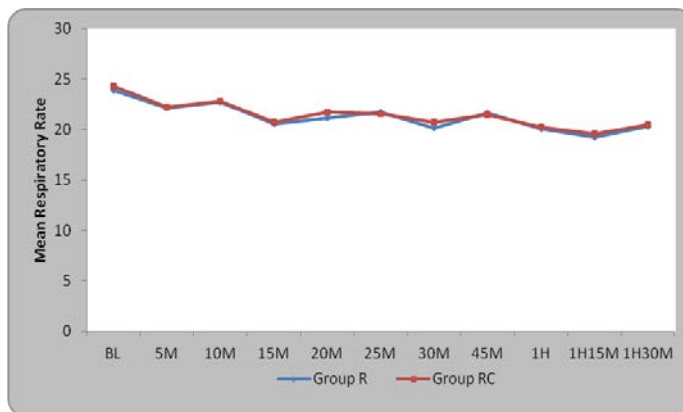


Table 18 Graph 18 shows Comparison of RR in two groups. Mean base line RR was 23.9 ± 0.4 in R group and 24.33 ± 1.83 in RC group and the difference was not statistically significant. Thereafter, too, difference in Mean RR in R group and RC group was not statistically significant ($P < 0.05$). There was no noticeable change in RR in both the groups.

Table 19: Comparison of RR in group R with baseline

	Mean	SD	t-value	p-value	% change
BL	23.90	0.40	-	-	
5M	22.13	0.43	22.494	0.0001,S	7.41
10M	22.73	0.78	12.042	0.0001,S	4.90
15M	20.60	1.04	5.943	0.0001,S	9.62
20M	21.16	0.91	19.074	0.0001,S	11.46
25M	21.73	0.98	16.979	0.0001,S	9.08
30M	20.13	0.90	32.953	0.0001,S	15.77
45M	21.60	1.04	14.366	0.0001,S	9.62
1H	20.03	0.72	48.779	0.0001,S	16.19
1H15M	19.23	1.25	24.856	0.0001,S	19.54
1H30M	20.30	0.92	23.062	0.0001,S	15.06

Graph 19: Comparison of RR in group R with baseline

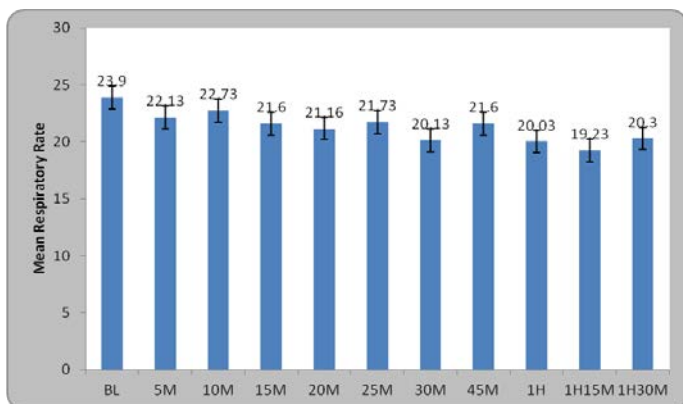


Table 19 Graph 19 shows comparison of RR in group R with Base line. Base line RR in group R was 23.90 ± 0.40 and at the end of 1 hour and 30 minutes it was 20.30 ± 0.92 . Percentage change in RR was 15.06%.

Table 20: Comparison of RR in group RC with baseline.

	Mean	SD	t-value	p-value	% change
BL	24.33	1.83	-	-	
5M	22.23	1.01	7.822	0.0001,S	8.63,S
10M	22.77	1.14	4.590	0.0001,S	6.41,S
15M	20.77	1.74	13.429	0.0001,S	14.63,S
20M	21.70	1.57	4.521	0.0001,S	10.81,S
25M	21.53	1.57	7.167	0.0001,S	11.51,S
30M	20.77	1.48	10.887	0.0001,S	79.23,S
45M	21.47	1.07	8.746	0.0001,S	11.76,S
1H	20.20	1.00	10.884	0.0001,S	16.97,S
1H15M	19.53	1.01	13.214	0.0001,S	19.73,S
1H30M	20.50	1.38	10.973	0.0001,S	15.74,S

Graph 20: Comparison of RR in group RC with baseline.

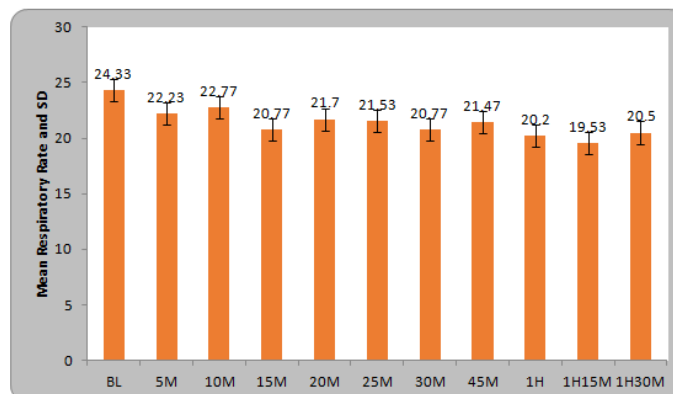


Table 20 Graph 20 shows comparison of RR in group RC with Base line. Base line RR in group RC was 24.33 ± 1.83 and at the end of 1 hour and 30 minutes it was 20.50 ± 1.38 . Percentage change in RR was 15.74%.

Table 21: Comparison of mean Apgar Score in two groups Student's unpaired t test.

	N	Mean	Std. Deviation	Std. Error Mean	t-value	p-value
Group R	30	8.30	0.46	0.08	1.58	0.11,NS
Group RC	30	8.50	0.50	0.09		

Graph 21: Comparison of mean Apgar Score in two groups.

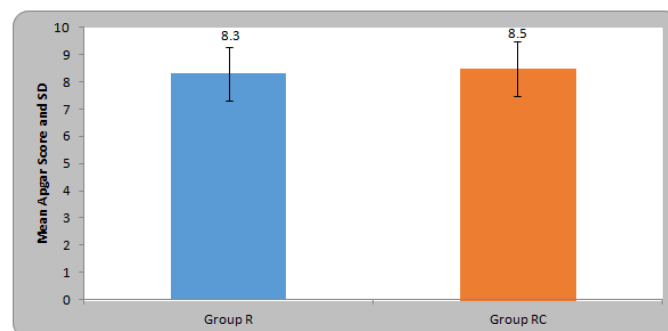


Table 21 Graph 21 shows comparison of mean Apgar score in two groups. The mean in R group was 8.30 ± 0.46 and RC was 8.50 ± 0.50 . The difference between the two groups was not statistically significant ($p > 0.05$, t -value 1.58)

Table 22: Comparison of duration of anaesthesia in two groups. Student's unpaired t test.

	N	Mean	Std. Deviation	Std. Error Mean	t-value	p-value
Group R	30	128.43	4.07	0.74	20.57	0.0001,S
Group RC	30	160	7.34	1.34		

Graph 22: Comparison of duration of anaesthesia in two groups

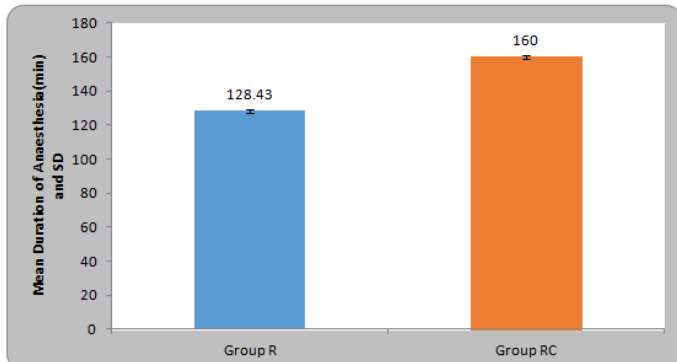


Table 22 Graph 22 shows comparison of duration of anaesthesia in two groups. The mean in R group was 128.43 ± 4.07 and RC was 160 ± 7.34 . The duration of anaesthesia was more in RC group as compared to R group, therefore difference between the two groups was statistically significant ($p < 0.05$, t -value 20.57).

Table 23: Comparison of Postoperative complication in two groups.

	Group R	Group RC	χ^2 -value	p-value
Nausea/Vomiting	6(20%)	9(30%)	0.80	0.37,NS
Sedation	0(0%)	0(0%)	0.00	1.00,NS
Shivering	9(30%)	3(10%)	3.75	0.05,NS
Dry Mouth	0(0%)	7(23.33%)	7.92	0.005,S

Graph 23: Comparison of postoperative complication in two groups

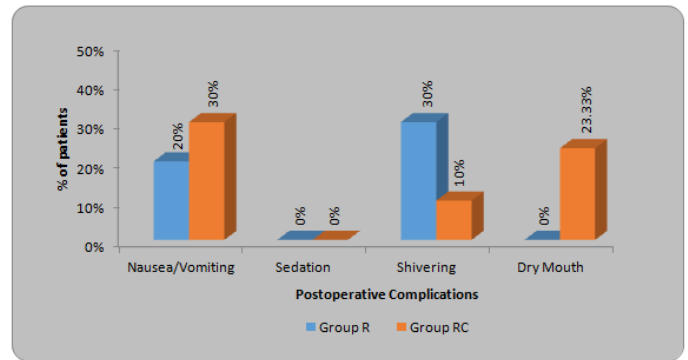


Table 23 Graph 23 shows comparison of postoperative complication in two groups. In R group the Nausea/vomiting was 20% and in RC group was 30%, therefore the difference between two groups were not statistically significant ($p > 0.37$). In R group the sedation was 0% and in RC group was 0%, therefore the difference between two groups were not statistically significant ($p > 0.05$). In R group the shivering observed was 30% and in RC group it was 10%, therefore the difference between two groups were not statistically significant ($p > 0.05$). In R group the incidence of dry mouth was 0% and in RC group 23.33% were observed, therefore the difference between two groups was statistically significant ($P < 0.05$)

Statistical analysis was done by using descriptive and inferential statistics using chisquare test, students paired and unpaired t test and software used in the analysis were SPSS20.0 version and GraphPad Prism 6.0 version and $p < 0.05$ is considered as level of significance.

Discussion

There are numerous studies on the use of epidural ropivacaine for inducing painless labor and deliveries.⁷⁰ The addition of various adjuvants to epidural ropivacaine for achievement of labor analgesia with subsequently lesser dose requirement of the ropivacaine has been studied to some extent.⁴ Although intrathecal clonidine as an adjuvant to ropivacaine has been studied

extensively, till date there has been hardly any study which has detailed data on the epidural use of ropivacaine and clonidine for caesarean section. Though ropivacaine is slightly less potent as compared to bupivacaine, its pharmacological profile is almost comparable to the latter. Various studies and literary evidence have concluded that cardiotoxicity of ropivacaine is far less than that of bupivacaine.⁵⁸ Clonidine is a selective partial agonist for alpha-2-adrenoreceptors. It is known to increase both sensory and motor block of local anaesthetics¹⁹. The analgesic effect following its intrathecal administration is mediated spinally through activation of post synaptic alpha-2- receptors in substantia gelatinosa of spinal cord. The rationale behind intrathecal administration of clonidine is to achieve a high drug concentration in the vicinity of alpha-2-adrenoreceptors in the spinal cord and it works by blocking the conduction of C and A delta fibres, increases potassium conductance in isolated neurons in vitro and intensifies conduction block of local anaesthetics. Dobrydnjov et al⁶⁶ their study in orthopaedic patients, on postoperative pain relief following intrathecal bupivacaine combined with intrathecal or oral clonidine (150 mg), found that addition of intrathecal clonidine prolonged analgesia and decreased morphine consumption postoperatively more than oral clonidine. Hypotension was less pronounced after intrathecal than oral clonidine.

The present study was undertaken to compare the epidural ropivacaine with a combination of ropivacaine and clonidine for elective caesarean sections with major emphasis on onset, intensity and duration of block, maternal cardiorespiratory parameters, postoperative analgesia and Apgar score. In this study only epidural route was chosen and not combined spinal epidural because there have been no studies comparing

these drugs through epidural route solely.

Secondly, epidural route provides a better control on maternal hemodynamic parameters as compared to intrathecal drugs⁴⁹. Thirdly, the study also provide the patients a postoperative pain-free stay in hospital and to avoid systemic analgesics⁵⁶. Finally, it was an indirect effort to educate these patients about the beneficial effects of regional epidural anaesthesia thereby removing their false notions associated with the pain and other misinterpretations of regional anaesthesia, which are so much prevalent in our society.

Total 60 patients undergoing elective caesarean section were selected and randomly allocated to two groups of 30 each who received 20ml plain isobaric Ropivacaine and Ropivacaine(0.75%) 20ml + 30µg clonidine.

The intention behind selecting 30µg of Clonidine as a fixed dose for epidural use was that lower doses such as 15 µg and 20 µg of Clonidine did not significantly enhance the quality and intensity of sensory and motor block and did not prolong post-operative analgesia, whereas, higher dose of 75 µg of epidural Clonidine prolonged sensory and motor block and gave a high quality anaesthesia, but was associated with systemic side effects like sedation and hypotension.

Therefore, 30 µg of intrathecal Clonidine was chosen as a fixed dose with effective prolongation of post-operative analgesia and minimal side effects⁴⁸.

All the demographic data like weight, height, age were comparable in patients amongst both the groups and the difference was non-significant (p-value>0.05, NS)

Duration of surgery: the mean duration of surgery among the two groups was 67.86±8.07 min in group R and 67.66±8.33 min in group RC. There was no statistically significant difference in both the groups in relation to the duration of surgery.

Comparison of Block Characteristics:

1. **Onset time at T10-T11(min):** Onset of anaesthesia at T10-T11 mean time required for onset in R group was 20.66 minutes and in RC group 12.63 minutes and difference was statistically significant ($p < 0.05$). When compared with the study done by Christelis et al in 2005 have studied, a comparison of epidural ropivacaine 0.75% and bupivacaine 0.5% with fentanyl for elective caesarean section, they found that mean time to achieve sensory blockade to T4 for ropivacaine was 15.8 min, while bupivacaine/fentanyl was 18.7 min, $P = 0.13$) or to S1 (ropivacaine 18.3 [4.6] min, bupivacaine/fentanyl 17. However, ropivacaine produced a motor block that was denser, and of longer duration which was also proved in our study.

1. **Time to sensory blockade at T6-T7 (min):** Mean time required to achieve sensory blockade upto level T6-T7 in R group was 27.66 minutes and 14.20 minutes in RC group and the difference was statistically significant ($P < 0.05$) This observed data was compared with the study done by Bajwa SJ et al⁴⁶ in 2010 where the mean time taken to achieve the sensory blockade at T6-T7 was 15.12 ± 4.36 min in group Ropivacaine and 12.26 ± 3.18 min in group Ropivacaine Clonidine. Thus time required to achieve sensory blockade at T6-T7 was shorter in Clonidine group, which is comparable to our study.

2. **Time to complete motor block(min):** Mean time required for complete motor blockade was 26.93 ± 0.58 minutes in R group and 16.73 ± 1.01 minutes in RC group and difference was statistically significant ($P < 0.05$) RC.

This observed data was compared with the study done by Bajwa SJ et al⁵⁰ in 2010 where the mean time taken to achieve the motor blockade 21.70 ± 4.20 min in group

Ropivacaine and 17.34 ± 4.48 min in group Ropivacaine Clonidine. Thus time required to achieve motor blockade was shorter in Clonidine group.

Haemodynamic Parameters:

1. **Pulse Rate:** In our study mean baseline pulse rate was 117.6 ± 5.92 in R group and 116 ± 4.2 in Rc group and difference was not statistically significant.

At 5 minutes, Mean pulse rate in R group was 116.6 ± 4.665 and in Rc group was 117 ± 0.5 and difference was not statistically significant.

At 10 min, difference in Mean pulse rate in R and RC group was not statistically significant.

At 15 minutes, Mean pulse in R group was 116.96 ± 3.28 and in RC group 105 ± 4.96 and difference was statistically significant.

After 15 minutes difference between mean pulse rate in R and RC group was statistically significant ($P < 0.05$). The decrease in heart rate in RC group after 15 minutes was possibly due to effect of clonidine.

There was no incidence of bradycardia in both the groups and no intervention required.

In the study done by Gonul Sagiroglu et al⁴⁸ 6/24 patients had bradycardia receiving 30 mcg clonidine compared to 15 mcg and plain ropivacaine group in which none of the patients had bradycardia.

De Kock et al⁴² also observed that the need for atropine was more in group with 45 mcg and 75 mcg clonidine than in group with 15 mcg and in plain ropivacaine. Thus, it shows that bradycardia due to clonidine is dose dependent.

2. **Blood pressure:** Mean base line SBP was 136.73 ± 4.34 in R group and 138.7 ± 6.06 in RC group and the difference was not statistically significant. Even at 5 minutes, difference in Mean base line SBP in R group and RC group was not statistically significant.

At 10 minutes Mean base line SBP was 134.03 ± 1.49 in R group and 130.86 ± 5.13 in RC group and the difference was statistically significant ($P < 0.05$). There after difference in Mean SBP in R group and RC group was statistically significant ($P < 0.05$). Mean base line DBP was 90.66 ± 1.42 in R group and 91.93 ± 3.94 in RC group and the difference was not statistically significant. Even at 5 minutes, difference in Mean base line DBP in R group and RC group was not statistically significant. At 10 minutes Mean base line DBP was 87.66 ± 1.58 in R group and 84 ± 4.29 in RC group and the difference was statistically significant ($P < 0.05$). There after difference in Mean DBP in R group and RC group was statistically significant ($P < 0.05$). Mean base line MAP was 106.13 ± 1.67 in R group and 107.53 ± 3.95 in RC group and the difference was not statistically significant. Even at 5 minutes, difference in Mean base line MAP in R group and RC group was not statistically significant. At 10 minutes Mean base line MAP was 103.1 ± 0.8 in R group and 99.7 ± 3.41 in RC group and the difference was statistically significant ($P < 0.05$). There after difference in Mean MAP in R group and RC group was statistically significant ($P < 0.05$). These all differences might be due to hypotension action of clonidine in RC group. Transient hypotension was seen in two patients in RC group requiring 5mg ephedrine in the study done by **Sadhana Kulkarni et al**⁵³. However, **De Kock et al**⁴² have observed relative reduction in arterial blood pressure lasting from 60 to 150 minutes but none of the patients required vasopressor.

Klimsha et al³⁵ suggested that when a larger dose of local anesthetic is used, the hypotensive action of clonidine is masked by dense axonal blockade produced by the local anesthetic. The relatively low dose of ropivacaine (8mg) used with $45 \mu\text{g}$ clonidine by

De Kock et al⁴², might have unmasked the effect of clonidine leading to hypotension. In our study, hypotension was seen in the first half- hour which could be due to dense blockade by the local anaesthetic. **Klimscha et al**³⁵ stated that hypotension after 20-30 minutes of injection, is due to local spinal and systemic supraspinal actions as peak concentrations occur in CSF. Lipid solubility and elimination of clonidine in CSF results in lack of delayed hypotension.

Gonul Sagiroglu et al⁴⁸ also observed more need of vasopressors in their patients where 30mcg clonidine was used. When compared with bupivacaine in the study done by McNamee et al⁶³ intraoperative hypotension requiring treatment with i.v. ephedrine occurred in 12% of patients in ropivacaine groups (range 5 ± 35 mg) and in 26% of patients in the bupivacaine group (range 5 ± 35 mg), suggesting that hypotension is more common with hyperbaric solutions.

3. **RESPIRATORY RATE:** Mean base line RR was 23.9 ± 0.4 in R group and 24.33 ± 1.825 in RC group and the difference was not statistically significant. Thereafter, too, difference in Mean RR in R group and RC group was not statistically significant ($P > 0.05$). There was no noticeable change in RR in both the groups.

APGAR SCORE

The mean of Apgar score in R group was 8.30 and RC group was 8.50. The difference between the two groups was not statistically significant ($p > 0.05$, t-value 1.58). **Kothari et al**⁶⁹ in 2011, studied analgesic effect of intrathecal clonidine 50mcg along with Bupivacaine in caesarean section concluded that Apgar score of babies (at 1, 5 and 10 min) was unaffected when 50mcg clonidine used in caesarean section.

Singh et al in 2013⁷⁰ studied addition of intrathecal clonidine to hyperbaric bupivacaine on post-op pain in LSCS has found no difference in neonatal outcome.

Tuijil et al⁷¹ in 2006 found no difference in neonatal outcome after addition of intrathecal clonidine to hyperbaric bupivacaine.

Duration of Anaesthesia

The mean in R and RC group was 128.43 and 160 respectively. so there was significant difference seen in the duration of anaesthesia.

Bajwa SJ et al⁵⁰ in 2010 have concluded that epidural ropivacaine combined with epidural clonidine causes profound motor block with rapid onset and prolongs the duration of analgesia as compared to plain ropivacaine and they have also concluded that epidural anaesthesia for elective caesarean section has got the advantage in that analgesia can be prolonged in the postoperative period and further helped in smooth shifting of patients to recovery beds and better maternal comfort with top-up doses of local anaesthetics.

SIDE EFFECTS :The comparison of postoperative complication in two groups In R group the Nausea/vomiting was 20% and in RC group was 30%, therefore the difference between two groups were not statistically significant ($p>0.37$) In R group and group RC there was no evidence of any sedation therefore the difference between two groups were not statistically significant ($p>0.05$).

In R group the shivering observed was 30% and in RC group it was 10%, therefore the difference between two groups was not statistically significant ($p>0.05$).

In R group the incidence of dry mouth was 0% and in RC group 23.33% were observed, therefore the difference between two groups was statistically significant ($P<0.05$).

Bajwa SJ et al⁵⁰ in 2010, compared two groups as far as the side effects are concerned. There was no significant

difference in both the groups with regard to nausea, vomiting, sedation, shivering, respiratory depression or headache ($P > 0.05$). Nine patients complained of dry mouth as compared to none in the R group which was statistically significant ($P < 0.05$). This can be attributed to the side effects of clonidine.

Conclusion

Epidural 0.75% of isobaric ropivacaine given epidurally provides efficient and safe anaesthesia for caesarean section delivery. The addition of 30 μ g clonidine to isobaric ropivacaine results in prolonged complete and effective analgesia with similar block properties and helped to reduce the effective dose of ropivacaine and improved the intraoperative surgical conditions when compared with plain ropivacaine for caesarean delivery. Clonidine combination with ropivacaine did not affect maternal and neonatal outcome. The regular use of epidural ropivacaine and clonidine for elective caesarean sections is safe and provides better perioperative conditions, unaffected Apgar scores, postoperative maternal comfort and uneventful neonatal outcome with minimum side-effects.

Abbreviations :

PACU	:	Post anaesthesia care unit
CSF	:	Cerebrospinal fluid
V/Q	:	Ventilation/Perfusion
CNS	:	Central nervous system
NMDA	:	N-methyl-D-aspartate
VAS	:	Visual analogue scale
FEV1	:	Forced expiratory volume in 1st second
FRC	:	Functional residual capacity
SD	:	Standard deviation
μ g	:	microgram
Kg	:	kilogram
MAC	:	Minimum alveolar concentration

FDA	:	Food and drug administration
GPCRs	:	G-protein coupled receptors
MAP	:	Mean arterial pressure
ED	:	Effective dose
LSCS	:	Lower segmental caesarean section
ASA	:	American Society of Anesthesiologists
HR	:	Heart rate
RR	:	Respiratory rate
SBP	:	Systolic blood pressure
DBP	:	Diastolic blood pressure
SpO2	:	Peripheral Oxygen saturation
IV	:	Intravenous
Min	:	minute
S	:	Significant
NS	:	Non significant
ng	:	Nanogram

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