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Clinical Investigation

Comparison of Intrathecal 0.75% Isobaric Ropivacaine and 0.75% Isobaric Ropivacaine with Dexmedetomidine, for below Umbilical Surgeries in Adults

Authors

Dr Vani. K. Venu[1], Dr Anzer Shah. M[2*], Dr Santhosh Surendran[3]

[1]Senior Resident, Dept. of Anaesthesiology, Govt. TD Medical College, Alappuzha
[2]Assistant Professor, Dept. of Anaesthesiology, Govt. TD Medical College, Alappuzha
[3]Additional Professor, Dept. of Anaesthesiology, Govt. TD Medical College, Alappuzha
*Corresponding Author
Dr Anzer Shah. M
Assistant Professor, Dept. of Anaesthesiology, Govt. TD Medical College, Alappuzha, India

Abstract

Background and Objectives: *Ropivacaine has reduced risk of cardiotoxicity, neurotoxicity with rapid recovery of motor function. We have conducted an observational study on effect of intrathecal 0.75% isobaric ropivacaine and combination of 0.75% isobaric ropivacaine with dexmedetomidine in spinal anesthesia for below umbilical surgeries, based on duration of analgesia, duration of motor blockade, hemodynamic profile and side effects.*

Methods: *After ethical committee approval and informed consent from patients, a prospective observational study was performed on 34 patients scheduled for below umbilical surgeries under subarachnoid block (SAB). This study was done among two group of patients belonging to ASA 1 and 2. Both the groups of patients were comparable with respect to sex, height and weight. Patients were divided into 2 groups according to the drugs they received, Group R: Received 2.5ml volume of 0.75% isobaric ropivacaine and 0.5ml normal saline(n=17). Group D: Received 2.5ml volume of 0.75% isobaric ropivacaine and 5µg dexmedetomidine in 0.5ml normal saline (n=17). Computer software SPSS version-22 (IBM SPSS Statistics, Somers NY, USA) was used for statistical analysis. Independent t test and chi-square test were used and p <0.05 was considered as significant.*

Results and Discussion: *The mean onset of Analgesia in Group R was 2.8 ± 1.0 min and in Group D was 6.6 ± 3.4 min (P <0.001).Mean Duration of Analgesia in Group R was 201.6 ± 16.0 min and in Group D was 263.6 ± 12.7 min12.7 min (P <0.001). Mean Onset of motor block in Group R was 9.2 ± 2.5 min and in Group D was 11.8 ± 4.4 min (P = 0.05).Mean Duration of motor block in Group R was 104 ± 12.1 min and in Group D was 182.9 ± 18.4 min (P <0.001). Incidence of hypotension (P = 0.037 < 0.05) were more in patients who received dexmedetomidine*

Conclusion: *Intrathecal administration of dexmedetomidine with ropivacaine prolongs duration of analgesia and duration of motor blockade and associated with increased incidence of hypotension.*

Keywords: *ropivacaine. dexmedetomidine. isobaric.*

Introduction

The clinically used local anesthetics include bupivacaine, ropivacaine, and levobupivacaine.[1-4] Bupivacaine is widely used as a spinal anesthetic, either as a hyperbaric solution at a concentration of 0.5% with 8% dextrose or by using the nearly isobaric 0.5% solution. Ropivacaine, has reduced risk of cardiotoxicity, neurotoxicity than bupivacaine. Ropivacaine is slightly less potent than (1:1.3 to 1:1.5) bupivacaine for regional anesthesia and produce slightly less motor block and earlier recovery.[1]

Spinal additives allow for a reduction in the required dose of local anesthetic, with the

advantage of motor block sparing and faster recovery while still producing the same degree of analgesia. α2-Agonists- Clonidine, and dexmedetomidine, act on prejunctional and postjunctional α2 receptors in the dorsal horn of the spinal cord. Activation of presynaptic receptors reduces neurotransmitter release and postjunctional receptor activation results in hyperpolarization and reduction of impulse transmission. [5-10]

Dexmedetomidine is a highly selective α-2 adrenergic agonist with eight times greater affinity for receptors than clonidine. It has high selectivity for alpha 2 adrenoreceptors (alpha 2 / alpha 1: 1620 / 1) compared to clonidine (alpha 2 / alpha 1: 220 / 1). It has anxiolytic, analgesic and sympatholytic properties.[11] Neuraxial route is appropriate for administration of adjuvant because of its high lipophilicity. It can prolong motor and sensory block without hemodynamic compromise.[1] Dexmedetomidine has been used intrathecally in varying doses ranging from 3 – 15 µg. A low dose of 5 µg was used in this study [4]

This study compared the effect of intrathecal 0.75% isobaric ropivacaine and combination of 0.75% isobaric ropivacaine with dexmedetomidine in spinal anesthesia for below umbilical surgeries, based on time of onset of analgesia, duration of analgesia, time to reach peak sensory level, onset of motor blockade, duration of motor blockade, hemodynamic profile and side effects.

Materials and Methods

34 patients undergoing elective below umbilical surgeries who fulfilled the inclusion and exclusion criteria were included in the study and allocated into two study groups of 17 each, according to the drug they received intrathecally, and were observed.

Inclusion Criteria

- Age between 18 and 60 years, of both sexes.
- ASA physical status class I and II.
- Weight: 50kg to 70 kg.
- Height between 155 cm to 170cm.

Exclusion Criteria

- Pregnancy
- Patients with sinus bradycardia (Heart rate<50/min)

Sample size was calculated from the data obtained from the pilot study conducted in patients coming for orthopaedic surgery of lower limb by using formula-

Sample size = $(Z\ \alpha/2 + Z\beta)2\ X(SD)^2 \times 2] \div d^2$

$Z\ \alpha/2 = 1.96$

$Z\beta = 0.84$

On substituting values with time to achieve Bromage score 0

Group R 229.37± 28.74minutes

Group D 258.55 ± 30.46minutes

$= [16\ X\ (29.6)^2] \div (29.18)^2$

= 16.46, in one arm

Therefore, a sample size of 34 was arrived.

Study Procedure

After getting clearance from institutional research and ethical committees, study subjects were selected based on inclusion and exclusion criteria. Age, gender, weight and height of participating patients were recorded. Detailed preanesthetic check-up was done. Vitals and detailed physical examination including airway assessment was done. A written informed consent was obtained from these patients. Preoperatively all selected patients were explained about the spinal anaesthesia and visual analogue scale.

Premedication

All selected patients were given T. Alprazolam 0.25mg, C. Omeprazole 20mg and T. Ondansetron 4mg on preoperative day at 10:00 pm and at 6 am on the day of surgery.

Preparation

The anaesthesia machine was checked. Laryngoscopes with appropriately sized blades, endotracheal tubes, oropharyngeal airways, stylet and working suction apparatus were kept ready. All the necessary drugs were drawn in syringes,

labelled and kept ready before the patient was brought to the operation theatre.

When the patient reached thepar anaesthesia room, intravenous line was established using an 18G cannula. Intravenous fluid was started. Patient was shifted to the operation theatre. Standard patient monitors such as ECG, pulse oximeter, non-invasive blood pressure was attached. Sedation was given with Inj. Midazolam 1 mg IV.

Procedure

Patients were placed in right lateral decubitus position. Under strict asepsis and local infiltration with 2ml of 2% lignocaine, lumbar puncture is performed at L3-L4 interspace through a mid-line approach using a 25-guage Quincke Babcock needle.

Patients were divided into 2 groups according to the drugs they received,

Group R: Received 2.5ml volume of 0.75% isobaric ropivacaine and 0.5ml normal saline.

Group D: Received 2.5ml volume of 0.75% isobaric ropivacaine and 5µg dexmedetomidine in 0.5ml normal saline.

Assessment

Study Variables and Measurements

- **Peak sensory dermatome level**: tested by pinprick along midclavicular line, bilaterally, every minute, using a blunt 25-guage needle, until the level is stabilised for two consecutive tests. Testing was done every 10 minutes until the point of 2 segment regression of sensory level.
- **Onset of analgesia**: Time interval from completion of spinal injection to loss of pinprick sensation at T 10.
- **Onset of Motor blockade**: Time interval from completion of spinal injection to inability to move both ankles.

The motor level will be assessed using modified Bromage scale

0 – No motor block

1 – Inability to lift extended legs, but can bend knees and feet

2 – Inability to lift extended leg and move knee, but can move feet

3 – Inability to flex ankle (complete motor block)

End point of analgesia: It is the time at which patient complained of pain of more than 50 in Visual Analogue Scale.

Duration of analgesia: It is the time period between the onset of analgesia to the end point of analgesia.

Other variables: Heart rate, mean arterial blood pressure, oxygen saturation, respiratory rate were monitored and recorded every 5 minutes till surgery finishes. Post –operatively heartrate, blood pressure,O2 saturation were recorded during 1st hour at 15 ,30 ,45 and 60 minutes and thereafter every hour during the study period

Adverse effects: The following adverse effects, if any were noted.

- Bradycardia.
- Hypotension.
- Respiratory depression.
- Nausea and vomiting.
- Pruritis.
- Shivering.

Statistical Analysis

Data was entered in Microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. Chi-square test was used as test of significance for qualitative data. Continuous data was represented as mean and SD. Independent t test or Mann Whitney U test was used as test of significance to identify the mean difference between two quantitative variables and qualitative variables respectively. Graphical representation of data: MS Excel and MS word was used to obtain various types of graphs such as bar diagram, Pie diagram. p value (Probability that the result is true) of <0.05 was considered as statistically significant after

assuming all the rules of statistical tests. Statistical software: MS Excel, SPSS version 22 (IBM SPSS Statistics, Somers NY, USA) was used to analyze data.

Results

The graphical representation, analysis and inference with respect to different study variables are as follows.

1. **Onset and duration of analgesia, motor block and other parameters comparison between two groups**

	Group				P value
	Group R		Group D		
	Mean	SD	Mean	SD	
Onset of Analgesia	2.8	1.0	6.6	3.4	<0.001*
Duration of Analgesia	201.6	16.0	263.6	12.7	<0.001*
Onset of motor block	9.2	2.5	11.8	4.4	0.05
Duration of motor block	104.0	12.1	182.9	18.4	<0.001*
Time for Maximum Sensory block	7.8	1.0	7.8	3.1	1.000
Two Segment Regression	68.2	9.5	112.4	6.6	<0.001*

Mean onset of Analgesia in Group R was 2.8 ± 1.0 min and in Group D was 6.6 ± 3.4 min. There was significant difference in mean onset of analgesia between two groups.

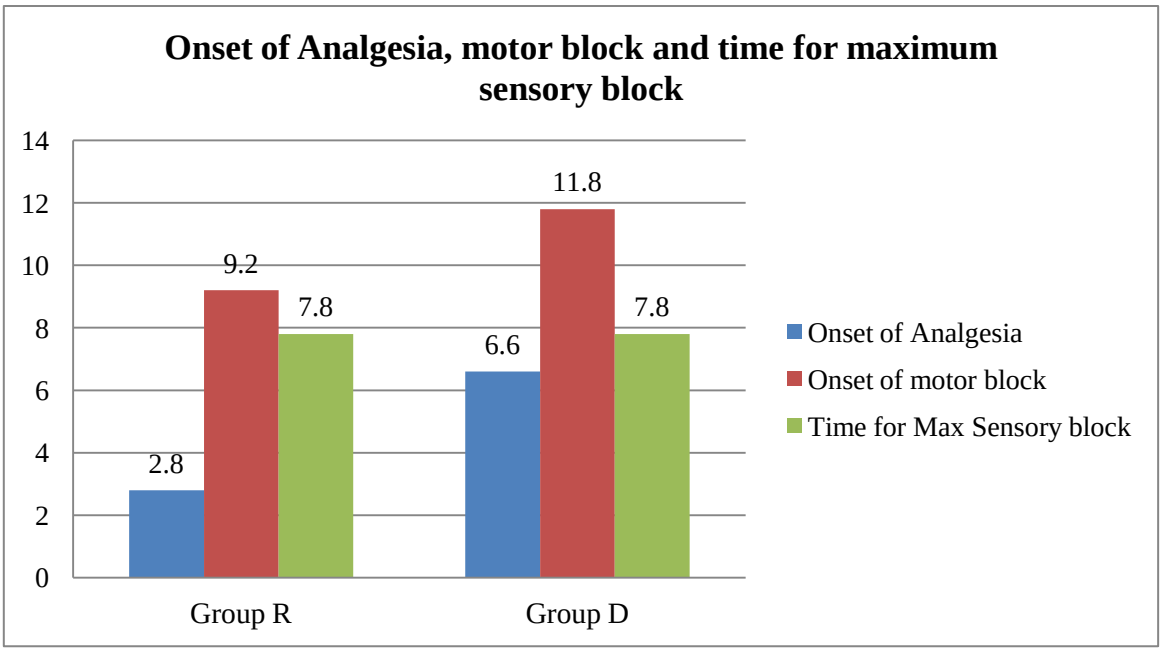
Mean Duration of Analgesia in Group R was 201.6 ± 16.0 min and in Group D was 263.6 ± 12.7 min. There was significant difference in mean duration of analgesia between two groups.

Mean Onset of motor block in Group R was 9.2 ± 2.5 min and in Group D was 11.8 ± 4.4 min. There was no significant difference in mean Onset of motor block between two groups.

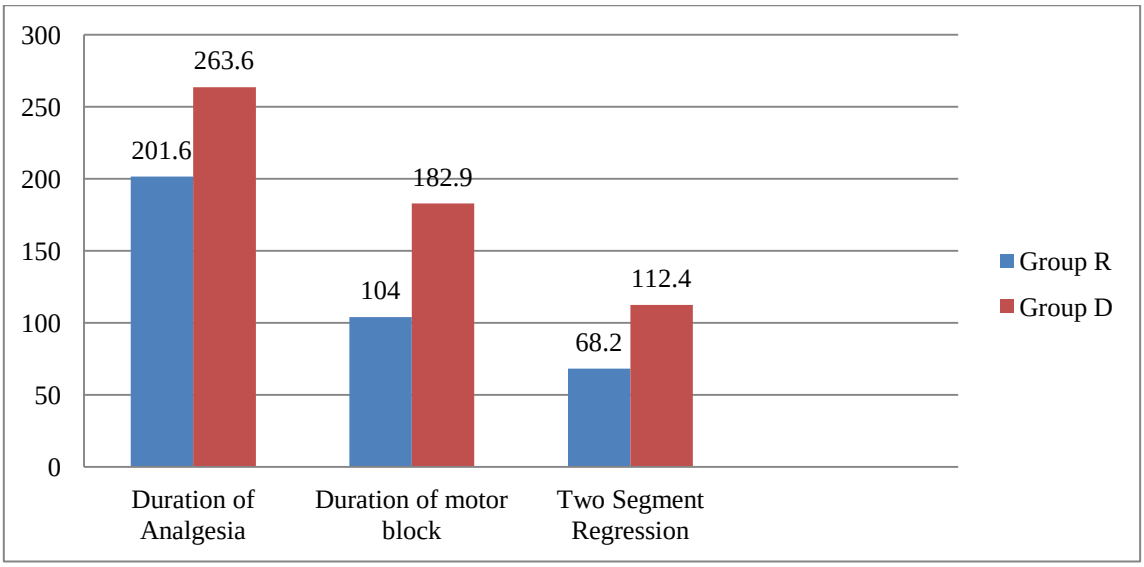
Mean Duration of motor block in Group R was 104 ± 12.1 min and in Group D was 182.9 ± 18.4 min. There was significant difference in mean Duration of motor block between two groups.

Mean Time for Maximum Sensory block in Group R was 7.8 ± 1.0 min and in Group D was 7.8 ± 3.1 min. There was no significant difference in mean Time for Maximum Sensory block between two groups.

Mean Two Segment Regression in Group R was 68.2 ± 9.5 min and in Group D was 112.4 ± 6.6 min. There was significant difference in mean Two Segment Regression between two groups.



Bar diagram showing Onset of Analgesia, motor block and time for maximum sensory block

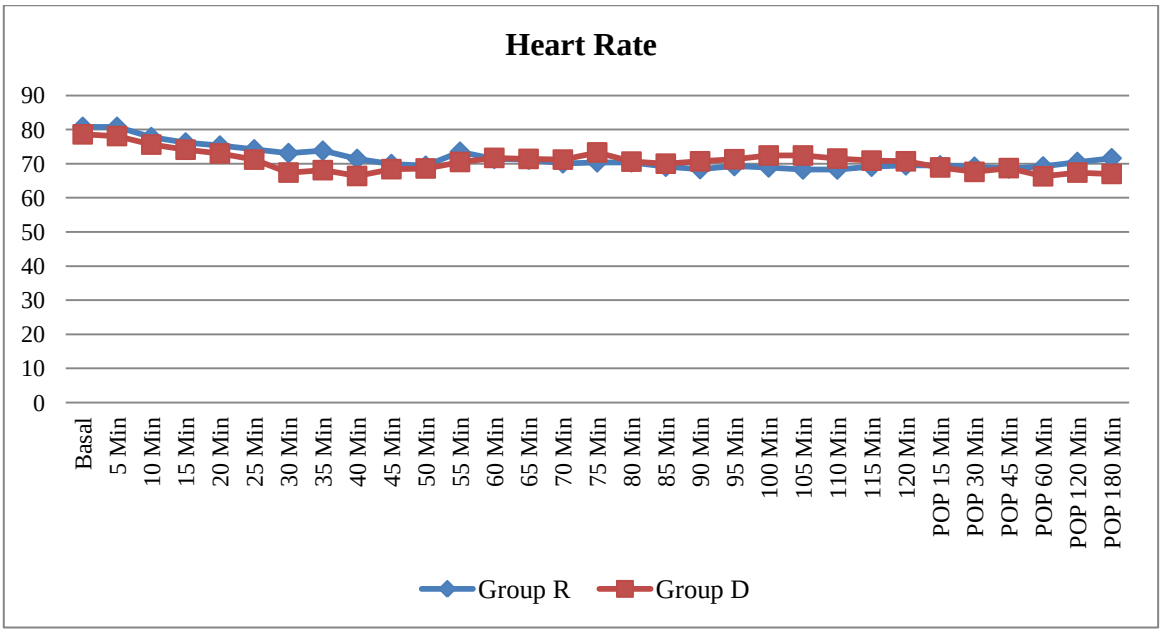


Bar diagram showing duration of analgesia, motor block, two segment regression comparison between two groups

2. Heart Rate Comparison between two groups at different time intervals

Heart Rate	Group				P value
	Group R		Group D		
	Mean	SD	Mean	SD	
Basal	80.8	14.5	78.6	15.9	0.688
5 Min	80.8	15.0	78.1	18.0	0.641
10 Min	77.8	15.0	75.6	16.0	0.685
15 Min	76.2	15.1	74.1	15.7	0.683
20 Min	75.3	16.0	73.0	16.0	0.679
25 Min	74.2	13.6	71.2	15.6	0.556
30 Min	73.1	12.1	67.4	15.0	0.231
35 Min	73.8	14.8	68.1	16.2	0.293
40 Min	71.4	14.0	66.4	14.2	0.310
45 Min	69.9	9.7	68.4	16.4	0.733
50 Min	69.4	13.3	68.6	19.5	0.895
55 Min	73.5	17.6	70.5	19.1	0.637
60 Min	71.4	13.6	71.7	19.3	0.959
65 Min	71.2	11.1	71.4	21.3	0.976
70 Min	70.1	9.3	71.2	19.4	0.832
75 Min	70.4	9.2	73.3	20.1	0.588
80 Min	70.4	9.6	70.6	18.5	0.972
85 Min	69.1	10.5	70.0	19.0	0.868
90 Min	68.4	10.9	70.7	19.4	0.666
95 Min	69.3	9.8	71.3	19.0	0.702
100 Min	68.9	10.5	72.4	19.5	0.523
105 Min	68.3	11.3	72.4	19.7	0.467
110 Min	68.3	10.5	71.5	20.1	0.567
115 Min	69.1	10.6	70.9	19.6	0.747
120 Min	69.5	10.1	70.7	20.2	0.831
POP 15 Min	69.5	11.7	68.9	18.2	0.920
POP 30 Min	69.1	11.7	67.6	17.1	0.772
POP 45 Min	68.6	12.2	68.7	16.4	0.981
POP 60 Min	69.2	11.9	66.3	17.1	0.564
POP 120 Min	70.5	12.0	67.4	17.4	0.548
POP 180 Min	71.6	11.7	67.0	16.2	0.352

In the study there was no significant difference in mean Heart rate between two groups from baseline to 120 min Post Op.

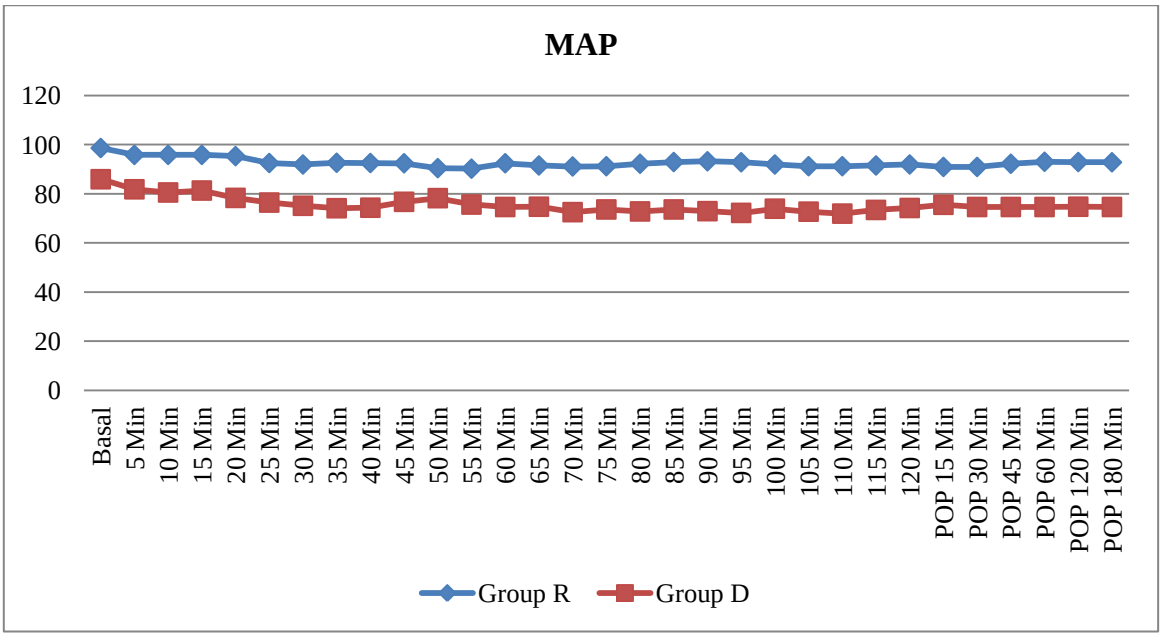


Line diagram showing Heart Rate Comparison between two groups at different time intervals

3. MAP Comparison between two groups at different time intervals

MAP	Group				P value
	Group R		Group D		
	Mean	SD	Mean	SD	
Basal	98.6	10.5	85.9	9.8	0.001*
5 Min	95.8	13.3	81.8	14.9	0.007*
10 Min	95.8	11.6	80.5	10.5	<0.001*
15 Min	95.8	11.3	81.3	10.6	0.001*
20 Min	95.3	11.8	78.3	10.0	<0.001*
25 Min	92.5	9.2	76.4	8.0	<0.001*
30 Min	91.9	8.2	75.1	7.0	<0.001*
35 Min	92.6	9.2	74.1	7.5	<0.001*
40 Min	92.5	11.8	74.3	7.9	<0.001*
45 Min	92.4	10.5	76.7	10.0	<0.001*
50 Min	90.4	14.4	78.2	12.4	0.012*
55 Min	90.2	13.3	75.6	11.8	0.002*
60 Min	92.4	8.4	74.6	9.0	<0.001*
65 Min	91.5	7.8	74.7	10.3	<0.001*
70 Min	91.1	7.3	72.5	8.2	<0.001*
75 Min	91.2	6.6	73.6	7.7	<0.001*
80 Min	92.2	6.5	72.8	7.6	<0.001*
85 Min	92.9	5.9	73.6	7.5	<0.001*
90 Min	93.2	7.1	72.9	6.8	<0.001*
95 Min	92.8	6.3	72.2	6.8	<0.001*
100 Min	91.9	4.8	73.9	8.6	<0.001*
105 Min	91.2	4.7	72.7	6.6	<0.001*
110 Min	91.2	5.4	71.9	6.9	<0.001*
115 Min	91.5	4.1	73.4	6.9	<0.001*
120 Min	91.9	3.6	74.2	8.5	<0.001*
POP 15 Min	90.9	6.8	75.5	11.6	<0.001*
POP 30 Min	90.9	7.4	74.6	8.6	<0.001*
POP 45 Min	92.2	4.1	74.6	9.8	<0.001*
POP 60 Min	93.0	6.2	74.6	10.9	<0.001*
POP 120 Min	92.9	8.0	74.7	9.4	<0.001*
POP 180 Min	92.8	6.5	74.6	8.8	<0.001*

In the study there was significant difference in Mean MAP between two groups from baseline to 120 Min post op. Mean MAP was significantly higher in Group R than in Group D.



Line diagram showing bar diagram showing Heart Rate Comparison between two groups at different time intervals

4. **VAS Score Comparison between two groups at different time intervals**

VAS	Group				P value
	Group R		Group D		
	Mean	SD	Mean	SD	
1hr	4.7	6.2	3.5	4.9	0.708
2hr	20.0	11.7	20.0	11.7	1.000
4hr	40.0	.0	27.6	9.0	1.000
6hr	40.0	.0	40.0	.0	1.000
8hr	40.0	.0	40.0	.0	1.000
12hr	40.0	.0	40.0	.0	1.000
16hr	40.0	.0	40.0	.0	1.000
20hr	40.0	.0	40.0	.0	1.000
24hr	40.0	.0	40.0	.0	1.000

In the study there was no significant difference in VAS Score between two groups from 1 hr to 24 hrs.

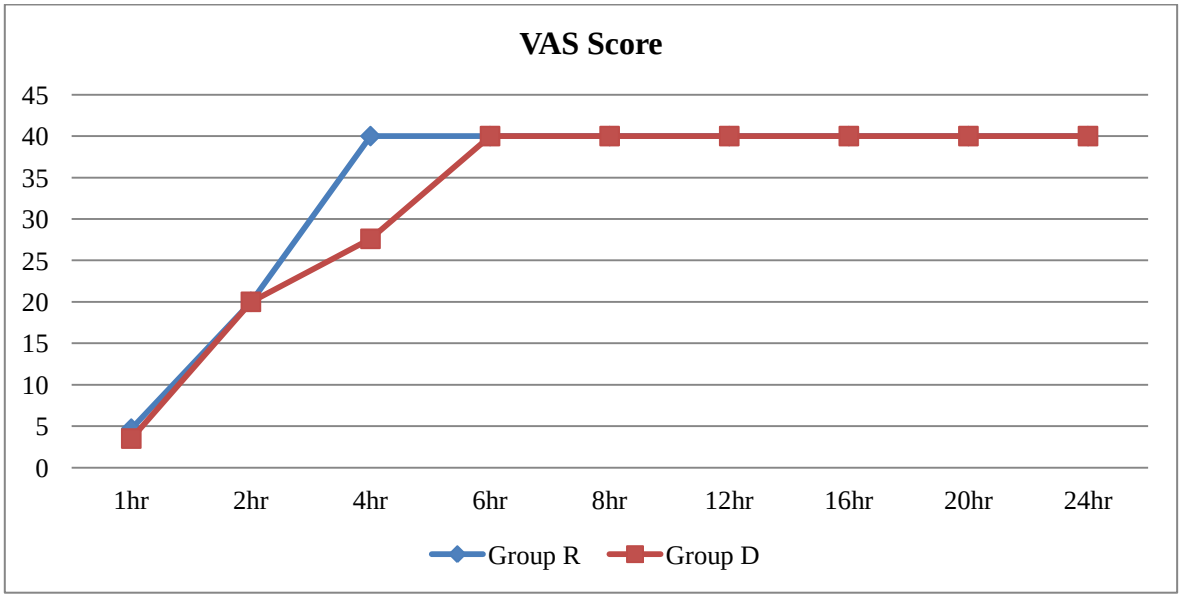


Figure 27: Line diagram showing VAS Score Comparison between two groups at different time intervals

5. Sensory level comparison between two groups

		Group			
		Group R		Group D	
		Count	%	Count	%
Sensory level	T4	0	0.0%	1	5.9%
	T6	17	100.0%	14	82.4%
	T8	0	0.0%	1	5.9%
	T10	0	0.0%	1	5.9%

$\chi 2 = 32.9$, df = 3, p = 0.349

In Group R, 100% had sensory level at T6. In Group D, 5.9% had at T4, 82.4% had T6, 5.9% had at T8 and 5.9% had at T10. There was no significant difference in sensory level between two groups.

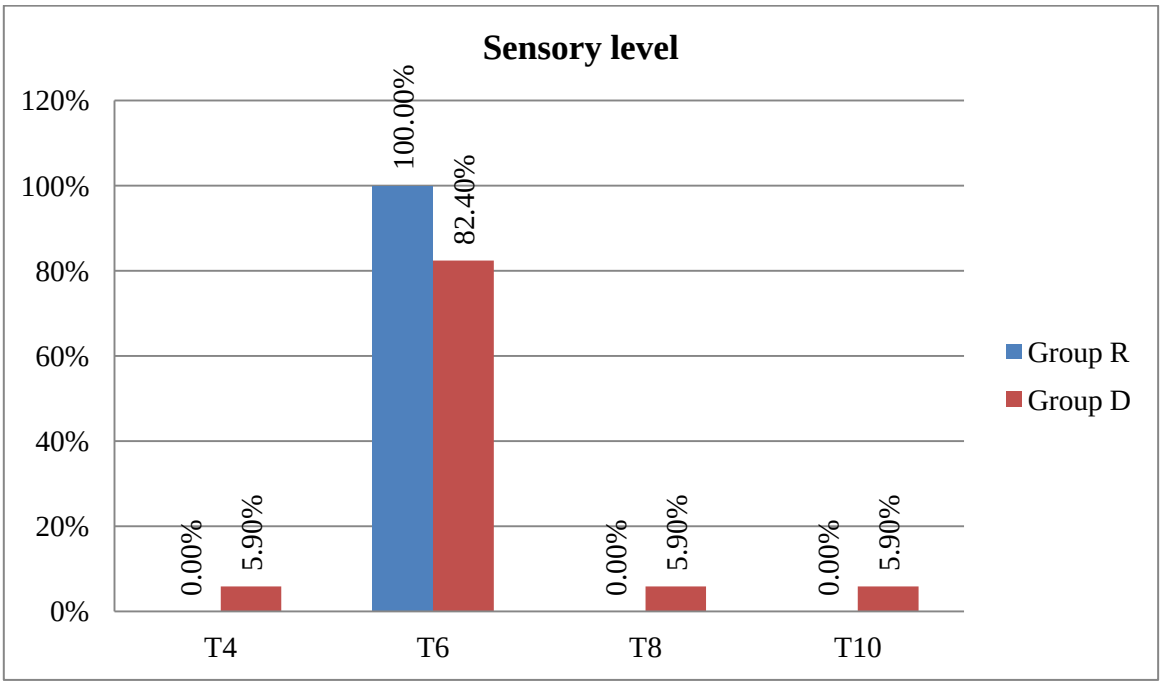
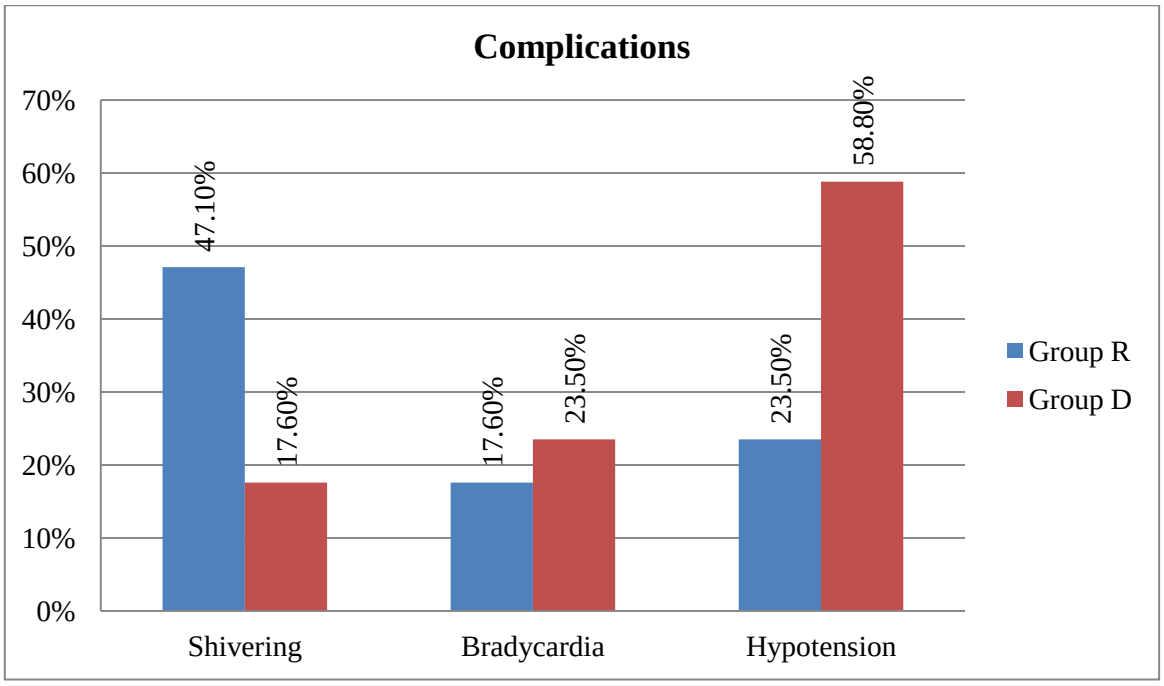


Figure 28: Bar diagram showing Sensory level comparison between two groups

6. Complications comparison between two groups

		Group				P value
		Group R		Group D		
		Count	%	Count	%	
Shivering	No	9	52.9%	14	82.4%	0.067
	Yes	8	47.1%	3	17.6%	
Bradycardia	No	14	82.4%	13	76.5%	0.671
	Yes	3	17.6%	4	23.5%	
Hypotension	No	13	76.5%	7	41.2%	0.037*
	Yes	4	23.5%	10	58.8%	

In Group R, 47.1% had Shivering, 17.6% had Bradycardia and 23.5% had Hypotension. In Group D, 17.6% had Shivering, 23.5% had Bradycardia and 58.8% had Hypotension. There was significant difference in Incidence of Hypotension between two groups. There was no significant difference in shivering and Bradycardia between two groups.



Bar diagram showing Complications comparison between two groups

Discussion

The α2 agonists are being extensively evaluated as an alternative with emphasis on opioid – related side effects such as respiratory depression, nausea, urinary retention, and pruritus. The and have been employed clinically to achieve the desired effects in regional anaesthesia.[1][4][9]

Dexmedetomidine pharmacologic properties of α–2 agonists have been extensively studied has been growing popularity and expanding its role in anaesthesia since then Dexmedetomidine became α_2 agonist of choice, due to its greatest α_2: α_1 affinity (8 times greater than clonidine).[20][21] The increased selectivity results in more predictable and effective sedation and analgesia and fewer side effects.

The Demographic profile of our patients was comparable with respect to mean age, bodyweight, height, gender and ASA physical status.

Onset and Duration of Analgesia: In our study, the mean time of onset of Analgesia in Group D was 6.6 ± 3.4 min,was significantly more than Group R 2.8 ± 1.0 min (p value <0.001).

The study had shown that addition of 5µg of dexmedetomidine to 2.5ml of 0.75% Ropivacaine in group D prolongs the duration of analgesia nearly 1 hour. In group R duration of analgesia was only 201.6 ± 16.0 min compared to group D 263.6 ± 12.7 min.

Onset and Duration of motor blockade:

Mean Onset of motor block in Group R was 9.2 ± 2.5 min and in Group D was 11.8 ± 4.4 min. Mean Duration of motor block in Group R was 104 ± 12.1 min and in Group D was 182.9 ± 18.4 min. addition of dexmedetomidine prolongs the duration of motor block about 80 min.

These results correlate with study done by Kanazi et al[24] who showed that the motor block duration was 250 +/- 76 min in dexmedetomidine group D, 216 ± 35 min in clonidine group C and 163 ± 47 min in plain bupivacaine group B.

Time for Maxiumum Sensory block: In Group R, it was 7.8 ± 1.0 min and in Group D was 7.8 ± 3.1 min. both groups were comparable

Time to Two Segment Regression: In Group R it was 68.2 ± 9.5 min and in Group D it was significantly prolonged to 112.4 ± 6.6 min.

Highest sensory level: obtained in both groups doesn't have much difference.

Hemodynamic stability

The heart rate mean arterial pressure remained stable both during the intraoperative and postoperative period. 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[23], kanazi et al[24].

Side Effects

In Group R, 47.1% had Shivering, 17.6% had Bradycardia and 23.5% had Hypotension. In Group D, 17.6% had Shivering, 23.5% had Bradycardia and 58.8% had Hypotension. There was significant difference in Incidence of Hypotension (p value = 0.037) between two groups. There was no significant difference in shivering (p value = 0.067) and Bradycardia (p value = 0.671) between two groups

Conclusion

This study was designed to compare intrathecal 0.75% isobaric ropivacaine and combination of 0.75% isobaric ropivacaine with dexmedetomidine for below umbilical surgeries. The study was conducted in 34 patients in the age group 18-60years, of both sexes, height between 155 cm to 170 cm, body weight between 50kg to 70kg and American society of Anaesthesiologists (ASA) physical status 1 and 2 scheduled for below umbilical surgeries.

The patients were allocated into two groups according to the drug they received.

Group R: Received 2.5ml volume of 0.75% isobaric ropivacaine and 0.5ml normal saline.

Group D: Received 2.5ml volume of 0.75% isobaric ropivacaine and 5µg dexmedetomidine in 0.5ml normal saline.

Pain was evaluated by visual analogue scale. In this scale 0 corresponds to no pain and 100 corresponds to the worst pain possible. Duration of analgesia was calculated from the time of onset of sensory blockade to the time when patients complained of pain >40 in the visual analogue scale. Pain was managed by Inj. Tramadol 100 mg and time was noted.

The addition of 5ug Dexmedetomidine to 0.75% Ropivacaine prolonged the duration of analgesia and duration of motor blockade compared to plain ropivacaine. The incidence of side effects such as hypotension was more in patients who received dexmedetomidine but were able to manage easily. Incidence of bradycardia were comparable in both groups. Noepisode 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.

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