A RANDOMISED CLINICAL TRIAL COMPARING THE EFFICACY AND SAFETY OF ROPIVACAINE 0.75% ALONE AND IN COMBINATION WITH DEXMEDETOMIDINE IN EPIDURAL ANAESTHESIA FOR LOWER LIMB SURGERIES

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ABSTRACT

AIM

This study was aimed to study the efficacy and safety of ropivacaine alone and in combination with dexmedetomidine in epidural anaesthesia in patients undergoing lower limb surgeries.

MATERIALS AND METHODS

A randomised study was conducted on 80 patients at Krishna Hospital, Karad, on those patients undergoing limb surgeries and efficacy of ropivacaine (0.75%) and ropivacaine with dexmedetomidine was compared. Eighty patients belonging to ASA physical status 1-2 were selected for the study and randomly allocated to two groups of 40 each, Ropivacaine (RN) group and Ropivacaine + Dexmedetomidine (RD) group. Group RN received 16 mL of 0.75% ropivacaine. Group RD received 16 mL of 0.75% ropivacaine + Dexmedetomidine.

RESULTS

The mean time of onset of sensory blockade in group RD was 1.73±0.73 min and group RN was 2.43±1.07 min. Onset of sensory blockade was clinically faster in group RD (p<004). The range of block in group RD was T10-T4 and in group RN was T10-T5 and was clinically and statistically not significant. The mean duration of analgesia in group RN was 205.53±36.36 min and group RD was 217.2±48.69 min. The duration of motor block in group RD was 195.83±29.24 mins and group RN was 187.26±33.75 min. Changes in haemodynamic parameters were not clinically significant.

CONCLUSION

This randomised, double blinded, clinical trial shows that ropivacaine 0.75% combined with dexmedetomidine in epidural anaesthesia provides faster onset of sensory block and longer duration of motor block compared to plain ropivacaine 0.75%.

KEYWORDS

Epidural, Ropivacaine, Dexmedetomidine.

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INTRODUCTION

Epidural anaesthesia is one of the most common regional anaesthetic techniques used for lower abdominal and lower limb surgeries. The advantages of epidural anaesthesia being

1. It provides effective surgical anaesthesia.
2. It can meet the extended duration of surgical needs.
3. It provides good postoperative analgesia.
4. It reduces incidence of haemodynamic changes with segmental blockade.

Different local anaesthetics are used for epidural anaesthesia, most popular in India being lignocaine and bupivacaine. Lignocaine has intermediate duration of action. Bupivacaine is clinically available as a racemic mixture of the enantiomers. The enantiomers of a chiral drug may vary in their pharmacokinetics, pharmacodynamics, and toxicity. Administering a racemic mixture is in reality administration of two different drugs (Ehrlich, 1992).[1]

A newly introduced long-acting amide linked local anaesthetic, bupivacaine congener "ROPIVACAINE" registered for use in 1996 (White side J B 2001),[2] but registered for use in India in 2009 only. Ropivacaine is a pure 'S' enantiomer with low lipid solubility, which blocks nerve fibers involved in pain transmission (A Delta and C Fibers). Ropivacaine has less motor blockade and shorter duration of action than bupivacaine. (Scott et al 1995; Markham et al 1996, Zaric et al 1996).[3,4,5]

Dexmedetomidine, a highly selective α-2 adrenoceptor agonist is the most recent and advanced agent. It has sedative, analgesic, haemodynamic stabilising effects in addition to reduction of anaesthetic drug requirement.[6]

As the combination of these two drugs is not extensively studied yet here is an attempt to study the synergistic effect, efficacy, and safety between dexmedetomidine and ropivacaine 0.75% in epidural anaesthesia and comparing this with 0.75% ropivacaine alone.

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METHODS

After obtaining ethical committee approval and informed written consent, 80 patients were randomly selected of age between 18-60 years of age, ASA 1-2, and scheduled for lower limb surgeries. Inclusion criteria were patients of ASA physical status I-II aged between 18 to 70 years of either sex. Exclusion criteria were patients with physical status of ASA III or greater, uncooperative patients, previous spinal surgeries, spine deformities, local site infection, and coagulation abnormalities, allergy to local anaesthetics (Amide group), neuromuscular diseases, patients with poorly-controlled hypertension, patients with haematological disease, neurologic, psychiatric disease, severe renal or hepatic derangement, and patients with history of drug abuse. Group RN received 16 mL of 0.75% ropivacaine. Group RD received 16 mL of 0.75% ropivacaine + dexmedetomidine.

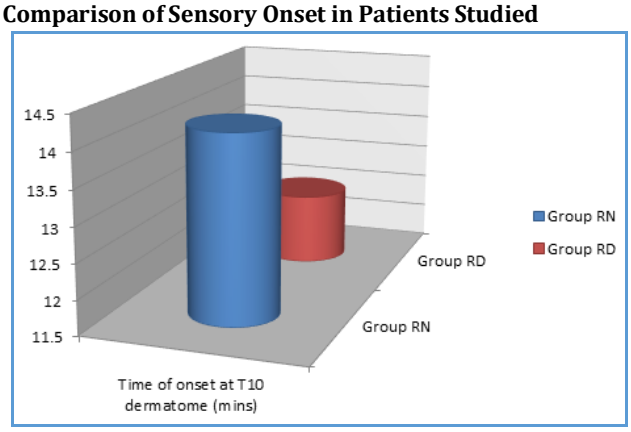
Either group received 16 mL of the respective local anaesthetic agent via epidural catheter. Preoperative assessment was done for each patient and written consent was taken. Intravenous line obtained with 18G cannula and preloaded with RL 500 mL half an hour before anaesthesia. Basal vital parameters like heart rate, blood pressure, SpO2 were noted. Patients were placed in flexed lateral positions. Epidural space was identified with loss of resistance to air technique using 18G Tuohy epidural needle at L2-3/L3-4 level. An epidural catheter was advanced in cephalad direction into the epidural space and fixed in the space for 3-5 cms. Test dose of 3 mL of 2% lignocaine with adrenaline (1:2,00,000) given after negative aspiration of CSF and blood. After confirming the correct position of the catheter, patient will be turned to supine position. Five minutes after test dose in the absence of any adverse squeal, 16 mL of study drug as per randomisation was given.

RESULTS

Comparison of Sensory Onset in Patients Studied

	Group RN	Group RD	P Value
Onset of sensory block to T10 dermatome (mins)	14.182±6.020	12.536±4.172	0.115

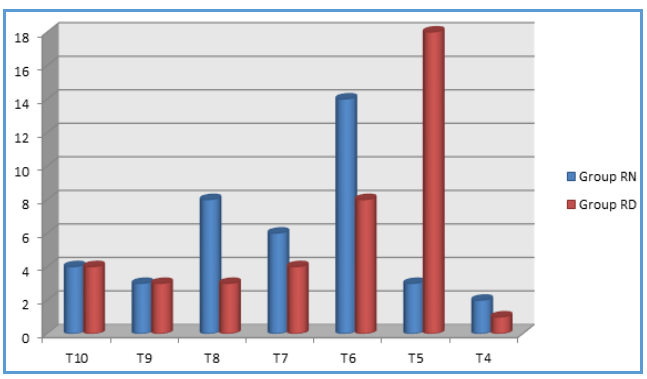
Comparison of Sensory Onset in Patients Studied



Comparison of Maximum Sensory Level of Patients Studied

Sensory Level	Group RN	Group RD
T10	4(10.0%)	4(10.0%)
T9	3(7.5%)	3(7.5%)
T8	8(20.0%)	3(7.5%)
T7	6(15.0%)	4(10.0%)
T6	14(35.0%)	8(20.0%)
T5	3(7.5%)	18(45.0%)
T4	2(5.0%)	1(2.5%)

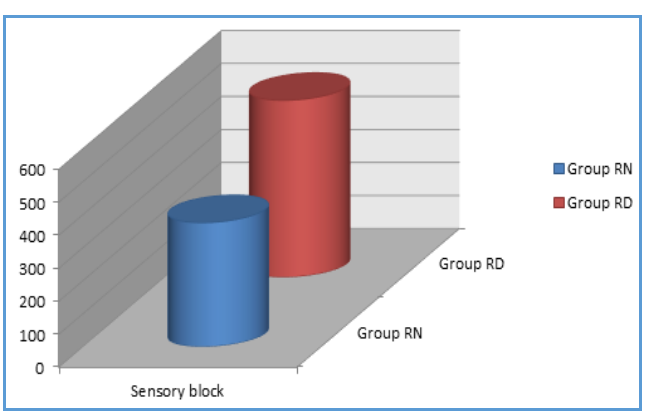
Comparison of Maximum Sensory Level of Patients Studied



Comparison for Duration for Maximum Sensory Level Reached

	Group RN	Group RD	P Value
Duration of analgesia (min)	375.20±15.97	535.18±19.85	0.000

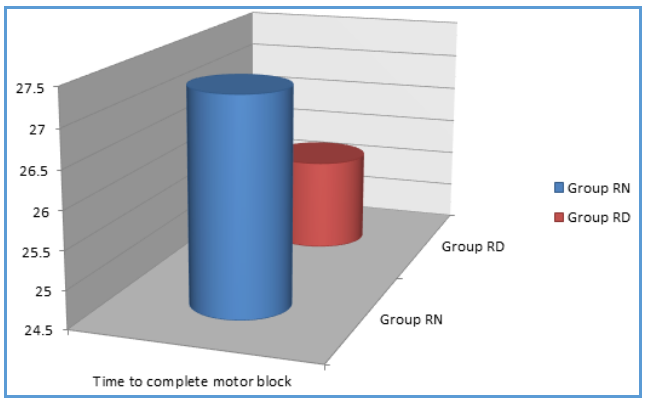
Comparison for Duration for Maximum Sensory Level Reached



Time to Complete Motor Block

	Group RN	Group RD	P Value
Complete motor block time (min)	27.34±5.970	25.73±4.172	0.123

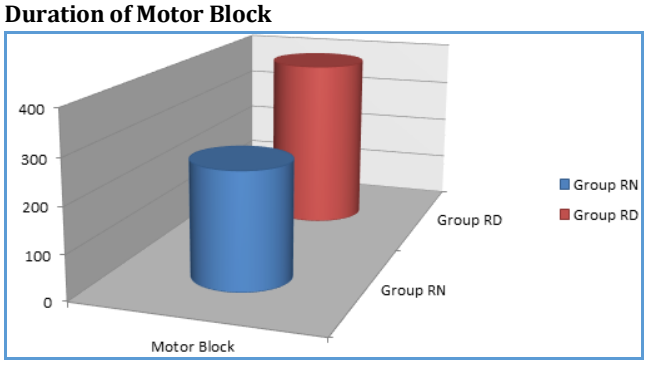
Time to Complete Motor Block



Duration of Motor Block

	Group RN	Group RD	P Value
Duration of Motor block (min)	259.80±15.486	385.92±17.719	0.000

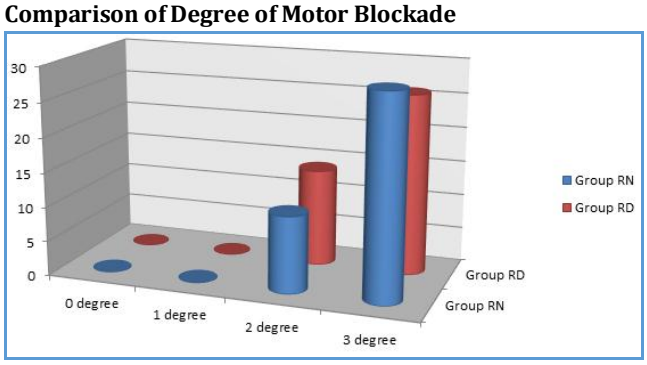
Duration of Motor Block



Comparison of Degree of Motor Blockade

Bromage	Group RN	Group RD	P Value
0 degree	0	0	0.75
1 degree	0	0	
2 degree	11	14	
3 degree	29	26	

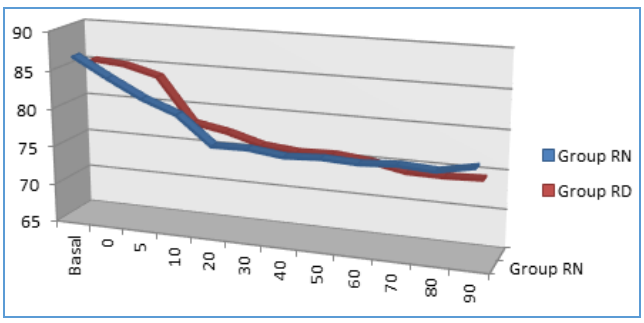
Comparison of Degree of Motor Blockade



Comparison of Heart Rate (BPM) in two Groups of Patients

Heart Rate	Group RN	Group RD	P Value
BASAL	86.66±8.71	85.3 ±13.39	0.641
0	84.16±8.23	84.9±13.45	0.799
5	81.86±7.15	83.73±13.86	0.514
10	80.2±6.54	78.03±9.68	0.314
20	76.58±12.20	77.2±9.16	0.535
30	76.66±6.02	75.9±8.16	0.680
40	76.1±5.79	75.46±7.67	0.719
50	76.36±5.56	75.6±7.68	0.659
60	76.16±4.96	75.13±7.49	0.531
70	76.46±5.27	74.23±7.60	0.191
80	76.2±4.75	74.16±7.30	0.206
90	77.13±6.22	74.36±7.08	0.113

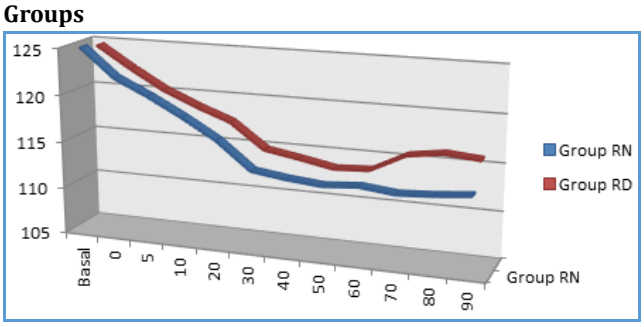
Comparison of Heart Rate (BPM) in Two Groups of Patients



Comparison of Systolic Blood Pressure between Two Groups

SBP (mmHg)	Group RN	Group RD	P Value
BASAL	125±10.38	124.56±14.36	0.893
0	122.±11.32	122.3±13.39	0.925
5	120.33±11.40	120.26±13.40	0.98
10	118.43±11.48	118.73±11.99	0.921
20	116.33±11.60	117.4±10.11	0.705
30	113.46±11.77	114.76±10.03	0.646
40	112.96±11.13	114.13±8.79	0.654
50	112.63±10.59	113.43±7.92	0.741
60	112.93±10.40	113.63±6.98	0.760
70	112.53±10.70	115.5±6.17	0.193
80	112.76±10.75	116.03±5.65	0.146
90	113.13±10.15	115.7±4.69	0.210

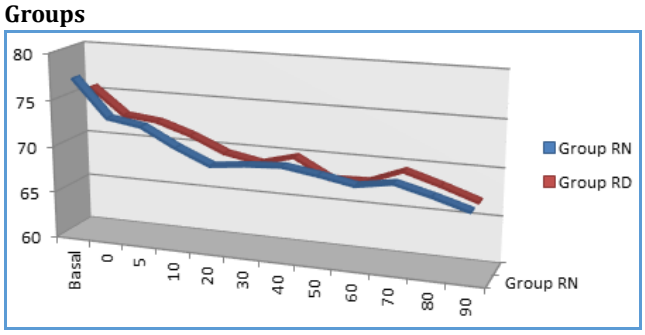
Comparison of Systolic Blood Pressure between Two Groups



Comparison of Diastolic Blood Pressure between Two Groups

DBP (mmHg)	Group RN	Group RD	P Value
BASAL	77.23±11.76	75.56±10.33	0.562
0	73.23±10.74	72.73±9.65	0.850
5	72.63±9.74	72.33±8.96	0.901
10	70.7±9.18	71.13±9.80	0.860
20	69.13±9.07	69.53±10.52	0.875
30	69.53±7.76	68.83±8.87	0.746
40	69.76±7.24	69.8±9.43	0.987
50	69.2±7.16	67.8±8.22	0.484
60	68.5±7.28	67.9±7.71	0.757
70	69.13±6.83	69.36±7.92	0.903
80	68.16±6.47	68.2±8.75	0.986
90	67.03±7.60	66.9±8.90	0.954

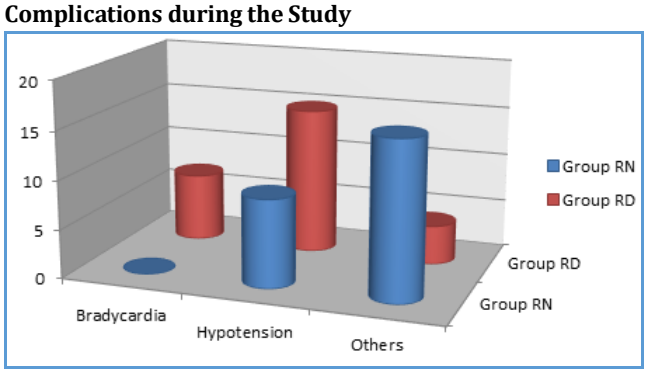
Comparison of Diastolic Blood Pressure between Two Groups



Complications during the Study

Adverse Effect	Group		P Value
	Group RN N (%)	Group RD N (%)	
Evidence of bradycardia	4(10%)	7(17.5%)	0.212
Evidence of hypotension	9(22.5%)	15(37.5%)	0.222
Others	16(40%)	4(10%)	0.0038

Complications during the Study



DISCUSSION

Orthopaedic surgeries and lower limb surgeries are usually associated with perioperative pain, which is a potent trigger for the stress response and autonomic system and is thought to be an indirect cause of various adverse effects like myocardial ischaemia, infarction, thromboembolic phenomena, impaired pulmonary function, ileus, fatigue, muscle catabolism, postoperative infection, and postoperative confusional states.

Epidural anaesthesia and analgesia is considered by many as the gold standard technique for major surgery. It has the potential to provide complete analgesia for as long as the epidural is continued. Epidural techniques are particularly effective at providing dynamic analgesia allowing the patient to mobilise and resume normal activities unlimited by pain. It also improves the postoperative outcome and attenuates the physiologic response to surgery in particular significant reduction in pulmonary infections, pulmonary embolism, ileus, acute renal failure, and blood loss.

A newly introduced long-acting amide linked local anaesthetic, bupivacaine congener "ROPIVACAINE" was registered for use in 1996 (Whiteside JB 2001), but registered for use in India in 2009 only.

Ropivacaine is a pure 'S' enantiomer with low lipid solubility, which blocks nerve fibers involved in pain transmission (A Delta and C fibers). Ropivacaine has less motor blockade and shorter duration than bupivacaine (Scott et al 1995, Markham 1996, Zarie et al 1996).

Dexmedetomidine is a highly selective α-2 adrenergic agonist with an affinity of eight times greater than that of clonidine. The anaesthetic and the analgesic requirements get reduced to huge extent by the use of this adjuvant because of its analgesic properties and augmentation of local anaesthetic effects as it causes hyperpolarisation of nerve fibres by altering transmembrane potential and ion conductance at locus coeruleus in brain stem.

The results of the present study show that supplementation of epidural ropivacaine with dexmedetomidine significantly prolongs the duration of sensory and motor block with improved quality of postoperative analgesia as compared to ropivacaine alone. The mechanism by which α-2 adrenergic agonists prolong the motor and sensory block of local anaesthetics maybe an additive or synergistic effect secondary to the different mechanisms of action of local anaesthetics. Dexmedetomidine act by binding to the presynaptic C-fibers and postsynaptic dorsal horn neurons.

They produce analgesia by depressing the release of C-fibre transmitters and by hyperpolarisation of postsynaptic dorsal horn neurons. The complimentary action of local anaesthetics and α-2 adrenergic agonists accounts for their profound analgesic properties. The prolongation of motor block maybe the result of binding α-2 adrenergic agonists to the motor neurons in the dorsal horn. The use of dexmedetomidine has been studied as an epidural adjuvant by various authors who have observed its synergism with local anaesthetics without any additional morbidity (Salgado PF et al, Bajwa SJS et al).[7,8]

In the present study, we used fixed dose and concentration of ropivacaine i.e. 16 mL of 0.75% ropivacaine in both the groups as the volume of the study drug because the influence of height and weight on the spread of epidural block is very little and usually not clinically relevant unless considering the extremes of the spectrum.

Time of onset of sensory block to T10 dermatome in Group RD (12.53±4.17 min) was found to be little earlier than Group RN (14.18±6.02 min) with a statistically non-significant (P > 0.05).

These results were in concordance with the results of Salgado PF et al who observed similar results with 20 mL of 0.75% ropivacaine (13.8 min) and with 0.75% ropivacaine and 1 µg/kg dexmedetomidine (11.5 min).

However, in study done by Bajwa SJS et al using 1.5 µg/kg dexmedetomidine, onset at T10 dermatome was 8.52±2.36 min.

The mean time taken to reach maximum sensory level in Group RN was 23.24±5.971 min and in Group RD was 21.63±4.172 min, which was almost comparable (p 0.122).

Bajwa SJS, et al in their study also observed a similar result (13.14±3.96 min) when dexmedetomidine was used as an adjuvant to ropivacaine. The epidural dexmedetomidine used in our study had shown comparable onset of Maximum Motor Block (27.34±5.970 min vs 25.73±4.172 min) (p 0.123) with significantly Prolonged duration of Motor Block (259.80±15.486 min vs 385.92±17.719 min) (p<0.001). Similar results were observed by Salgado PF et al and Bajwa SJS et al.

Total duration of motor block in Group RN was 259.80±15.86 min while in Group RD was 385.92±17.719

min ($p<0.001$), which is almost similar to the results of Salgado PF et al (300 min) and Brown D et al[9] (220 min).

Time for two segment regression of sensory block to T10 dermatome was earlier in Group RN (277.58±17.66 min) when compared to Group RD (404.18±17.93 min).

Similarly, comparable time (237±65 min) was observed by Brown D et al using 20 mL of 0.5% ropivacaine.

In the present study, patients remained haemodynamically stable in both groups and incidence of bradycardia and hypotension was comparable at all measured intervals, which reaffirms the established effects of α-2 agonists in providing a haemodynamically stable perioperative period.

CONCLUSION

Our study reveals that 16 mL of ropivacaine 0.75% along with dexmedetomidine when administered epidurally provides adequate anaesthesia for lower extremity surgery.

Onset of sensory blockade is slightly faster with dexmedetomidine while the level of sensory block was comparable.

Ropivacaine + dexmedetomidine group had earlier onset of motor blockade with longer duration of motor block and more intense motor block as compared to ropivacaine alone.

The haemodynamic effects were comparable in both the drugs.

Hence, we can conclude that ropivacaine along with dexmedetomidine can be used successfully for epidural anaesthesia in lower extremity surgery.

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