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ORIGINAL ARTICLE

COMPARATIVE STUDY OF INTRATHECAL ISOBARIC ROPIVACAINE AND ISOBARIC ROPIVACAINE CLONIDINE COMBINATION IN LOWER ABDOMINAL AND LOWER LIMB SURGERIES

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ABSTRACT

Background and Objective: Spinal anaesthesia is the most common approach which is used for lower abdominal and lower limb surgeries. Clonidine is an alpha-2 adrenergic agonist which acts on dorsal horn of spinal cord to produce analgesic effects and can be used as an adjuvant. Aim of the study is to evaluate the effects of addition of clonidine to intrathecal ropivacaine in lower abdominal and lower limb surgeries.**Methodology:**With sample random sampling technique, 60 patients of either sex belonging to age group 18 to 60 years, ASA I or II, posted for lower abdominal and lower limb surgeries under spinal anesthesia were selected who fulfill the inclusion, exclusion criteriae and divided them into two groups of 30 each.**Results:**The mean time for onset of sensory block was 134.97 ± 53.99 seconds in group R and 99.67 ± 29.39 seconds in group RC. Thus, onset of sensory block was faster in group RC when compared to group R and the difference was statistically significant.Time taken to regression to S2 level was 158.33 ± 29.69 mins in group R when compared to 215.00 ± 42.81 mins in group RC and the difference is statistically highly significant. Thus sensory block is prolonged in group RC compared to group R. The mean time to complete motor block in group R was 14.03 ± 4.35 mins, while it was faster, 6.03 ± 2.87 in group RC and the difference was statistically significant.**Conclusion:** Clonidine when used intrathecally along with ropivacaine significantly prolonged the duration of analgesia and there was no clinically significant adverse effects with addition of intrathecal clonidine, hence clonidine can be used as an adjuvant to ropivacaine in smaller doses to produce better quality of analgesia and motor blockade.

Keywords: Comparative Study, Lower Abdominal, Lower Limb Surgeries

1.INTRODUCTION

Ropivacaine is a new long acting amide local anaesthetic agent, related structurally to bupivacaine. It is developed as a pure S enantiomer of propivacaine. It is less lipophilic than bupivacaine and is therefore less likely to product neurotoxicity and cardiotoxicity(Albright,1979; Marx,1984). Moreover due to less liphophilicity it does not penetrate large myelinated motor fibres to a great extent resulting in a lesser degree of motor block.

Efforts have been made to improve the duration of surgical anaesthesia and analgesia provided by already existing local anaesthetic in spinal anaesthesia by adding various drugs as there is a complex system of different receptors for transmission and inhibition of nociception in the spinal cord.

These receptors include μ, κ, δ-opioid receptors (opioids), α2 adrenergic receptors (Clonidine and Dexmedetomidine), Gamma-amino butyric acid agonist (GABA) receptors (Midazolam), N-methyl-D-aspartate (NMDA) receptors (Ketamine) and muscarinic acetylcholine receptors. Epinephrine is the most commonly used adjuvant with local anesthetic. It prolongs the action of lignocaine by retarding its diffusion into blood vessels of the spinal cord but does not prolong the effect of ropivacaine. The addition of these drugs is associated with some unwanted side effects.

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Clonidine being a partial α2 adrenergic agonist, is being extensively evaluated as an adjuvant to intrathecal local anesthetics. It is known to increase both sensory and motor blockade and reduce the dose of local anesthetic required to produce the same quality of blockade, when administered alongwith. There are studies which have evaluated the efficacy of intrathecal clonidine in a wide range (15 to 150 µg)(Engelman and Marsala,2013)

Thus we have decided to take clonidine as an adjuvant to intrathecal isobaric ropivacaine for lower abdominal and lower limb surgeries.

2.METHODOLOGY

The study was undertaken after obtaining ethical committee clearance as well as informed consent from all patients.Sixty patients posted for elective lower abdominal and lower limb surgeries were grouped randomly into two groups (n=30). Randomization was done using simple sealed envelope technique. Group R (control group): received 22.5mg of 0.75% (Isobaric) Ropivacaine intrathecally with 0.2cc distilled water. Group RC (clonidine group): received 22.5mg of 0.75% (Isobaric) Ropivacaine and 30 mcg of Clonidine intrathecally.

Adult patients of either sex, aged between 18 and 60 years, belonging to ASA grade I and II scheduled for elective lower abdominal and lower limb surgeries were the group of patients selected for the study.

Under strict aseptic precautions, lumbar puncture done and test drug administered. The test drugs are prepared by the senior anaesthesiologist who is not involved in the study, Clonidine (Cloneon; 150 µg/ml of Neon laboratories) 0.2cc i.e 30µg is added or distilled water 0.2cc is added to 3cc i.e 22.5mg of Ropivacaine (Ropin; 7.5mg/ml of Neon laboratories). Both the observer and the patient are blinded for the study drug.

Onset of sensory blockade and motor blockade, maximum level of sensory blockade attained and the time taken for it, maximum level of motor blockade attained and the time taken for it, two segments sensory regression time, time to regression to S2, total duration of analgesia, total duration of sensory blockade were noted.

Sensory blockade was tested using pinprick method with a blunt tipped 27G needle at every minute for first 5 mins and every 5 mins for next 15 mins and every 10 mins for next 30 mins and every 15 mins till the end of surgery and there after every 30 mins until sensory block resolved. Quality of motor blockade assessed by modified Bromage scale. Total duration of surgery and side effects if any noted.

Haemodynamic monitoring was done during the block every 2mins for first 10mins and every 10 mins for until 60 mins and once in 15mins till the end of surgery and post operatively every 30 mins employing multi parameter monitor which displays heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), ECG and SpO2.

Onset of sensory blockade is defined as time taken from the completion of the injection of study drug till the patient does not feel the pin prick at L1 level. Time taken for maximum sensory blockade is defined as the time taken from the completion of the injection of the study drug to the maximum sensory blockade attained. Quality of motor blockade assessed by modified Bromage scale. Score 1- total motor block, score 2- total motor block, patient can only move his/her feet, score 3- partial motor block, patient can move his/her knees, score 4- patient can lift his/her leg but cannot hold the position, score 5- no hip function, patient can lift and hold his/her leg for ten seconds and score 6- no motor block.

Duration of two segment sensory regression is defined as the time taken from the maximum level of sensory block attained till the sensation has regressed by 2 segments.

Duration of analgesia is defined as the time taken from the completion of the injection of the study drug till the patient complaints of first feeling of pain. Duration of sensory blockade is defined as the taken from the time of injection till the sensory blockade has regressed to S2.

Intra-operatively if the patient's blood pressure fell below 80/60 mm of Hg, were considered hypotension and when the patient's heart rate declined to 50 beats/min or less, considered bradycardia. Patient monitored post-operatively for pain and the time of onset of pain and time to first rescue analgesic recorded. Pain assessed by Visual Analogue Scale.

3.RESULTS

The mean age of the patients, male to female ratio, ASA distribution, duration of surgery, mean systolic blood pressure, mean diastolic blood pressure, mean heart rate and mean $Sp0_2$ (Table 1-4 & Fig 1-3) were comparable between the groups.

Table-1: Age distribution

	R	RC	P Value
Age	41.10 ± 12.87	39.20 ± 10.297	>0.05

Z test

Table-2: Sex distribution

Sex	R	RC	P Value
Male	18	17	>0.05
Female	12	13	

Chi-square test

Table 3 ASA distribution

ASA	R	RC	P Value
ASA I	18	17	>0.05
ASA II	12	13	

Chi-square test

Table-4: Duration of Surgery

	R	RC	P Value
Duration of Surgery	97.33 ± 17.357	102.00 ± 16.692	>0.05

Z test

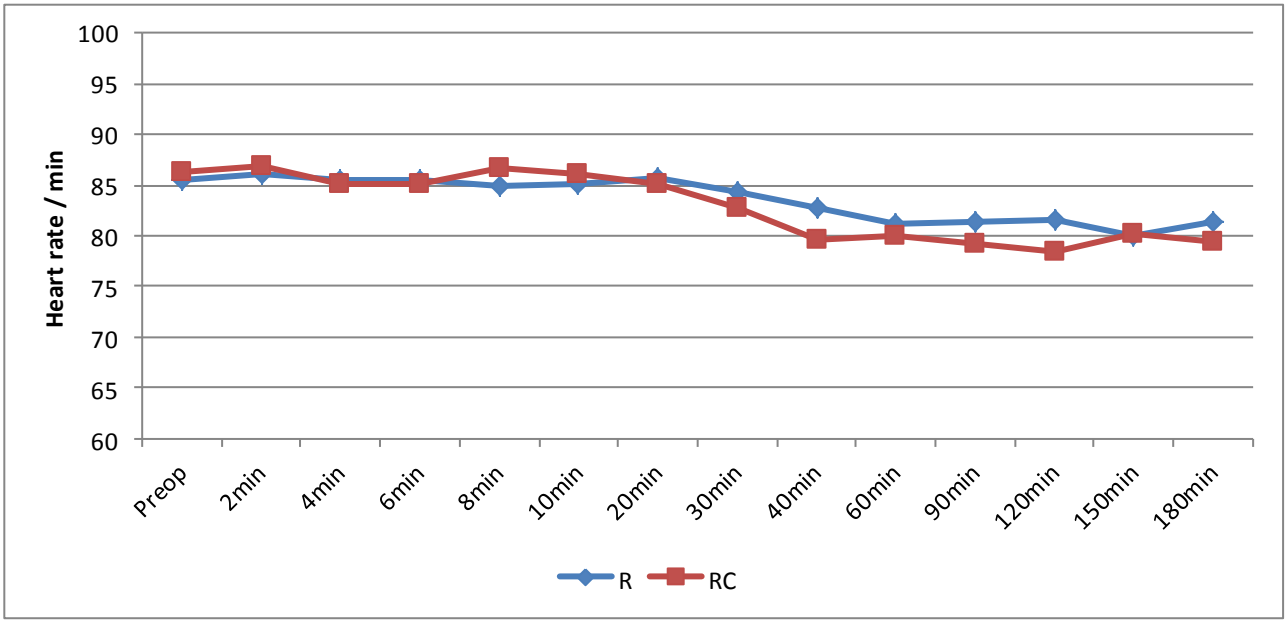

Fig. 1: Mean heart rate in both the groups

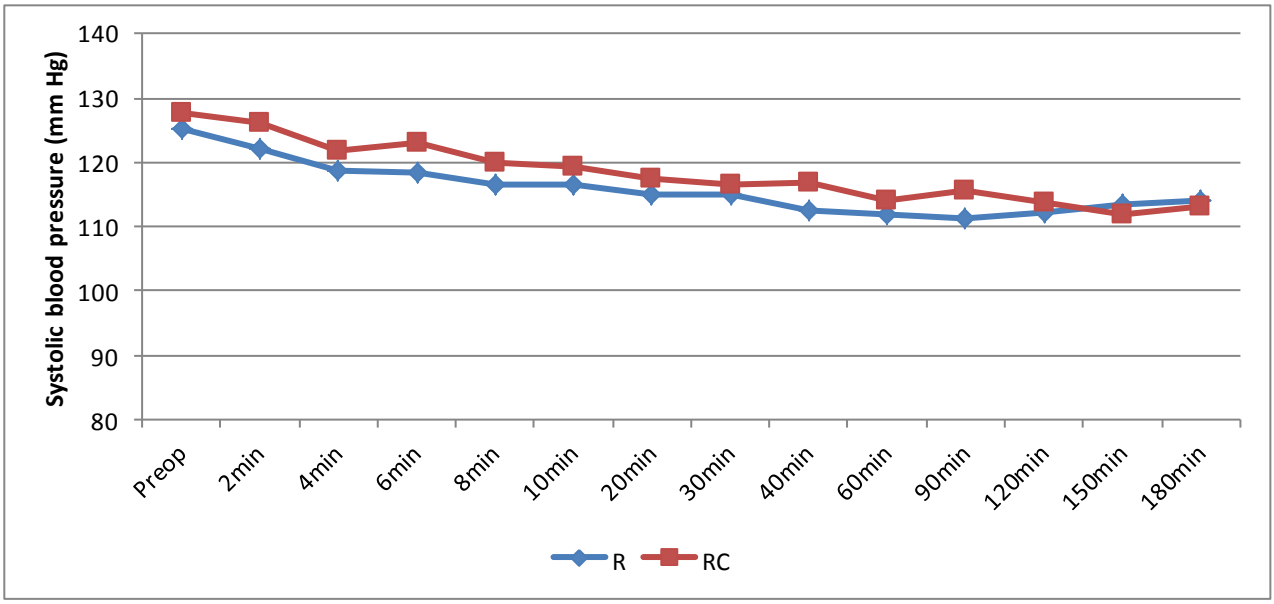

Fig. 2: Mean systolic blood pressure in both the groups

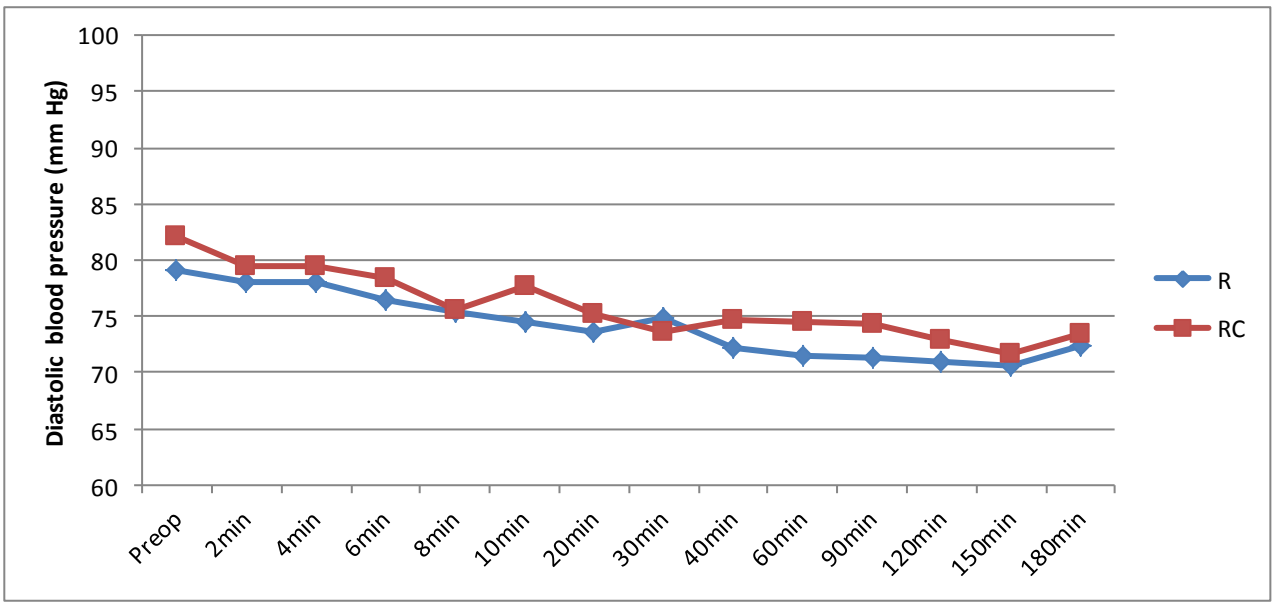

Fig. 3: Mean diastolic blood pressure in both the groups

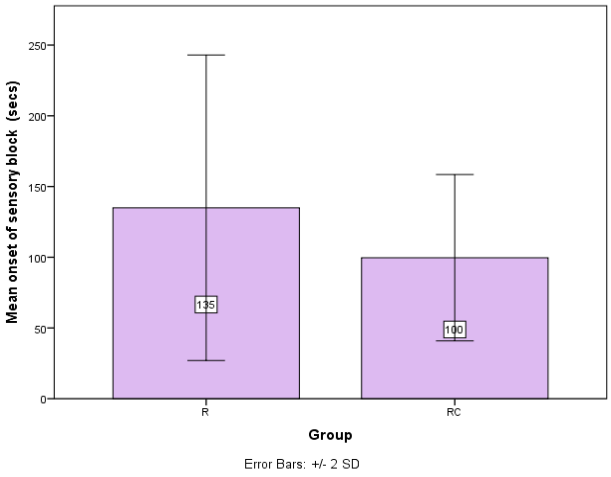

Fig. 4: Onset of sensory block

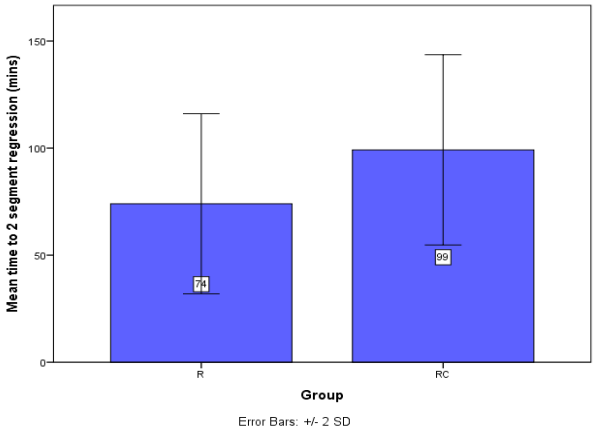

Fig. 5: Time to two segment regression

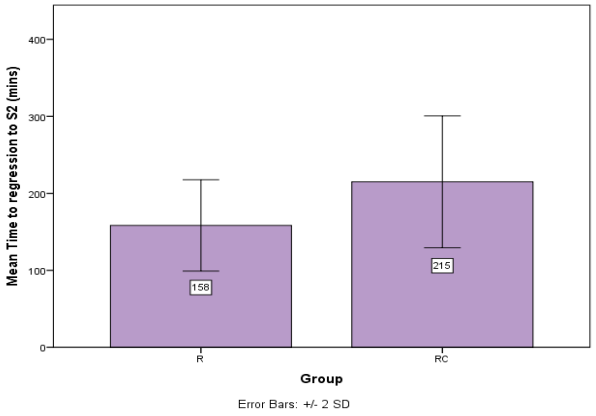

Fig. 6: Time to regression to S2

The mean time to onset of sensory block (Table-6 & Fig.4) was 134.97 ± 53.99 seconds in group R and 99.67 ± 29.39 seconds in group RC. Thus, onset of sensory block was faster in group RC when compared to group R and the difference was statistically significant. Time taken to achieve maximum level was 16.37 ± 3.87 mins in group R and 15.67 ± 5.08 mins in group RC and the difference was statistically insignificant. Time taken to two segment regression of level (Fig.5) was 74.00 ± 21.02 mins in group R and 99.17 ± 22.21 mins in group RC. It was earlier in group R than in group RC nd the difference was statistically highly significant. Time taken to regression to S2 (Fig.6) was 158.33 ± 29.69 mins in group R when compared to 215.00 ± 42.81 mins in group RC and the difference is statistically highly significant. Thus sensory block is prolonged in group RC compared to group R.

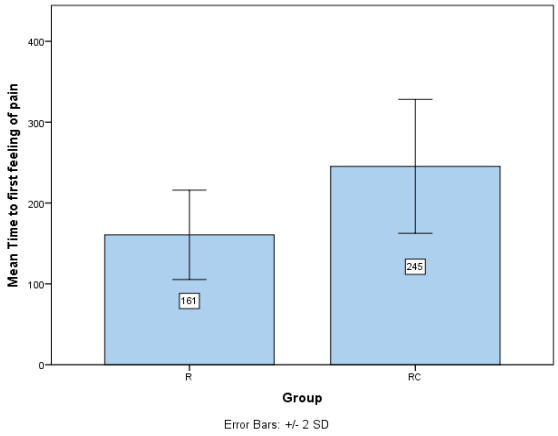

Fig. 7: Time to complete motor block

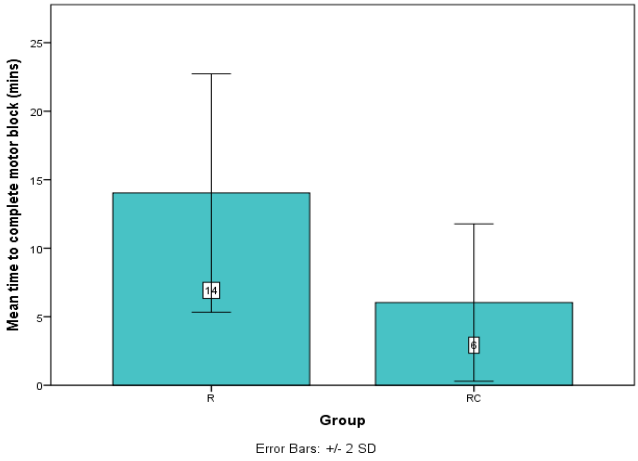

Table-5: Maximum sensory level achieved

Maximumsensory level achieved	Group R		Group RC	
	N	Percentage	N	Percentage
T3	1	3.33	0	0.00
T4	1	3.33	5	16.67
T6	11	36.67	17	56.67
T8	13	43.33	7	23.33
T10	4	13.33	1	3.33

Chi-square test (Cross tab), p value = 0.073

The mean time to complete motor block (Table.6 & Fig.7) in group R was 14.03 ± 4.35 mins, while it was faster, 6.03 ± 2.87 in group RC and the difference was statistically significant. The mean bromage level when sensory level was T10 (Table.6) was 2.30 ± 0.53 in group R and 2.13 ± 0.57 in group RC and the difference was statistically insignificant. The difference in achievement of maximum sensory level was statistically insignificant. 56.67% of the patients in group RC achieved a level of T6 whereas about 36.67% achieved T6 and 43.33%, T8 in group R. The time taken to first feeling of pain (Fig.8) after spinal anesthesia was 160.67 ± 27.63 mins in group R compared to 245.33 ± 41.42 mins in group RC and difference is statistically highly significant. The time to first rescue analgesic was 180.33 ± 30.31 mins in group R, while it was 282.33 ± 44.23 mins in group RC and the difference is statistically highly significant.

Haemodynamics (Fig.1-3) were preserved both intraoperatively and postoperatively. However there was a small number of patients who developed significant fall in blood pressure and bradycardia which were easily managed without any untoward effect. Three patients each in the clonidine group and two patients in the control group developed hypotension requiring

treatment. Two patients in the clonidine group alone developed bradycardia requiring treatment.

No patient had any respiratory depression, nausea, vomiting or shivering in either of the groups. In the present study the efficacy of intrathecal clonidine as an adjuvant to intrathecal ropivacaine has been found to produce better quality of anesthesia with prolonged postoperative analgesia without any adverse effects with low dose of clonidine.

Table 6: Summary of Spinal Block Characteristics

Spinal block characteristics	Group – R (Mean ± SD)	Group –RC (Mean ± SD)	P value
Onset of sensory block (seconds)	135±54	100±29	<0.05
Time to maximum level (minutes)	16±3.9	15.67±5	>0.05
Time to 2 segment regression (minutes)	74±21	99±22	<0.001
Time to regression to S2 (minutes)	158±30	215±43	<0.001
Time to complete motor block (minutes)	14±4.3	6±2.9	<0.001
Bromage level when T10	2.3±0.5	2.1±0.5	>0.05
Time to first feeling of pain (minutes)	161±28	245±41	<0.001

4.DISCUSSION

Sensory block characteristics

Onset of sensory blockade

In our study the mean time taken for onset of sensory block is 2.25±0.89mins in the control group, 1.67±0.5mins in the clonidine group. There is a statistically highly significant decrease in the onset of sensory blockade in clonidine group compared to the control group.

In a study conducted by Saxena et al(2010) authors observed the onset of sensory blockade to be 6.57±0.49 mins in control group and 2.58±0.33 mins, 2.54±0.34mins and 2.09±0.89 mins in clonidine groups (15 µg, 30 µg and 37.5 µg respectively) and in this study there was a significant reduction in the onset time which concurs with our study. But compared to our study the onset time of sensory block is higher and this could be possibly due to the drug effect of ropivacaine with clonidine in our study.

In a study conducted by Kanazi GE et al.[4] the authors observed the onset of analgesia to be 9.7±4.2 mins in control group and 7.6±4.4 mins in clonidine group which is more than the value in our study and there is no significant reduction in the onset time of sensory blockade .This could be due to the lesser dose.

In studies conducted by Dobrydnjov et al.(2003), Benhamou D et al.(1998) Grandhe et al.,(2008) and De Kock M et al.,(2001), authors observed a significant reduction in the onset time of sensory blockade in clonidine group which concurs with our study.

Time taken for maximum sensory blockade

The mean time taken for maximum sensory blockade in the present study is 16.37±3.87 mins in the control group and 15.67±5.08mins in the clonidine group. There is no statistically significant decrease in the mean time taken for the maximum sensory blockade in the clonidine group compared to the control group.

In a study conducted by De Kock et al., (2003) the authors observed that the time to peak sensory level to be 19±15 mins in the control group and 23±16, 25±14 and 30±15 in the clonidine group (15µg, 45µg and 75µg respectively). Though there is difference between the control group and clonidine group, the difference in longer time taken to achieve maximum level in this study compared to our study might be due to lesser dose of ropivacaine used.

Maximum level of sensory blockade achieved

In our study the maximum level of sensory blockade achieved is T3. One out of 30 patients in control group had T3 level of sensory blockade. 1 out of 30 patients in the control group and 5 out of 30 paients in the clonidine group achieved T4 level.

There is no statistically significant difference in the maximum level of sensory blockade in the clonidine group compared to the control group.

In the studies conducted by Strebel et al.,(2004) and Thakur et al.,(2013) there was no statistically significant difference in the maximum level of sensory blockade which concurs with our study.

Time to two segment regression

The time taken for regression of sensory block by two segments in the present study is 74±21 mins in the control group, 99±22 mins in the clonidine group. There is statistically significant increase in the mean time taken for regression of sensory block by two segments in clonidine group compared to the control group.

In a study conducted by De Kock MD et al.,(2001) the authors observed that the mean time to 2 segment regression was 75±22 mins in the control group and 90±32 mins, 96±28 mins and 100±31 mins in clonidine groups (15µg, 45µg, 75µg respectively), which concurs with our study. It can be seen that there is not much of difference between the doses of clonidine used.

Our study is also consistent with studies done by Dobrydnjov et al.,(2003), Saxena et al.,(2010), Sethi et al.,(2007) and Kanazi et al.,(2006), here the authors observed a statistically significant increase in the mean time taken for regression of sensory block by two segments.

The time taken for sensory block to regress to S2

The time taken for sensory block to regress to S2 in the present study is 158±30mins in the control group, 215±43 mins in the clonidine group. There is a statistically significant increase in the mean time taken for regression of sensory block to S2 in the clonidine group compared to the control group.

In a study conducted by Kock et al.,(2001) the authors observed that the mean time for sensory block to S2 was 132±38 mins in control group and160±37mins, 183±52 mins and 195±40 mins in the clonidine groups (15µg, 45µg, 75µg respectively) which is statistically significant, but less than our study in both the groups and this may be due to less dose of ropivacaine used in the study.

In studies conducted by Kanazi et al.,(2006) and Thakur et al.,(2013), the authors observed a statistically significant increase in the mean time taken for regression of sensory block to S2 dermatome in the clonidine group which concurs with our study.

The duration of sensory blockade was prolonged in our study comparable to studies done by Saxena et al.,(2010), Grandhe et al.,(2008), VanTuijl et al.,(2006), Kaabachi et al.,(2007), Strebel et al., (2004) and De Kock M et al.,(2001) in clonidine group.

Duration of analgesia

The mean duration of analgesia in our study is 160±28 mins in control group and 245±41 mins in the clonidine group, which is statistically highly significant in the clonidine group compared to the control group.

Our study concurs with the study conducted by Grandhe RP et al.[10], where authors observed the mean duration of analgesia of 3.8 ±0.7 hours in the control group and 6.3±0.8 hours when using clonidine of 1µg/kg with a mean weight of 60.6±19.4 kg.

In the studies conducted by Saxena et al.,(2010), Strebel et al., (2004), Dobrydnjov et al.,(2003) and Benhamou et al.,(998) the authors observed a statistically significant increase in the mean duration of analgesia in the clonidine group.

Time taken for complete motor blockade

The mean time taken for complete motor blockade in our study is 14±4mins in control group and 6±3mins in clonidine group. This is statistically significant.

But the grade of motor blockade in the study groups did not differ. All the groups had a motor blockade of modified Bromage scale 1.

This is consistent with the studies done by Sethi et al.,(2007) and Saxena et al.,(2010) who observed the complete motor blockade of the lower extremity in all patients in clonidine group.

In a study conducted by Kock et al.,(2001) the authors observed that the time to maximum motor block to be 24±12mins in the control group and 24±11, 20±12 and 24±13 in the clonidine group (15µg, 45µg and 75µg respectively). The difference between the control group and clonidine group was statistically not significant and also the time taken for maximum motor block is prolonged when compared to our study. This might be due to lesser dose of ropivacaine used in this study.

Bromage level when T10

The bromage level was two universally in all the patients in both the groups when he the sensory level was T10. This is comparable with the studies done by Kanazi et al.,(2006), Kaabachi et al.,(2007), DeKock et al.,(2001), Saxena et al.,(2010), Strebel et al., (2004), Dobrydnjov et al.,(2003), Sethi et al.,(2007), Grandhe et al., (2008) and Benhamou et al.,(1998).

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