

## Comparison of the Duration of Analgesia, Duration of Sensory and Motor Blockade and Incidence of Side Effects of Intrathecal 0.75% Isobaric Ropivacaine with Combination of 0.75% Isobaric Ropivacaine and Dexmedetomidine

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### Abstract

**Introduction:** Ropivacaine has a reduced risk of cardiotoxicity, neurotoxicity, and rapid recovery of motor function.

Postoperative pain relief is an important issue with Ropivacaine. Dexmedetomidine which is a highly selective  $\alpha$ -2 adrenergic agonist with eight times greater affinity for receptors than clonidine decrease the requirements of analgesics and augment the effects of local anaesthetics

**Aim and Objective:** Compare the analgesic efficacy of intrathecal isobaric 0.75% Ropivacaine with the combination of isobaric 0.75% Ropivacaine and Dexmedetomidine.

**Study design:** A prospective randomized double-blinded study.

**Sample size:** 100 patients were selected and allocated in two groups randomly.

#### Inclusion criteria

- ASAI & II
- Either sex
- 18-60 years for lower limb Orthopaedic surgery

#### Exclusion criteria:

- Patient refusal
- Patients who had contraindications for spinal anaesthesia
- Allergy to local anaesthetics
- Cardiac disease
- Hypertension

Patients were divided into two following groups randomly by lot method.

- **Group R:** Received 3ml volume of 0.75% isobaric ropivacaine and 0.5ml normal saline.
- **Group D:** Received 3ml volume of 0.75% isobaric ropivacaine and 5 $\mu$ g dexmedetomidine in 0.5ml normal saline

**Observations:** Ropivacaine vs. plain 0.75% isobaric Ropivacaine given intrathecally in patients who underwent lower limb orthopedic surgeries.

The following observations were made:

1. The addition of 5 $\mu$ g Dexmedetomidine to 0.75% Ropivacaine significantly prolonged the duration of analgesia and the time to demand analgesia.
2. The addition of dexmedetomidine intrathecally produced sedation that was arousable for many hours compared to plain ropivacaine group
3. The incidence of side effects such as hypotension and bradycardia were more in patients who received dexmedetomidine But shivering was greatly reduced in dexmedetomidine.
4. No episode of respiratory depression was noted in both the study groups which are more common with opioids.

**Keyword:** Ropivacaine, Dexmedetomidine, Intrathecal, Isobaric

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### Introduction

The technique and concept of spinal anaesthesia had improved with the use of local anaesthetics pure isomeric compounds such as Ropivacaine and

Levobupivacaine. Ropivacaine, first single enantiomer specific compound, reduced the risk of cardiotoxicity, neurotoxicity with rapid recovery of motor function. Postoperative pain relief was an important issue with Ropivacaine. So we decided to use an adjuvant with Ropivacaine to provide prolonged postoperative analgesia with better intraoperative haemodynamic conditions with minimal side effects.

Regionally applied opioids were effective analgesics. The first report on intrathecal opioid anaesthesia was published in 1901 and on epidural morphine in 1979. Besides morphine various other opioids and adjuvants have been introduced including

NMDA antagonists (ketamine, magnesium), GABA agonists (midazolam) and adrenergic agonists (clonidine, adrenaline), COX-inhibitors (ketorolac), Ach-esterase inhibitor (neostigmine) etc.

An ideal adjuvant provides a longer duration of analgesia and better hemodynamic stability. Dexmedetomidine, highly selective  $\alpha$ -2 adrenergic agonist with eight times greater affinity for receptors than clonidine. They also augment the effects of local anaesthetics by causing hyperpolarisation of nerve cells and alters the transmembrane potential and conduction of ion in the brain stem (Locus Coeruleus) (11,17,18,23,24).

With the knowledge of pharmacological properties and drug interactions, we designed prospective randomised controlled study in a double-blinded manner at our institution for the patients receiving spinal anaesthesia who underwent lower limb orthopaedic surgeries. Our aim was to compare the analgesic efficacy of intrathecal isobaric 0.75% Ropivacaine with the combination of isobaric 0.75% Ropivacaine and Dexmedetomidine.

### Aim of the Study

To compare the effect of dexmedetomidine as an adjuvant to intrathecal Ropivacaine on the duration of analgesia, duration of sensory and motor blockade and incidence of side effects.

### Materials and Methods

The ethical committee approval from the institution obtained. 100 patients were randomly selected based on inclusion criteria and allocated into two equal groups. Study design: A prospective randomized double-blinded study.

Sample size: A Hundred patients were selected and allocated in two equal groups randomly.

#### Inclusion criteria

- ASA I & II
- Either sex
- 18-60 years for lower limb Orthopaedic surgery

#### Exclusion criteria:

- Patient refusal
- Patients who had contraindications for spinal anaesthesia
- Allergy to local anaesthetics
- Uncontrolled systemic illness

#### Preoperative preparation

Patients, age, body weight and baseline vital parameters were recorded. History regarding previous anaesthesia, surgery and significant other comorbid illness, medications and allergy was recorded. Complete physical examination and airway assessment were done.

In the preoperative period all patients were instructed about the benefits of spinal anaesthesia and

10-point visual analogue scale and informed consent obtained from all the study group patients.

#### Premedication

All patients were premedicated with T. Ondansetron 4mg and T. Ranitidine 150 mg at 6 am on the day of surgery.

#### Materials Used

- Spinal needle (Quincke) 23 or 25G
- 5 ml syringe
- 4 ml ampoule of 0.75% isobaric Ropivacaine (Preservative-free)
- 1 ml ampoule of 100  $\mu$ g Dexmedetomidine.

#### Monitoring and intravenous access

Continuous ECG and pulse oximetry, automated intermittent non-invasive blood pressure monitoring was done. Intravenous access was done using 16 or 18 Gauge venflon and intravenous crystalloid was started.

#### Procedure

Preoperative heart rate, SpO<sub>2</sub>, blood pressure was obtained. Under strict aseptic precautions with the patients in sitting position subarachnoid block was performed using 23-25G Quincke needle at L3-4, or L4-5 space.

Patients were divided into two following groups randomly by lot method.

Group R: Received 3ml volume of 0.75% isobaric ropivacaine and 0.5ml normal saline.

Group D: Received 3ml volume of 0.75% isobaric ropivacaine and 5 $\mu$ g dexmedetomidine in 0.5ml normal saline.

The consultant who prepared the drug combination did not participate in the monitoring or assessment of the patient. The person who performed the spinal anaesthesia, as well as monitoring, was blinded to the groups the patient belongs to. Injections were given over approximately 10 to 15 seconds. Immediately after completion of the block, patients were made to the supine position.

Heart rate, SpO<sub>2</sub>, blood pressure were recorded every 5min for 30 min following the subarachnoid block and every 10min thereafter till surgery finishes. Oxygen 4L/min was administered through a face mask. Hypotension defined as a decrease in mean arterial pressure more than 30% from baseline or less than 80 mm Hg was treated with incremental intravenous (IV) doses of ephedrine 6 mg and boluses of IV fluid as required. The incidence of adverse effects such as nausea, vomiting, shivering, itching, pruritus, respiratory depression, sedation and hypotension was recorded.

The sensory level was assessed using the loss of pinprick sensation and the dermatomal level was tested every 2 minutes until the highest level had stabilised for 4 consecutive tests. Testing was done every 10 minutes until the point of two segment regression of the sensory level. Testing was performed by an anaesthetist who

was blinded to the patient group. Testing was continued every 20 minutes until the recovery of S1 dermatome.

Motor block was assessed using modified Bromage scale

- 0 - no motor block,
- 1 - Inability to lift the extended legs, but can bend knees and feet
- 2 - Inability to lift extended leg and move knee, but can move feet
- 3 - full motor block of the limb

The surgeon and the observing anaesthetist were blinded to the patient groups. Data regarding the highest dermatomal level of sensory blockade, the time to reach the highest sensory level from the time of injection, time to S1 sensory regression and incidence of side effects were collected.

Four-point verbal rating scale was used to assess the sedation (1 = no sedation, 2=light sedation, 3=somnolence, 4= deep sedation).

#### **Assessment of Pain using visual analogue score**

The pain was assessed using visual analogue scale was used to assess rating from 0 to 10 during the intraoperative period. Postoperatively, pain scores were recorded by using VAS between 0 and 10 (0 = no pain, 10 = the most severe pain), initially every 1 hour for 2 hours, then every 2 hours for next 8 hours and then after every 4 hours till 24 hours. Injection Diclofenac 75 mg intramuscular was given as rescue analgesia when VAS  $\geq 4$ .

#### **Recording of adverse effects**

During the intraoperative and postoperative period, adverse events like nausea, vomiting, shivering, dry mouth were noted. Nausea, vomiting were managed with 4mg of ondansetron intravenously. Shivering was treated with Inj. Tramadol 100mg slow IV.

#### **Observations and Results**

The following observations were made: Heart Rate, Blood pressure, SpO<sub>2</sub> every 5 minutes until 1 hour and at every 15 minutes for next one hour and then every 60 minutes for next 22 hours. Hypotension (defined as fall in systolic arterial pressure less than 90mmHg) was managed with inj.Ephedrine 6mg and bradycardia (pulse rate <50 /min) was treated with 0.3mg of inj.Atropine.

- Time to achieve maximum sensory block in minutes
- Time to two segment regression from highest sensory level in minutes
- Duration of motor blockade in minutes
- Duration of analgesia in minutes
- Highest VAS score
- Incidence of side effects

#### **Statistical Analysis**

Data were analysed using INSTAT 3 (Graph Pad Software, California, USA).Two sided independent student' s t tests to analyse continuous data, Fisher's exact test and chi-square test for categorical data were used. P<0.05 was considered as statistically significant.

#### **Results**

##### **Demographic data**

The two groups were comparable with respect to their age, weight, sex and ASA Physical status. There was no statistically significant difference among two groups in demographic profile and saturation.

The mean duration of analgesia was 204.7 $\pm$  20.61minutes in Group R and 430.9 $\pm$  33.08minutes in Group D. There was statistically significant difference among two groups in the mean duration of analgesia (P<0.05).

There is no difference in highest sensory level obtained in between two groups. Both group R and group D were comparable in respect to the highest level of the sensory block obtained (p value0.8143 i.e >0.05).The mean time to attain highest sensory block was 8.18 $\pm$  1.7921minutes in Group R and 5.52 $\pm$ 2.159 minutes in Group D. There was a significant difference among two groups in the time to attain highest sensory block (P<0.05). The mean time for two segment regression was 96  $\pm$  4.94minutes in Group R and 134  $\pm$  6.06minutes in Group D. There was a significant difference among two groups in the duration two segment regression (P<0.05).

The mean duration of motor blockade was 144.06  $\pm$  18.75 minutes in Group R and 271.46  $\pm$  33.40 minutes in Group D. There was statistically significant difference among two groups in the mean duration of analgesia (P<0.05).

Sedation, as assessed by four-point verbal scale, was significant during 10min-360min of the observing period between the two groups while not significant during the first 5min and after 360min as shown by the p values. VAS score between group R and group D were found to be significant during the whole period of observation (p<0.05).

The intraoperative mean heart rate in Group R was 90.1 $\pm$  4.39 and in Group D 67.136  $\pm$ 10.7was, which was found to be statistically significant (p<0.05). The postoperative mean heart rate in Group R 94.25 $\pm$  2.818 was and in Group D 60.64  $\pm$ 0.599 was, which was found to be statistically significant (p<0.05). The intraoperative and postoperative mean arterial pressure in Group R was 95.76 $\pm$  7.45 and 109 $\pm$  11.53 respectively. Group D intraoperative and postoperative mean arterial pressure were 83.04 $\pm$ 16.12 and 87.74 $\pm$ 4.46 which was statistically significant (p<0.05).

#### **Discussion**

An ideal adjuvant provides a longer duration of analgesia, better hemodynamic stability with fewer side

effects. Dexmedetomidine had widened the scope of  $\alpha$ -2 agonists usage in the neuraxial blockade. Rapid onset of local anaesthetics action, the longer period of analgesia and better cardiovascular parameters have increased dexmedetomidine intrathecal use.

In our study 5 $\mu$ g of dexmedetomidine (made up to 0.5ml with normal saline) was added to 3ml of 0.75% Ropivacaine or 3ml of 0.75% Ropivacaine with normal saline 0.5ml added. The efficacy of dexmedetomidine as an adjuvant in neuraxial analgesia was studied in 50 patients in each group who underwent elective lower limb orthopedic surgeries.

The patients in both the groups with respect to age, weight, ASA Physical status did not show statistically significant difference.

### Duration of analgesia

The study had shown that addition of 5 $\mu$ g of dexmedetomidine to 3ml of 0.75% Ropivacaine in group D prolongs the duration of analgesia about 2 times of the plain Ropivacaine group R. In group R duration of analgesia was only 204.7  $\pm$  20.61mins compared to group D which was almost 2 times of group R 430.9  $\pm$  33.08 mins. This result was concurrent with the Gupta R et al (1): (2011; 55:347-51) study where they concluded that the duration of analgesia was prolonged for about 478 $\pm$ 20.9 minutes in group D compared to group R which as only 241.67 $\pm$ 21.67 minutes duration. This result was also correlated with the study Shukla et al(16), where they concluded that onset of anesthesia was faster with prolonged duration of analgesia in the group (D).

### Time to Regression of Block to S1

The time to regression of sensory blockade to S1 in group D was 423.3  $\pm$  32.66 mins and in Group R was 189 $\pm$ 23.44 mins was statistically significant. This result was correlated with study done by Gupta R et al (1) in their study the mean time for S2 segment regression was 468.3  $\pm$  36.78 minutes in group D and 239.33  $\pm$  16.8 minutes in group R. Kanazi GE et al(19): had observed that patients in dexmedetomidine group D and Clonidine group C had early onset time of motor block and a prolonged sensory and motor regression times than plain bupivacaine group B which was statistically significant. The mean time of S1 segment regression was 303  $\pm$  75 mins in group D, 272 $\pm$ 38 mins in group C and 190 $\pm$ 48 mins in group B. Gupta R et al (20): had observed that the mean time of sensory level regression to S1 dermatome was 476  $\pm$  23 mins in dexmedetomidine group D and 187  $\pm$  12 mins in fentanyl group F (P<0.001). Shukla et al(16): had found that faster onset and longer duration of anesthesia in the dexmedetomidine group (D).

### Duration of motor blockade

There was significant prolongation in the duration of the motor blockade in group D with 271.46 $\pm$ 33.40

mins when compared to group R i.e. 144.06 $\pm$ 18.75 mins. These results correlate with study done by Kanazi et al(19) who showed that the motor block duration was 250  $\pm$  76 min in dexmedetomidine group D, 216  $\pm$  35 min in clonidine group C and 163  $\pm$  47 min in plain bupivacaine group B. Gupta et al(20): evaluated the motor block duration was about 421  $\pm$  21 min in dexmedetomidine group D and about 149 $\pm$ 18 min in fentanyl group F (P<0.001). They found out that the spinal dexmedetomidine was associated with longer duration of motor and sensory block. Al-Mustafa MM et al(21) concluded that Dexmedetomidine had an effect on the onset and regression of sensory and motor block in a dose-dependent manner when used as an intrathecal adjuvant to bupivacaine. Eid HEA et al (22) concluded that the Intrathecal dexmedetomidine in two different doses (10 $\mu$ g and 15 $\mu$ g) significantly prolonged the anesthetic and analgesic effects of intrathecal bupivacaine in a dose-dependent manner. Shukla et al (16) recorded onset time to reach peak sensory and motor level, the regression time for sensory and motor block, hemodynamic changes and side effects. They founded that faster onset of anesthesia with prolonged duration of analgesia in the dexmedetomidine group.

### Sedation score

The results of our study clearly indicate the sedation score between the two groups was similar in the initial period after study drug administration and they had profound sedation but arousable by gentle tactile stimulation (i.e. four-point verbal rating scale of 2). After 10mins, the percentage of dexmedetomidine group patients who have scored higher sedation scores is more compared to group R. There was a significant sedative effect for dexmedetomidine group of patients.

### Hemodynamic stability

The heart rate, mean arterial pressure remained stable both during the intraoperative and postoperative period. Although a fall in heart rate and blood pressure (both systolic and diastolic) was noted in both the groups, it never decreased below the 20% of baseline values. But hypotension and bradycardia were observed more in group D patients which are statistically significant and was correlated with the results of Gupta et al(1), Kanazi et al(19).

### Side Effects

The incidence of bradycardia in Group R was 30% and in Group D was 70% and there was statistically no significant difference in both groups (p>0.05). The incidence of nausea and vomiting in Group R 70% and in Group D was 30% which was statistically not significant (p>0.05). The incidence of shivering in Group R was 90% and in Group D was 10% and there was statistically significant difference in both groups (p<0.05).

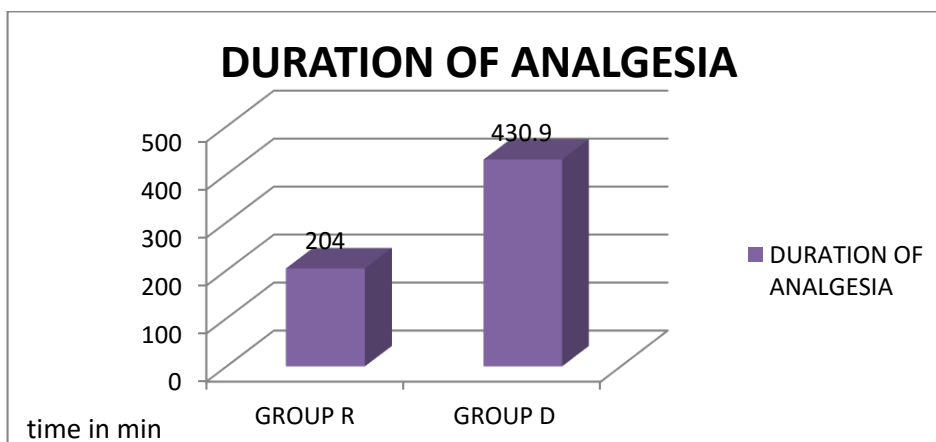
The incidence of dry mouth in Group C was 50% and in Group D 50%. Statistically, there was no significant difference in both groups ( $p > 0.05$ ). These results had concurrence with the results of Eid HEA et al(22).

**Vas Score**

VAS score between group R and group D were found to be significant during the whole period of observation ( $p < 0.05$ ) which correlated with study done by Gupta et al(1). which showed the maximum visual analogue scale score for pain was less in group D ( $4.4 \pm 1.4$ ) as compared to group R ( $6.8 \pm 2.2$ ).

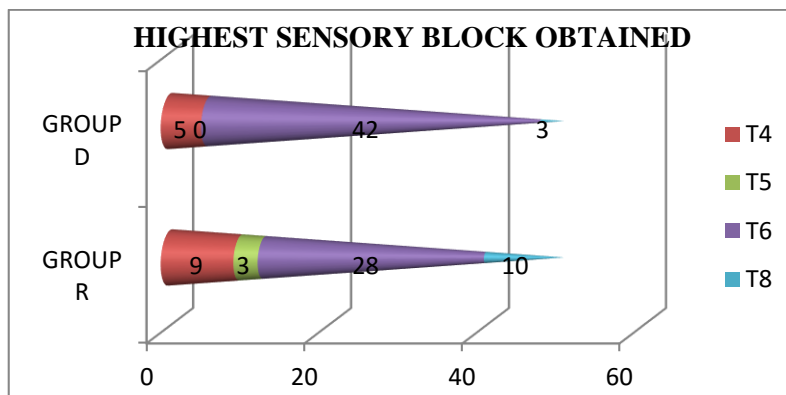
**DURATION OF ANALGESIA(In Min)(Student T Test) In Minutes**

	No. of Cases	Mean±S.D	p value
Group R	50	204.7± 20.61	0.0001
Group D	50	430.9± 33.08	



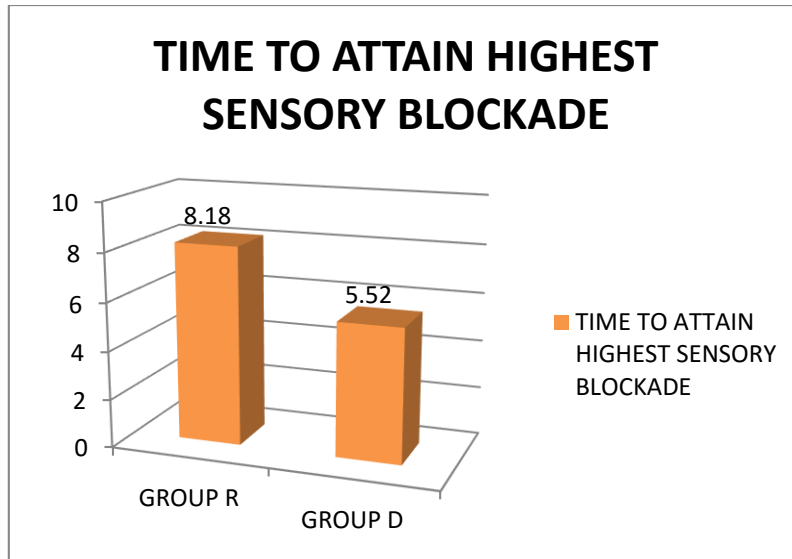
**HIGHEST SENSORY BLOCK OBTAINED number of patients**

Level	Group R	Group D	P value
T4	9(18%)	5(10%)	0.8143
T5	3(6%)	0(0%)	
T6	28(56%)	42(84%)	
T8	10(20%)	3(6%)	



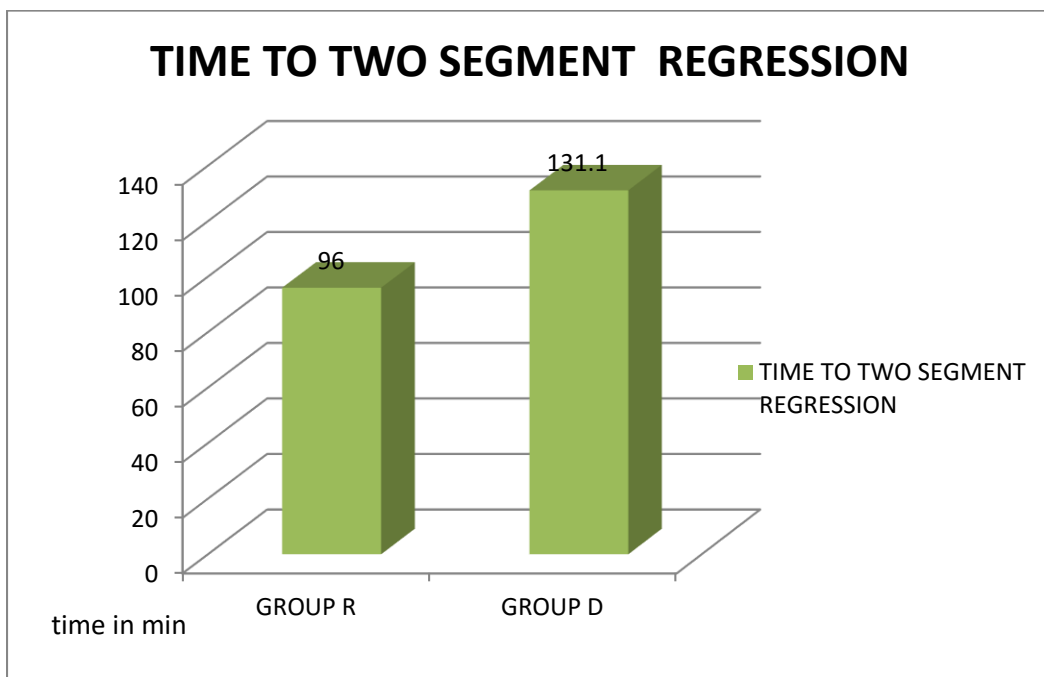
**TIME TO ATTAIN HIGHEST SENSORY BLOCK in min (student's t test) in minutes**

	No. of Cases	Mean±S.D	p value
Group R	50	8.18± 1.7921	0.0001
Group D	50	5.52±2.159	



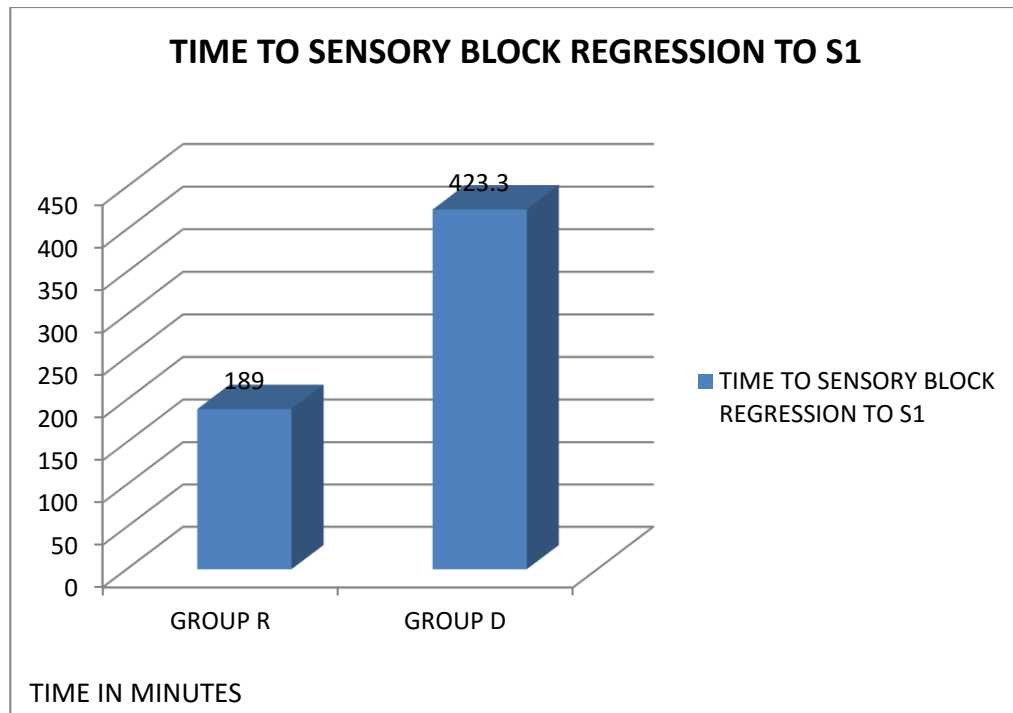
**TIME TO TWO SEGMENT REGRESSION in min (student's t test) in minutes**

	No. of Cases	Mean±S.D	p value
Group R	50	96± 4.94	0.0001
Group D	50	134±6.06	



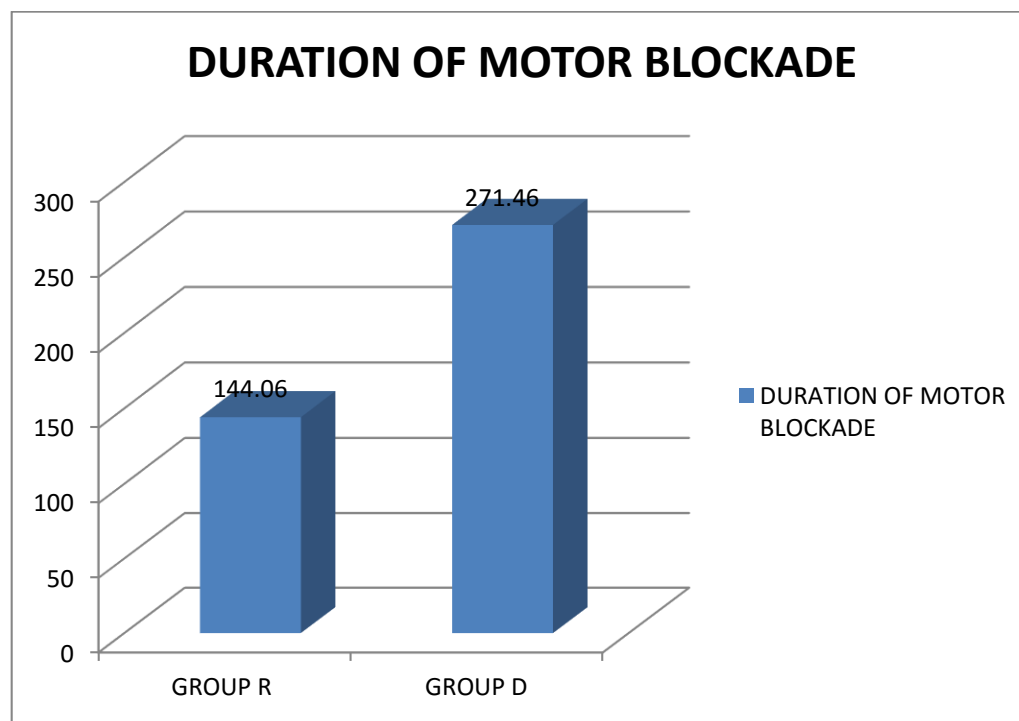
**DURATION OF REGRESSION TO S1 (student's t test) in minutes**

	No. of Cases	Mean±S.D	p value
Group R	50	189.1± 23.44	0.0001
Group D	50	423.3± 32.66	



**DURATION OF MOTOR BLOCKADE (student's *t* test) in minutes**

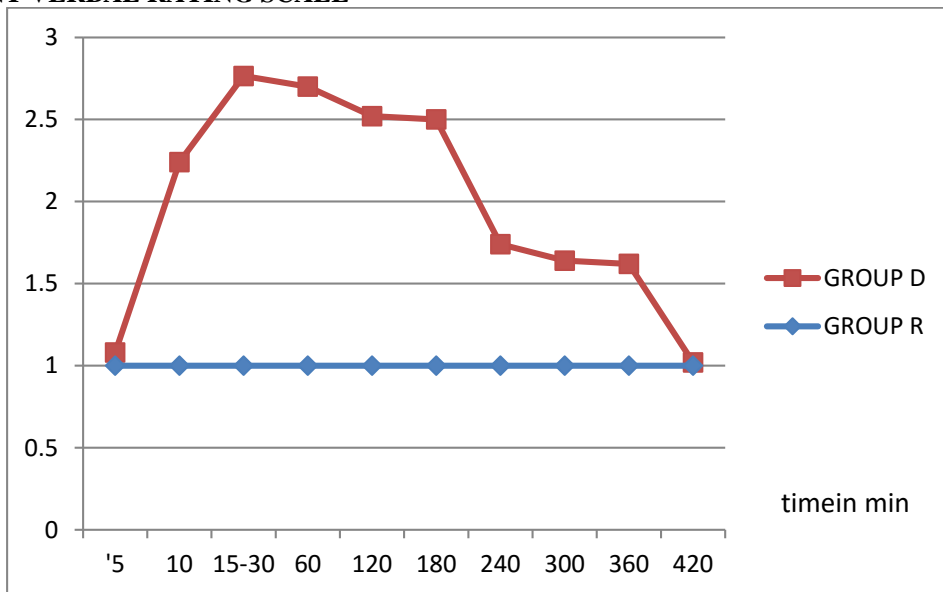
	No. of Cases	Mean±S.D	p value
Group R	50	144.06 ± 18.75	0.0001
Group D	50	271.46 ± 33.40	



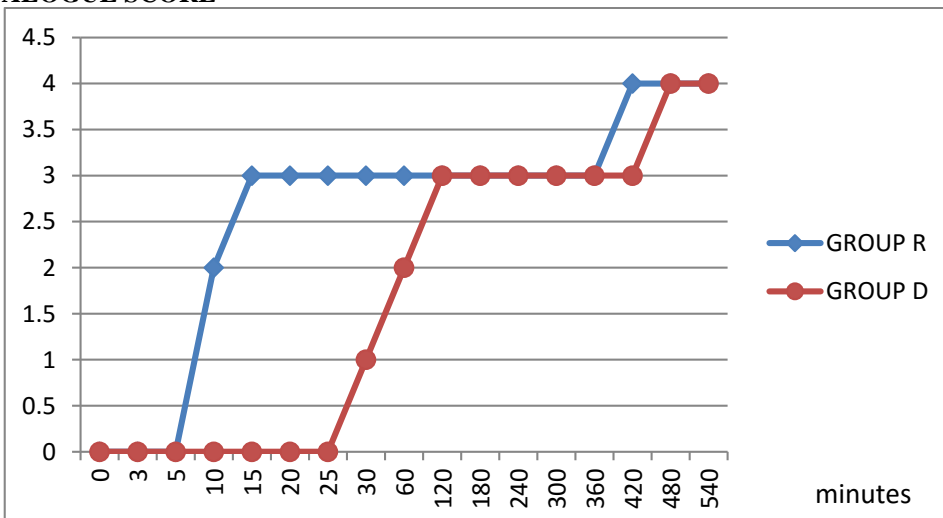
**FOUR POINT VERBAL RATING SCALE (student's t test)**

Time in Minutes	No. of Cases	Group R	Group D	P Value
5	50	1	1.08±0.2740	0.0416
10	50	1	2.24±0.4314	0.0001
15-30	50	1	2.765±0.425	0.0001
60	50	1	2.7±0.4529	0.0001
120	50	1	2.52 ±0.504	0.0001
180	50	1	2.5±0.505	0.0001
240	50	1	1.74±0.4646	0.0001
300	50	1	1.64±0.4848	0.0001
360	50	1	1.62±0.4848	0.0001
420	50	1	1.02±0.1414	0.3197

**FOUR POINT VERBAL RATING SCALE**



**VISUAL ANALOGUE SCORE**





**VISUAL ANALOGUE SCORE (student's t test)**

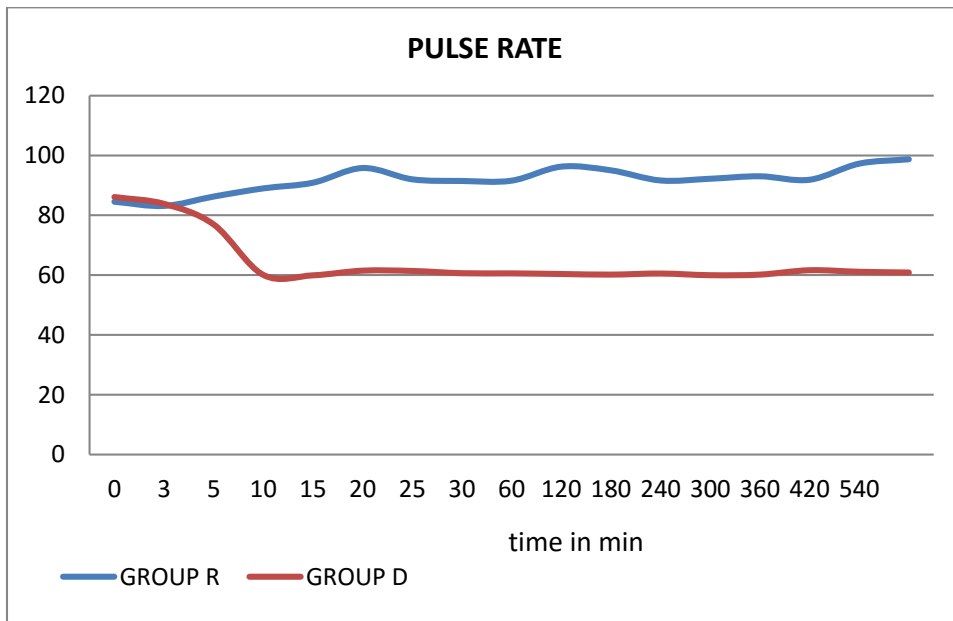
Time in Minutes	No. of Cases	Group R	Group D	P value
30	50	1.79±1.506	0.125±0.35	0.0001
60	50	3.14±0.78	1.78±0.79	0.0001
120	50	3.18±0.74	2.74±0.44	0.0005
180	50	3.18±0.74	2.74±0.44	0.0003
240	50	3.18±0.74	2.52±0.5	0.0001
300	50	3.18±0.74	2.52±0.5	0.0001
360	50	3.18±0.74	2.72±0.45	0.0003
420	50	4±0	2.42±0.57	0.0001
480	50	4±0	2.88±0.65	0.0001
540	50	4±0	2.92±0.92	0.0001

**INTRAOPERATIVE PULSE RATE (student's t test) rate per minute**

	No. of Cases	Mean ± S.D	p value
Group R	50	90.1± 4.39	0.0001
Group D	50	67.136 ±10.7	

**POSTOPERATIVE PULSE RATE (student's t test)**

	No. of Cases	Mean ± S.D	p value
Group R	50	94.25± 2.818	0.0001
Group D	50	60.64 ±0.599	

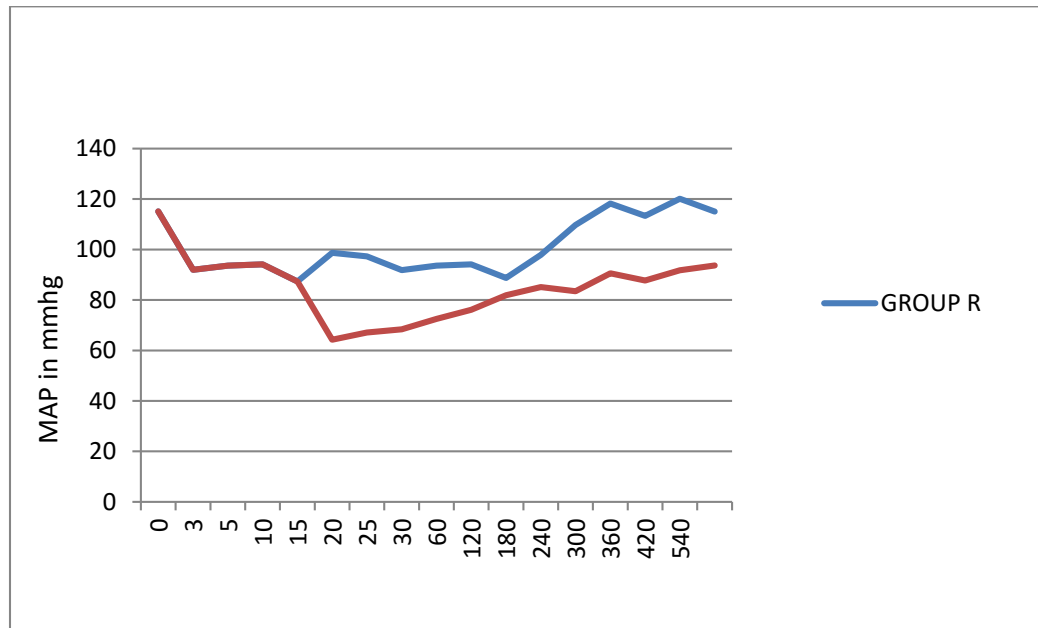


**INTRAOPERATIVE PERIOD MAP (student's t test) im mmhg**

	No. of Cases	Mean ± S.D	p value
Group R	50	95.76± 7.45	0.0001
Group D	50	83.04±16.12	

**POSTOPERATIVE PERIOD MAP (student's *t* test) in mmhg**

	No. of Cases	Mean $\pm$ S.D	p value
Group R	50	109 $\pm$ 11.53	0.0001
Group D	50	87.74 $\pm$ 4.46	

**Conclusion**

The addition of 5ug Dexmedetomidine to 0.75% Ropivacaine significantly prolonged the duration of analgesia, the time to demand analgesia and produced sedation that was arousable for many hours compared to plain ropivacaine. The incidence of side effects such as hypotension and bradycardia were more in patients who received dexmedetomidine but were able to manage easily. No episode of respiratory depression was noted in both the study groups which are more common with opioids. Dexmedetomidine may be a better adjuvant to Ropivacaine intrathecally in the prolonging duration of analgesia with fewer side effects.

**Conflict of Interest: None****Source of Support: Nil****References**

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