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Effects of low Doses of Intrathecal Clonidine and Dexmedetomidine with Bupivacaine on The Duration of Sensory and Motor Block in Abdominal and Lower Limb Surgeries- A Prospective Randomised Double Blinded Study

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ABSTRACT
BACKGROUND: The purpose of this study is to compare the duration of sensory and motor block in elective lower limb and abdominal procedures following intrathecal administration of bupivacaine along with adjuvants either clonidine or dexmedetomidine.
METHODS: A prospective randomised double blinded study. 120 study participants were randomly allocated to three groups- Group A was given 12.5 mg of hyperbaric bupivacaine, Group B was given 3 mcg dexmedetomidine along with 12.5 mg hyperbaric bupivacaine and Group C was given 30 mcg of clonidine along with hyperbaric bupivacaine. The duration of sensory and motor block was recorded.
RESULTS: Group B and C study participants showed significantly longer duration of sensory and motor block when compared to Group A. The mean duration of sensory block in Group A was 92.5 minutes, Group B 124.5 minutes Group C (119.4 minutes) (A vs B, A vs C $p<0.001$). The mean duration of motor block in group A 149.1 min, group B 252.5 min, Group C 217 min (A vs B, A vs C, B vs C $P<0.001$)
CONCLUSION: By adding 3 mcg dexmedetomidine or 30 mcg clonidine to hyperbaric bupivacaine duration of sensory and motor block was significantly prolonged.

INTRODUCTION

Neuraxial anesthesia is usually given for lower abdominal and lower limb surgeries. The subtypes of neuraxial anesthesia are spinal anesthesia, epidural anesthesia and combined spinal-epidural. In neuraxial anesthesia the needle is placed in between the vertebra and the drug is injected either into subarachnoid space for spinal anesthesia or into epidural space for epidural anesthesia. The local anesthetic drug which is injected into the cerebrospinal fluid anesthetizes the nerves which exit from the spinal cord.

The first anesthetic agent which was injected intra thecally was cocaine. Procaine and tetracaine were introduced later into clinical practice. 2 chloro procaine, lidocaine, bupivacaine, mepivacaine and ropivacaine are the drugs given intrathecally.

Bupivacaine, an aminoacyl local anesthetic was discovered in 1957 and is one of the most widely used local anesthetic for spinal anesthesia. It produces adequate anesthesia and analgesia for intermediate to long duration surgical procedures. Unlike lidocaine bupivacaine has low incidence of transient neurologic symptoms.

Adjuvants are agents which when co-administered with local anesthetic agents decreases the time of onset and increases the duration of sensory and motor block with increase in duration of analgesia. Many adjuvants have been used till date like opioids, vasoconstrictors and acetyl cholinesterase inhibitors and alpha 2 agonists to increase analgesia duration. Adjuvants like fentanyl, ketamine, tramadol, dexmedetomidine, neostigmine and clonidine usually increase the analgesic effect of the local anesthetic. Dexmedetomidine and clonidine are alpha 2 agonists. Clonidine is a partial alpha 2 agonist. It has a good efficacy and safety margin. (1) When we add clonidine to local anesthetic agent intrathecally the duration of both motor and sensory blockade are increased (2-4). Dexmedetomidine is an intravenous sedative and a co analgesic agent. It is selective alpha 2 agonist and has a preferential binding to 2A receptor subtype and hence dexmedetomidine has a more effective analgesic effect than clonidine without much

cardiovascular effects secondary to alpha 1 receptor activation.The dose of dexmedetomidine and clonidine used in various studies were different. In our study we evaluated the efficacy of low dose intrathecal clonidine (30 microgram) and dexmedetomidine (3 microgram), equipotent doses, as an adjuvant to bupivacaine and determined its effect on duration of sensory and motor blockade

AIM OF THE STUDY

In our study we aimed to compare the duration of sensory and motor block when intrathecal bupivacaine was supplemented with low dose of dexmedetomidine or clonidine.

MATERIALS AND METHODS

The study was conducted in the Department of Anesthesiology and Pain Medicine in Sri Ramachandra Institute of Higher Education and Research after getting the approval from Institution Ethical Committee (Ref No IEC /21/AUG/164/48)

Duration of study – September 2021 to October 2022

TYPE OF STUDY:

Prospective randomized double blinded study

SAMPLE SIZE:

Sample size was calculated as per the pilot study based on duration of sensory and motor block in 3 groups. Other parameters considered for sample size calculation included 95% power of study and 5% alpha error. The required sample size was 36 subjects in each group. To account for a loss of follow up of about 10% another 4 subjects were included in each group. Hence the final sample size was taken as 40 subjects in each group.

INCLUSION CRITERIA

- Adult patients of both sexes
- 18-60 years of age
- ASA 1and 2
- Posted for elective lower limb surgeries and lower abdominal surgeries

EXCLUSION CRITERIA

- Patients on alpha 2 adrenergic antagonist, calcium channel blockers, ACE inhibitors
- Coronary artery disease and valvular heart disease
- Dysrhythmia
- Body weight more than 120 kg
- Height less than 140 cm
- Post spinal surgeries, spinal deformities
- H/o allergy to study drugs
- Pregnancy
- Coagulopathy
- Neurological disorder

Institution Ethics Committee approval was obtained. Trial was registered in CTRI. Patients who fit into inclusion criteria were enrolled into the study after obtaining informed consent.

PREOPERATIVE

Data collection included

1. Demographic data
2. Preoperative assessment on the day before surgery (including Baseline vitals)
3. Written informed consent was obtained for participation in the study
4. Nil per oral orders was given according to department protocol

Patients were randomly allocated to three groups by using computer generated random table.

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Before arrival to the operating room, anesthesiologist assigned to the case opened a sequentially numbered sealed opaque envelope containing assignment to either group A, B or C.

- Normal saline and 2.5ml (12.5 mg) of 0.5% hyperbaric bupivacaine was given to group A
- 2.5ml (12.5 mg) of 0.5% hyperbaric bupivacaine and 3mcg of dexmedetomidine was given to group B.
- 2.5ml (12.5 mg) of 0.5% hyperbaric bupivacaine with 30 mcg of clonidine make up Group C.
  To make it a total volume of 3.0 ml normal saline was added in all the groups.

INTRAOPERATIVE:

Once the patient was wheeled into the holding area, baseline vitals – heart rate, oxygen saturation, blood pressure were monitored.

- After arrival of patient in operating room, iv access was checked for patency.
- Standard monitoring devices including NIBP cuff, ECG lead, pulse oximetry probe was attached to patient. Baseline BP and HR were recorded
- Injection Phenylephrine (20 micrograms/ml), Injection Ephedrine (6milligram/ml) and Injection Atropine (0.6milligram/ml) were loaded before procedure.
- After taking all aseptic precautions and proper draping, lumbar interspace L3-L4 was identified in sitting position.
- Subarachnoid space was identified by using 27 guage pencan or 25 guage Quincke spinal needle and once free flow of cerebrospinal fluid appeared, drug solutions was injected slowly
- The patient was placed in supine position after the injection was given.
- Drug solutions was made by one anesthetist and the observations were made by the attending anesthetist.
- Onset of sensory block was assessed by loss of cold sensation every 2 minutes with ice cube bilaterally till highest level is attained.
- Higher level was used for statistical analysis when there was a difference between the right and left.
- Onset of motor block was measured every 2 minutes from time of administering spinal anesthesia till Modified Bromage Scale III was attained
- As soon as the sensory block reached the necessary level, the procedure was allowed to start.
- Motor block was assessed using modified Bromage scale vitals like BP and HR will be recorded 5,10,15,20, 25 and 30 min after injection and subsequently every 15 min
- VAS scores were recorded 5 min before and after injection and every 15 min thereafter till the score was more than 4
- The spinal injection time was used as the starting point for all calculations, denoted by time 0.
- Time of onset of sensory block was measured from time of spinal injection till highest dermatomal block attained
- Time of onset of motor block was measured from time of spinal injection till modified Bromage scale III attained

POST OPERATIVE

After surgery patient was shifted to PACU

- Level of sensory and motor block was assessed every 15 min
- Duration of sensory block was taken as time for two segment regression
- Duration of motor block was taken as time taken to reach BMS 0

PRIMARY OUTCOME

- Duration of Sensory block
- Duration of Motor block

OBSERVATIONS AND RESULTS

No patients were excluded during the study. Intergroup analysis and the chi square test were used for the statistical analysis of the data that had been gathered. Range, mean, and standard deviation were used to represent the results. A "p" value of less than 0.05 was regarded as statistically significant.

The collected data were then analyzed using IBM SPSS Statistics for Windows, Version 23.0. (Armonk, NY: IBM Corp). For describing the data descriptive statistics frequency analysis, percentage analysis was used for categorical variables and the mean & S.D were used for continuous variables. To find the significant difference in the multivariate analysis the one way ANOVA with Tukey's Post-Hoc test was used. To find the significance in qualitative categorical data Chi-Square test was used. In all the above statistical tools the probability value .05 is considered as significant level

Table 1: Comparison of Age between the Groups

Variable	Groups	N	Mean	SD	F-value	p-value
Age	Group A	40	44.8	11.0	0.490	0.614 #
	Group B	40	42.6	12.5		
	Group C	40	42.5	12.4		
# No Statistical Significance at p > 0.05 level						

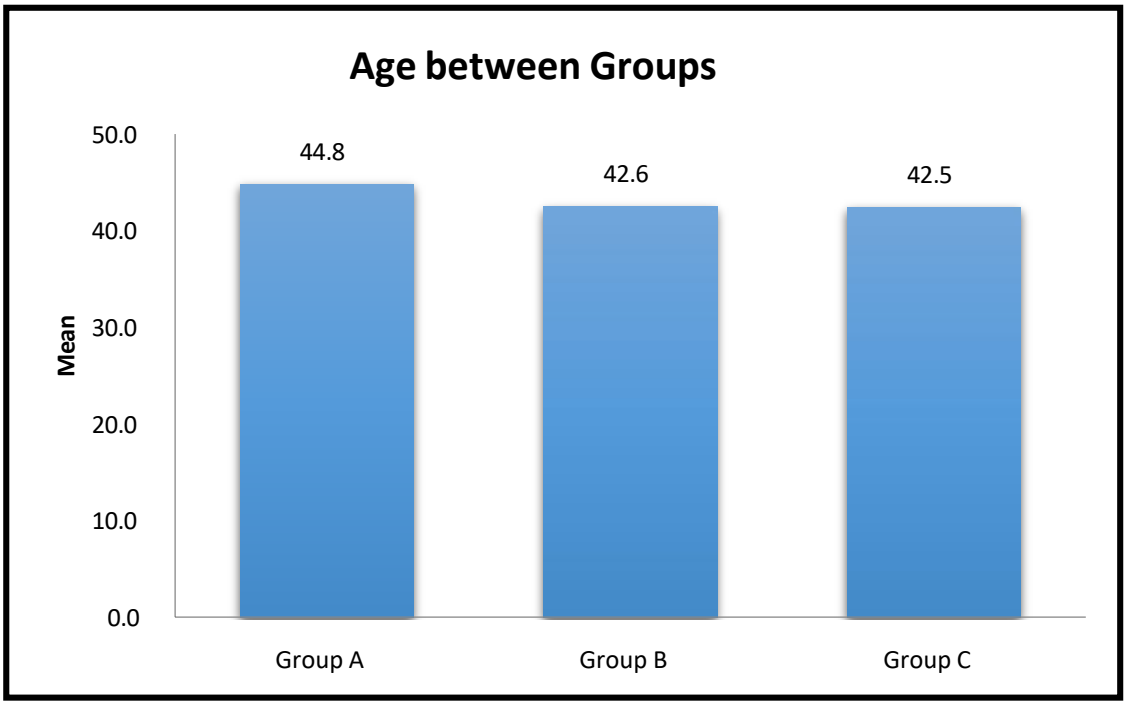

Figure 1

The above table shows the comparison of Age between Groups. The mean age group of patients in Group A was 44.8 years. Group B mean age group was 42.6 years. Group C consisted of patients with mean age group of 42.5 years.

Table 2: Comparison of Gender between the Groups by Pearson's Chi-Square test

			Groups			Total	χ 2 - value	p-value
			Group A	Group B	Group C			
Gender	Female	Count	21	17	19	57	0.802	0.670 #
		%	52.5%	42.5%	47.5%	47.5%		
	Male	Count	19	23	21	63		
		%	47.5%	57.5%	52.5%	52.5%		
Total		Count	40	40	40	120		
		%	100.0%	100.0%	100.0%	100.0%		
# No Statistical Significance at p > 0.05 level								

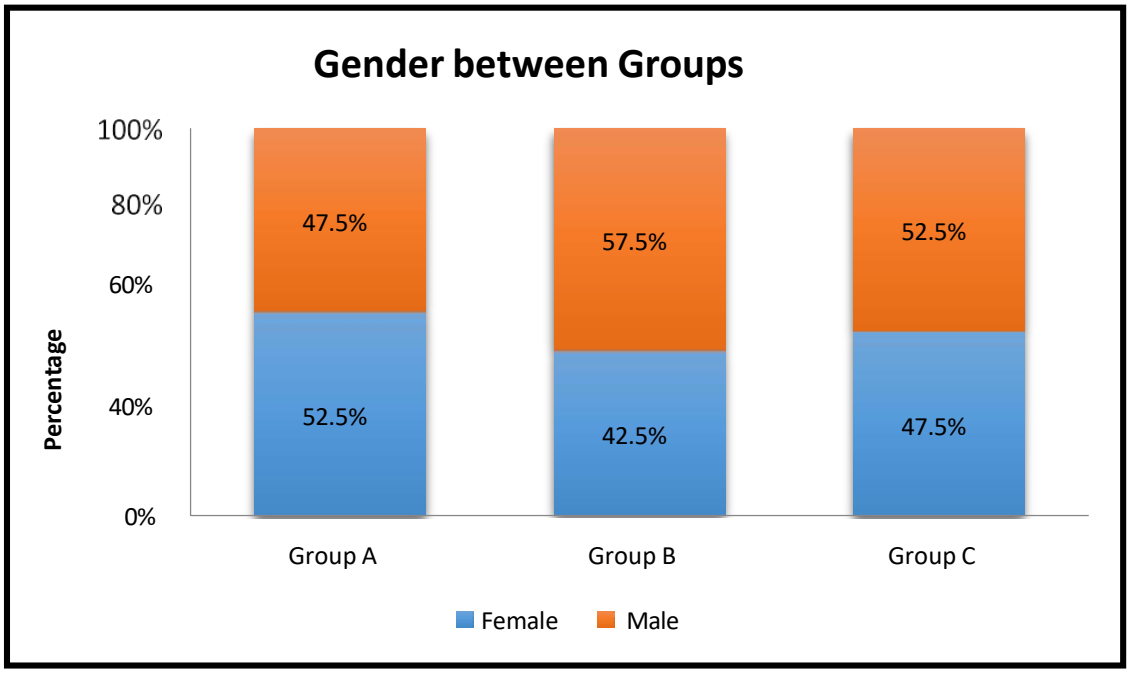

Figure 2

The above table shows comparison of Gender between Groups by Pearson's Chi-Square. Out of 120 patients 63 patients were male and 57 patients were females.

Table 3: Comparison of BMI between the Groups

Variable	Groups	N	Mean	SD	F-value	p-value
BMI	Group A	40	25.9	4.0	0.485	0.617 #
	Group B	40	26.8	3.5		
	Group C	40	26.3	4.1		
# No Statistical Significance at p > 0.05 level						

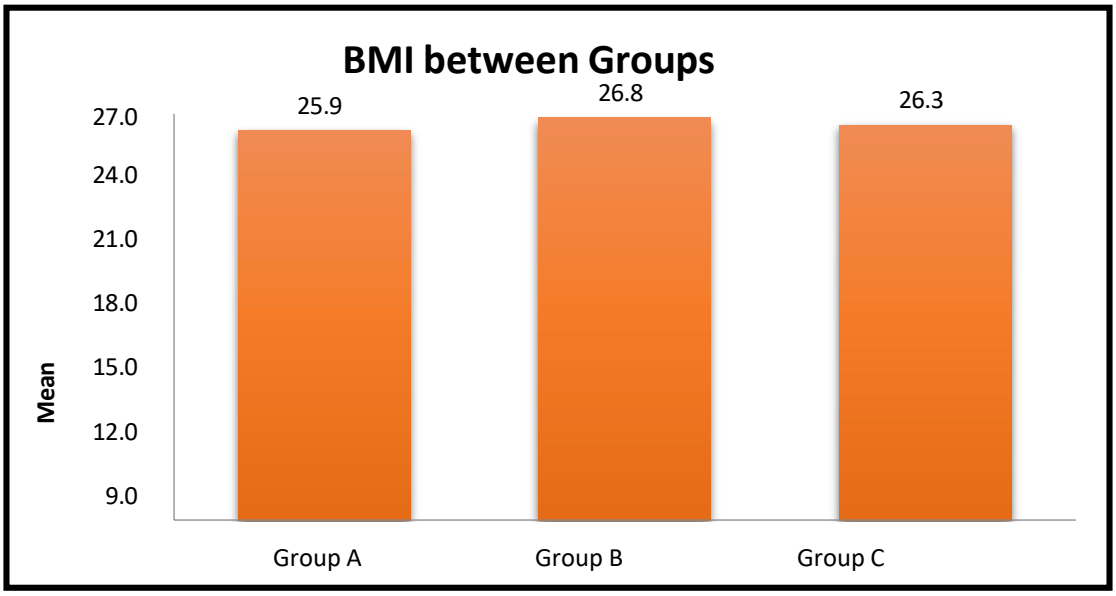

Figure 3

The above table shows the comparison of BMI between Groups. Patients in group A had an average BMI of 25.9. The mean BMI in group B was 26.8, while in group group C it was 26.3.

Table 5: Comparison of Peak Sensory Block Attained between the Groups

			Groups			Total	χ 2 - value	p-value
			Group A	Group B	Group C			
Peak Sensory Block Attained	T2	Count	0	2	2	4	50.688	0.0005 **
		%	0.0%	5.0%	5.0%	3.3%		
	T4	Count	1	21	22	44		
		%	2.5%	52.5%	55.0%	36.7%		
	T6	Count	22	16	15	53		
		%	55.0%	40.0%	37.5%	44.2%		
	T8	Count	13	1	0	14		
		%	32.5%	2.5%	0.0%	11.7%		
	T10	Count	3	0	1	4		
		%	7.5%	0.0%	2.5%	3.3%		
	T12	Count	1	0	0	1		
		%	2.5%	0.0%	0.0%	.8%		
Total		Count	40	40	40	120		
		%	100.0%	100.0%	100.0%	100.0%		
** Highly Statistical Significance at p < 0.01 level								

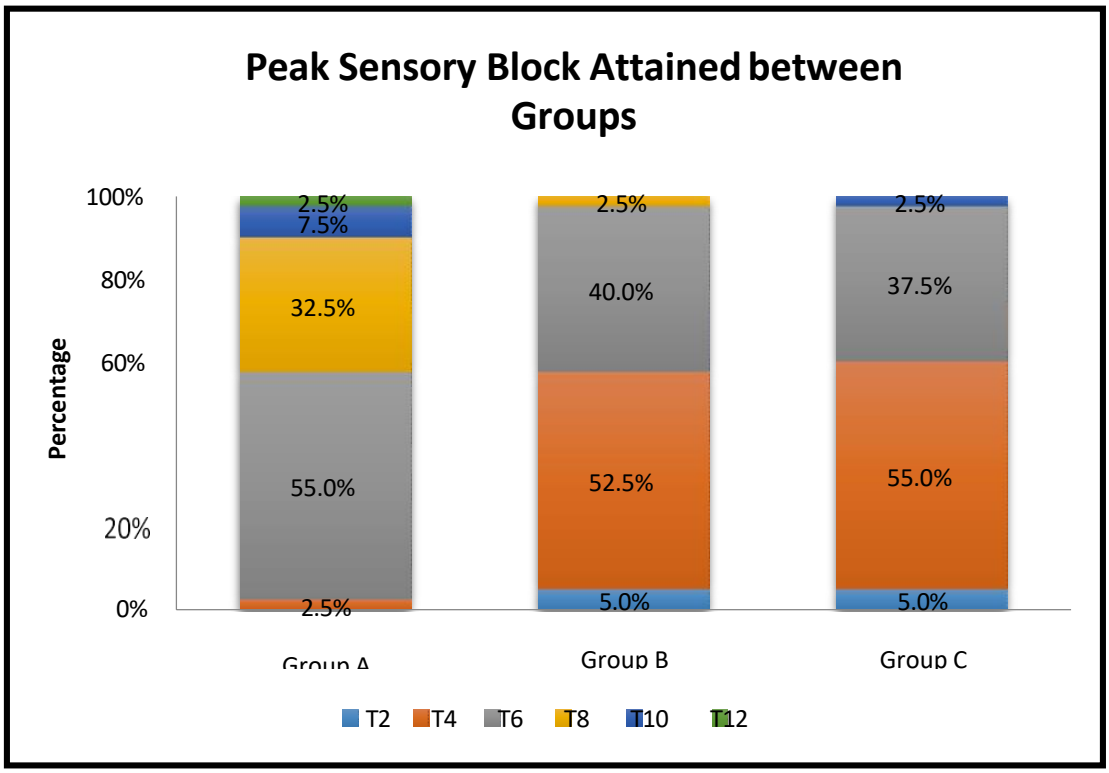

Figure 5

The above table shows comparison of Peak Sensory Block Attained between Groups. The highest degree of sensory blockade was T2. T2 level of sensory blockade was present in 2 out of 40 patients in the dexmedetomidine group B and 2 out of 40 patients in the clonidine group C. T4 level sensory blockade was seen in 1 out of 40 patients in Group A (control group), 21 out of 40 patients in Group B (dexmedetomidine group), and 22 out of 40 patients in Group C (clonidine group). T6 level sensory blockade was present in 22 out of 40 patients in Group A, 16 out of 40 patients in Group B, and 15 out of 40 patients in Group C. T8 level sensory blockade was present in 13 out of 40 patients in Group A, 1 out of 40 patients in Group B, and 0 out of 40 patients in Group C. T10 level sensory blockade was present in 3 out of 40 patients in Group A, 0 out of 40 patients in Group B, and 1 patient in Group C. There was a T12 level of sensory blockade in 1 out of 40 patients in Group A, but none in Group B or Group C

Table 7: Comparison of Time For 2 Segment Regression between the Groups

Variable	Groups	N	Mean	SD	F-value	p-value
Time For 2 Segment Regression	Group A	40	92.5	13.1	35.926	0.0005 **
	Group B	40	124.5	22.7		
	Group C	40	119.4	17.3		
** Highly Statistical Significance at p < 0.01 level						

Post Hoc Tests - Tukey HSD - Multiple Comparisons							
Dependent Variable			Mean	Std. Error	p-value	95% C.I	
			Difference (I-J)			LB	UB
Time For 2 Segment Regression	Group A	Group B	-32.0000*	4.0566	0.0005 **	-41.630	-22.370
		Group C	-26.9000*	4.0566	0.0005 **	-36.530	-17.270
	Group B	Group C	5.1000	4.0566	0.422 #	-4.530	14.730
** Highly Significant at p < 0.01 and # No Statistical Significance at p > 0.05							

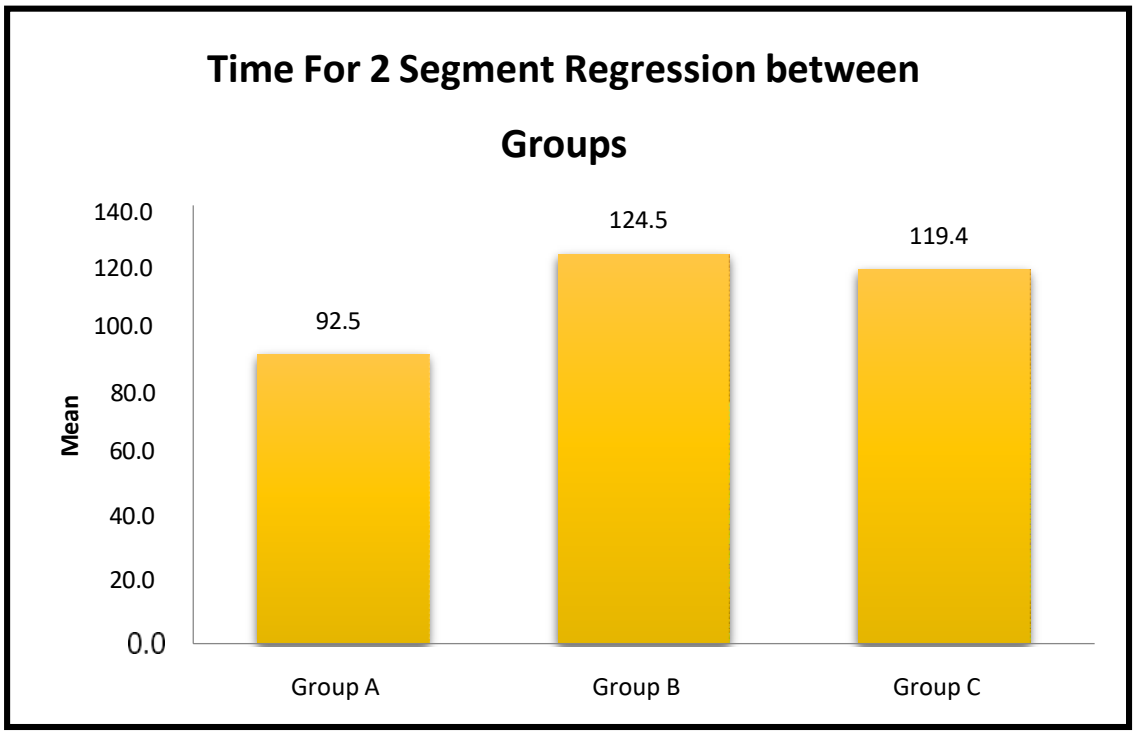

Figure 7

The above table shows the comparison of Time For 2 Segment Regression between Groups. Patients in group A took an average of 92.5 minutes for a two-segment regression, but patients in groups B and C took 124.5 and 119.4 minutes, respectively.

Table 8: Comparison of Motor Regression Time between the Groups

Variable	Groups	N	Mean	SD	F-value	p-value
Motor Regression Time	Group A	40	149.1	19.5	261.413	0.0005 **
	Group B	40	252.5	24.2		
	Group C	40	217.0	17.3		
** Highly Statistical Significance at p < 0.01 level						

Post Hoc Tests - Tukey HSD - Multiple Comparisons							
Dependent Variable			Mean Difference (I-J)	Std. Error	p-value	95% C.I	
						LB	UB
Motor Regression Time	Group A	Group B	-103.3750*	4.5943	0.0005 **	-114.282	-92.468
		Group C	-67.8750*	4.5943	0.0005 **	-78.782	-56.968
	Group B	Group C	35.5000*	4.5943	0.0005 **	24.593	46.407
** Highly Statistical Significance at p < 0.01 level							

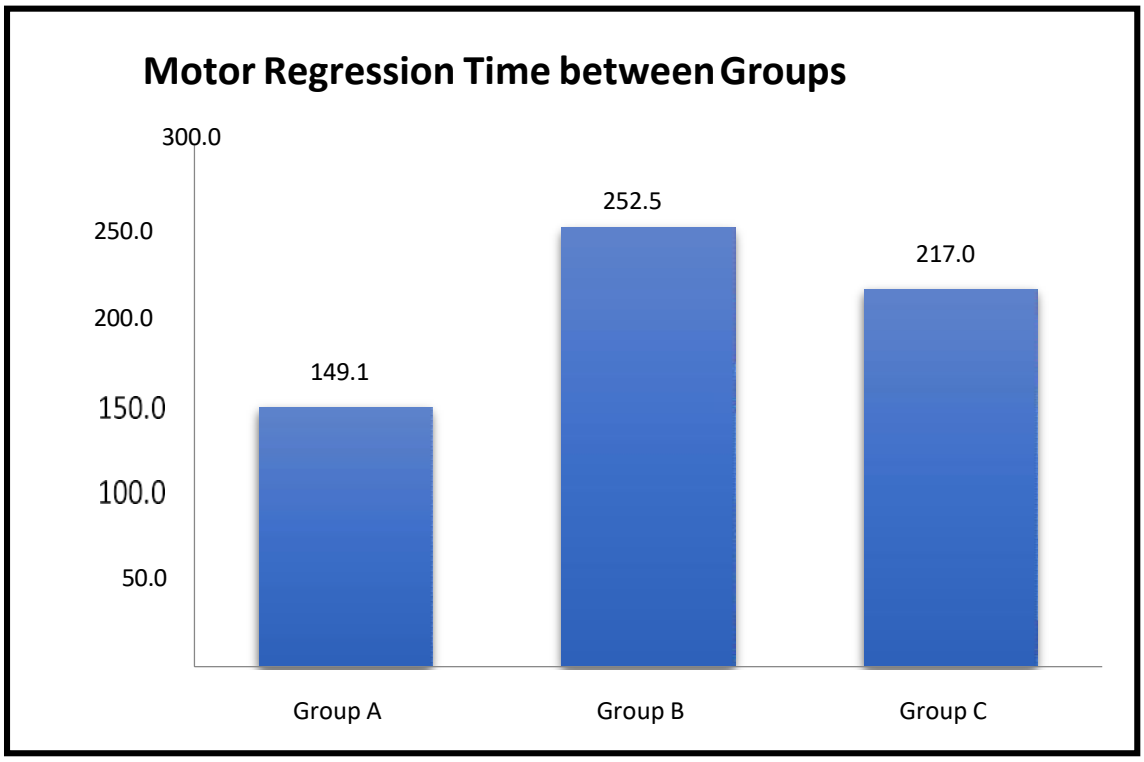

Figure 8

The above table shows the comparison of Motor Regression Time between Groups. In patients in group A, the mean motor regression time was 149.1 minutes, whereas in group B, it was 252.5 minutes. The mean motor regression time for group C was 217 minutes. Table 9: Comparison of Duration of Analgesia between the Groups

DISCUSSION

120 patients admitted for elective lower extremity and lower abdominal surgeries belonging to American Society of Anesthesiology (ASA) Grade-I and Grade-II were selected randomly into 3 groups (n=40). Through the use of a computer-generated random table, patients were divided into three groups at random. Before entering the operating room, the assigned anesthesiologist opened a sealed, opaque envelope with a sequential number that contained the patient's placement in group A, B, or C.

Age, sex, and body mass index comparisons in the demographic data revealed no statistically significant differences between the group. 30 micrograms of clonidine and 3 micrograms of dexmedetomidine were the dosages of drugs taken in our study. It has been shown in various literature studies that dexmedetomidine and clonidine have a 1:10 binding affinity to the spinal alpha-2 receptors. Different researchers used various doses of dexmedetomidine and clonidine in their studies and published their papers. For example, dexmedetomidine and clonidine were utilised in studies by Sarma et al. at dosages of 5 micrograms and 50 micrograms, respectively. Dexmedetomidine and clonidine were utilised in studies by Kanazi et al. (5) at dosages of 3 micrograms and 30 micrograms, respectively. In the literature after extensive pharmacological studies, they have demonstrated that dexmedetomidine and clonidine dosages were equipotent at a 1:10 ratio and they found out that they would have a similar impact on the properties of bupivacaine spinal anaesthesia. Clonidine was therefore chosen in our study at a dosage of 30 micrograms, which is 10 times the dosage of dexmedetomidine.

We found that our control group A took 21.3 mins, the dexmedetomidine group B took 26.1 mins, and the clonidine group C took 18.7 mins to reach maximum sensory block. When comparing the clonidine group to the control group, there was no statistically significant decrease in the mean time required for attaining the maximum sensory block. When compared to groups A and C, the mean time required for attaining the greatest sensory block was statistically longer in the dexmedetomidine group B. Our study was comparable with the study quoted by Kanazi et al (5) in 2006, where the peak sensory level in control (bupivacaine)

group B was mentioned as 20.2 +/- 8.4 minutes whereas in group C (clonidine) it was noted to be 18.7 +/- 9.2 minutes and in group D (dexmedetomidine) it was 24.5 +/- 14.8 minutes. Saxena et al. (6) found that the mean duration to reach the maximal sensory level in the control group was 7.3 mins, and that it was 6.8 mins, 7.4 mins, and 6.7 mins in the clonidine groups (15 mcg, 30 mcg, and 37.5 mcg, respectively) in his study group.

The median and range of the peak sensory level reached in a study documented by Kanazi et al. (5) were as follows - T6 was the peak sensory block attained in group B (control group), T6. 5 was the level attained in group C (clonidine group) and T6 was the level attained in group D (dexmedetomidine group), with no difference in variations between the groups. There was also no statistically significant difference in the maximal level of sensory block between groups in various studies quoted in literature (2, 7, 8,9) with dexmedetomidine and clonidine which was consistent with our work.

We found that the mean time taken for the onset of motor blockade in the current study was 10.8 minutes in the control group, 3.1 minutes in group B (dexmedetomidine) and 3.7 minutes in group C (clonidine). When compared to the control group, the mean time taken for the onset of motor blockade was significantly shorter in the dexmedetomidine and clonidine groups. There was no significant difference between group B and group C with regards to the mean time taken for the onset of motor blockade. Saxena et al. (6) and various other studies in the clonidine group (10), Kanazi et al. (5) along with other studies in the dexmedetomidine group (11, 12) noticed a significant reduction in the mean time for onset of motor block which correlated with our study.

It took 92.5 minutes in control group, 124.5 minutes in dexmedetomidine group and 119.4 minutes in clonidine group for 2 segments of the sensory block to regress in our study. When a comparison was made with the control group, there was a statistically significant increase in the mean time required for the regression of the sensory block by 2 segments in the dexmedetomidine and clonidine groups. Time taken for 2 segments of sensory block to regress was not statistically significant between group B and group C. Kanazi et al. (5) found that 2 segment regression of the sensory block took 80 min in the control group, 101 mins in the clonidine group and 122 mins in the dexmedetomidine group during their study. This finding was comparable to our current study in that it showed a significant prolongation of 2 segment regression compared to the control group. Our study was in line with findings by Sethi et al. (13) and other studies in clonidine group (6) and studies done by Gupta et al (8) and various other quoted studies in the dexmedetomidine group (9). In all of these studies of literature, the authors noticed a statistically significant 2 segment increase in the mean time required for sensory block regression

Mean duration time for the motor block in our study was 149.1 minutes in control group A, 252.5 minutes in the dexmedetomidine group and 217 minutes in the clonidine group. In comparison to the control group, there was a significant increase in duration of motor block in the dexmedetomidine group B and the clonidine group C. Additionally, we observed a statistically significant increase in duration of motor block in group B compared to group C. Kanazi et al. (5) showed that in their study the mean duration time of motor block was 163±47 minutes in the control group, 216±35 minutes in the clonidine group, and 250±76 minutes in the dexmedetomidine group which was comparable to our study. Our study nearly agreed with that of Kaabachi et al. (14), who found that administering the drug clonidine at a dose of 1 microgram/kg caused a motor block that lasted an average of 252 minutes. Similar outcomes were noted in various other studies conducted by Al Ghanem et al. (7,8,9,11) in dexmedetomidine group and in studies conducted by Saxena et al. (6) and similar (2, 3,7,13) in the clonidine group.

LIMITATION OF THE STUDY

Normal saline was added to the test solutions which might alter the baricity of the local anesthetic used.

CONCLUSION

We compared the duration of sensory and motor blocks in our study between the three groups – Group A (Control), Group B (Dexmedetomidine) and Group C (Clonidine) in elective lower limb and lower abdominal surgeries and we observed that there was

- Significant increase in duration of sensory block in dexmedetomidine and clonidine group
- Significant increase in duration of motor block in dexmedetomidine group and clonidine group

- When compared to the clonidine group, the dexmedetomidine group had a significant increase in duration of motor block.

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