Section A-Research paper

A Comparative Study of Dexmedetomidine and Clonidine as Adjuvants to Ropivacaine 0.75% for Epidural Anaesthesia in Patients Undergoing Lower Limb Orthopedic Surgeries

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Received Date: 12/04/2023 Revised Date: 06/05/2023 Accepted Date: 28/05/2023

ABSTRACT

Background: Over the last few decades, anaesthetic techniques used during the surgery have evolved and improved drastically. Many new drugs have been introduced which help in reducing the anxiety of the patients. Epidural anaesthesia is very popularly used in lower abdominal as well as lower limb surgeries. Ropivacaine has less cardiac toxicity and hence can be used as an ideal local anaesthetic for epidural anaesthesia. **Methodology:** A study was conducted at Chettinad Hospital and Research Institute, Chennai. A total of 100 patients belonging to ASA I and ASA II (American Society of Anaesthesiologists) were enrolled and divided into two groups based on the inclusion and exclusion criteria. Group A received 0.75% ropivacaine with clonidine (1 mcg/kg) with a total volume of 20 ml while Group B received 0.75% ropivacaine with dexmeditomidine (1 mcg/kg) with a total volume of 20 ml. **Results:** Clonidine to Ropivacaine, showed statistically significant difference in the onset of sensory and motor blockade between Ropivacaine with clonidine and Ropivacaine with dexmedetomidine group. Ropivacaine and dexmedetomidine group produced more intense motor blockade than Ropivacaine with clonidine group. Duration of sensory block is prolonged with ropivacaine and dexmedetomidine group compared to Ropivacaine with clonidine group. Duration of motor block is also prolonged with ropivacaine and dexmedetomidine group compared to Ropivacaine and clonidine group. **Conclusion:** The addition of the dexmeditomidine 1mcg/kg to 0.75% ropivacaine solution in epidural anaesthesia showed early onset of sensory and motor blockade and prolonged the duration of analgesia when compared to Ropivacaine with clonidine.

Keywords: Dexmedetomidine, clonidine, ropivacaine, anaesthesia, lower limb

Introduction: Surgical methods and the anaesthetic techniques have evolved and improved drastically over the last few decades. Many techniques and drugs were tried to reduce the anxiety of patients during regional anaesthesia. Central neuraxial blockade like epidural blockade is very popular for lower abdominal and lower limb surgeries as these techniques avoid the disadvantages associated with general anaesthesia.[1,2] The advantages of epidural anaesthesia are, it provides effective surgical anaesthesia and the duration can be extended for surgical needs, it provides extended post-operative analgesia, decreases the incidence of hemodynamic changes as a result of sympathetic blockade as it produces segmental anaesthesia.[3] Unlike spinal anaesthesia, in epidural anaesthesia there is no incidence of post-dural puncture headache as the dura is not pierced.[4,5] Different local anaesthetics are used for epidural anaesthesia, most popular are lidocaine and Bupivacaine. The drawback of lidocaine is its short duration of action and the drawback of bupivacaine though long acting, is increased incidence of cardiac toxicity because of accidental intravascular injection. Ropivacaine and levobupivacaine are the newer long acting amide local anaesthetics which have a wide margin of safety compared to bupivacaine, with all its advantages.[6-7]
Ropivacaine has all the advantages of bupivacaine with less cardiac toxicity, it can be an ideal local anaesthetic for epidural anaesthesia. Many studies found ropivacaine to be an effective local anaesthetic for epidural anaesthesia.[8-11] Ropivacaine was less potent than bupivacaine in terms of conduction blocks of Aβ fibers, but ropivacaine blocked Aδ and C fibers to a greater extent than bupivacaine. It is also being found that, lipid solubility of Ropivacaine is 2.9 compared with 3.9 of bupivacaine.[12,13] Sedation, stable haemodynamics and an ability to provide smooth and prolonged post-operative analgesia are the main desirable qualities of an adjuvant in neuraxial anaesthesia.[14] α-2 adrenergic receptor agonists has both sedative and analgesic properties when used in regional anaesthesia as adjuvents.[8]
Hence, a study was undertaken to compare 0.75% ropivacaine with Dexmedetomidine (1 mcg/kg) with a total volume of 20 ml and 0.75% ropivacaine with clonidine(1 mcg/kg) with a total volume of 20 ml in epidural anaesthesia for orthopedic surgeries of the lower limbs.

Materials And Methods

Study design and place- It is a prospective double blind randomized study conducted at Chettinad Hospital and Research Institute, Kelambakkam, Chennai.

Inclusion criteria- Patients with ASA physical status class (ASA) 1 and 2, patients age between 18 – 60 years, belonging to both the genders, undergoing Elective surgeries of lower limb.

Exclusion criteria- Patients with ASA physical status class (ASA) 3 and above, unwilling to participate, having Psychiatric disease, history of drug abuse and allergy to local anaesthetics, having haematological disease bleeding or coagulation test abnormalities, having skin infection at injection site and spine abnormalities.

Sample size- A total of 100 patients belonging to ASA I and ASA II (American Society of Anaesthesiologists) were enrolled in the study. Further they were divided into two groups, i.e Group A and Group B of 50 patients each using the computer generated randomization code.

Ethical concern- This study has been approved by the Institutional Ethical committee(IEC) at the participating hospital. Written informed consent was taken from the patients.

Group A - 0.75% ropivacaine with clonidine (1 mcg/kg) with a total volume of 20 ml

Group B - 0.75% ropivacaine with dexmeditomidine (1 mcg/kg) with a total volume of 20 ml

Tab.Pantoprazole 40mg (before food) and Tab.Diazepam 5mg (after food) were given as premedication the night before surgery to all patients.

Good intra venous access with 18 G intra venous cannula.

Patient was explained about the procedure well in advance. In sitting position injection under aseptic precaution epidural block was performed using 18G needle in L2L3 space, and catheter was secured into epidural space. Test dose of 3ml of 2% Lignocaine hydrochloride solution containing adrenaline 1:2, 00,000 was injected.
All patient received 20 ml of 0.75 % ropivacaine + 1 microgram per kg of Dexmedetomedine or 1 microgram per Kg Clonidine as per the randomization code.
Sensory Level was evaluated by loss of sensation to cold using a cold ice pack (chill it gel) and pin prick sensation using a 23gauge needle and Motor block assessed by modified bromage scale. Adverse effects like nausea, vomiting, shivering, dizziness, dry mouth, respiratory depression, urinary retention, if any, were noted.

Table 1: BROMAGE SCALE

SCORE	CRITERIA
1	Complete block (unable to move feet or knees)
2	Almost complete block (able to move feet only)
3	Partial block (just able to move knees)
4	Detectable weakness of hip flexion while supine (full flexion of knees)
5	No detectable weakness of hip flexion while supine
6	Able to perform partial knee bend

Results

Table 2: Descriptive Statistics: Age_Grp1, Age_Grp2 (Group 1 – Grp1, Group 2 – Grp2)

Variable N* Mean SE_Mean Std. Dev Minimum Maximum
Age_Grp1 0 39.60 1.62 11.43 20.00 62.00
Age_Grp2 0 36.24 1.60 11.28 18.00 60.00

Variable	N*	Mean	SE_Mean	Std. Dev	Minimum	Maximum
Age_ Grp 1	0	39.60	1.62	11.43	20.00	62.00
Age_ Grp 2	0	36.24	1.60	11.28	18.00	60.00

N* - No of missing variables
SE_Mean – Standard error of mean
StDev – Standard deviation

The minimum age in groups 1 and 2 were 18 and 20 years respectively. The maximum age in both groups 1 and 2 was 60 and 62 years respectively. There was no significant difference in the age of patients between the Group R and Group RD. Both groups were similar with respect to age distribution ($p>0.05$).

Table 3: Type of surgical procedure

Type of surgery	Group 1 (Ropivacaine and clonidine group)		Group 2 (ropivacaine and dexmedetomidine group)	
	Number of patients	Percent	Number of patients	Percent
# Hip	13	26	12	24
# Femur	25	50	23	46
# Both bones leg	12	24	15	30

There is no difference in the type of surgical procedures in both the groups

Table 4: Mean duration of surgery Descriptive Statistics: Comparison of 2 groups in terms of mean duration of surgery (Hours)

Variable	N*	Mean	SE_Mean	Std. Dev	Minimum	Maximum
Grp1_Dur_of_surgery (hours)	0	3.505	0.438	3.096	1.000	24.000
Grp2_Dur_of_surgery (hours)	0	3.589	0.114	0.808	1.750	6.160

Variable N* Mean SE Mean StDev Minimum Maximum
Grp1_Dur_of_surgery (hours) 0 3.505 0.438 3.096 1.000 24.000
Grp2_Dur_of_surgery (hours) 0 3.589 0.114 0.808 1.750 6.160

Table 5: Descriptive Statistics: Mean duration of surgery (minutes)

Variable	N*	Mean	SE_Mean	Std. Dev	Minimum	Maximum
Grp1_Dur_of_surgery (min)	0	210.4	26.3	185.8	60.0	1440.0
Grp2_Dur_of_surgery (min)	0	215.50	6.86	48.52	105.00	370.00

Variable N* Mean SE Mean StDev Minimum Maximum
Grp1_Dur_of_surgery(min) 0 210.4 26.3 185.8 60.0 1440.0
Grp2_Dur_of_surgery(min) 0 215.50 6.86 48.52 105.00 370.00

95% CI for mean difference: (-60.7, 50.5)
T-Test of mean difference = 0 (vs ≠ 0): T-Value = -0.18
P-Value = 0.855
The mean duration of surgery is 210.4 ± 185.8 mins in group 1 and 215.50± 48.52 mins in group 2. There is no statistically significant difference between the groups.

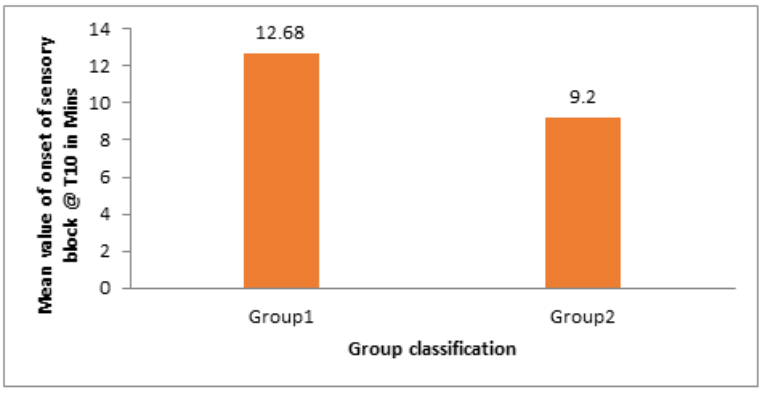

Figure 1: Mean time for onset of sensory block at T10 (minutes)

Two-sample T for G1 vs G2 for Onset of Sensory block at T10
95% CI for mean difference: (2.074, 4.886)
T-test of mean difference =0**(**vs ≠ 0) T-Value = 4.98 P-Value = 0.000

Table 6: Mean time for onset of sensory and motor block (minutes)

	Mean time for sensory onset (mins)	**SD**	**p-value**	**Mean time for motor onset (mins)**	**SD**	**p value**
Group 1	12.680	4.26	0.000	15.36	3.28	0.000
Group 2	9.2	3.19	0.000	11.22	2.61	0.000

The mean time of onset of sensory blockade in group 1 is 12.680±4.26 mins and in group 2 is 9.2±3.19 mins. There is highly statistical significant difference between the groups (p=0.000). The mean time taken for the onset of motor blockade is15.36±3.28 mins in group 1 and 11.22 2.61 mins in group 2. There is statistical significant difference between the groups (p=0.000).

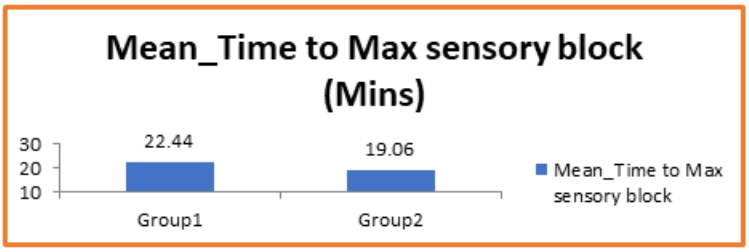

Figure 2: Mean time to max sensory block in minutes

Two-sample T for G1 vs G2 for Time to maximum sensory block (Mins)
95% CI for mean difference: (1.557, 5.203)
T-Test of mean difference = 0 (vs ≠ 0): T-Value = 3.73 P-Value = 0.001
Group 2 had the highest level of T4 and highest level in group 2 was T6. There was significant difference between the two groups(p-0.001)

Table 7: Duration of sensory blockade (hours)

Variable	**Mean**	**Std. Dev**	**Minimum**	**Maximum**
Grp1 Dur of sensory bloc	5.984	1.230	3.450	10.250
Grp2 Dur of sensory bloc	7.023	1.276	5.000	10.300

Variable Mean StDev Minimum Maximum
Grp1 Dur of sensory bloc 5.984 1.230 3.450 10.250
Grp2 Dur of sensory bloc 7.023 1.276 5.000 10.300

Table 7 1: T test for Duration of sensory blockade(hr)

N	Mean	Std. Dev	SE	Mean
G1	50	5.984	1.230	0.174
G2	50	7.023	1.276	0.180
Difference	50	-1.039	1.809	0.256

N Mean	StDev	SE	Mean
G1	50 5.984	1.230	0.174
G2	50 7.023	1.276	0.180
Difference 50 -1.039	1.809	0.256	

95% CI for mean difference: (-1.553, -0.524)

T-test of mean difference=0 (vs≠ 0): T-value=-4.06 P-value=0.000

The duration of sensory blockade in group 1 is 5.98±1.23 hours and in group 2 is 7.023±1.27 hours. There is highly statistical significant difference between the groups (p=0.000). 06

Table 8: Duration of motor blockade (Hrs)

Variable	Mean	Std. Dev	Minimum	Maximum
Grp1 Dur of motor blockade	6.498	1.131	4.000	10.400
Grp2 Dur of motor blockade	7.165	1.278	5.400	10.400

Variable Mean StDev Minimum Maximum
Grp1 Dur of motor blockade 6.498 1.131 4.000 10.400
Grp2 Dur of motor blockade 7.165 1.278 5.400 10.400

Table 8 1: T test for Duration of motor blockade (Hrs)

N	Mean	Std. Dev	SE	Mean
G1	50	6.498	1.131	0.160
G2	50	7.165	1.278	0.181
Difference	50	-0.667	1.750	0.248

N Mean	StDev	SE	Mean
G1	50 6.498	1.131	0.160
G2	50 7.165	1.278	0.181
Difference 50 -0.667	1.750	0.248	

95% CI for mean difference: (-1.164, -0.170)

T-test of mean difference=0 (vs ≠ 0): T-value =-2.69 P-value=0.010

The mean time motor blockade in group 1 is 6.49±1.31 hours and in group 2 is 7.16±1.27 hours. There is highly statistical significant difference between the groups (p=0.010).

Results

In our study, the drugs selected for epidural anaesthesia were ropivacaine, clonidine and dexmedetomidine. Ropivacaine is being regularly used for epidural anaesthesia for lower limb orthopedic surgeries hospital. Ropivacaine is structural similar to bupivacaine without any cardio toxic effects of bupivacaine. Clonidine has been compared and studied by various authors as an adjuvant to epidural anaesthesia. Dexmedetomidine has been studied by various authors as an adjuvant to epidural local anaesthetic.[15-18] Very few studies have compared ropivacaine with clonidine and dexmedetomidine as adjuvants for epidural anaesthesia. Hence, ropivacaine with clonidine and ropivacaine with dexmedetomidine combination was selected for our study to compare their efficacy.

The potency of the local anaesthetics is correlated to the lipid solubility of the drug. The lower lipid solubility of ropivacaine would predict that it is likely to produce a greater differential block of sensory and motor function than bupivacaine.[19]

Ropivacaine is less lipophilic than bupivacaine due to substitution of the pipecoloxylidine with a 3 – carbon side chain instead of a 4-carbon side chain.[20] Casati et al.[6] in their study reported that patients receiving 0.5% ropivacaine more frequently had an inadequate motor blockade during surgery than those receiving bupivacaine. Many of the patients had inadequate sensory and motor blockade with 0.5 % ropivacaine. Hence in our study 0.75% ropivacaine was selected instead of 0.5% ropivacaine. Dexmedetomidine and clonidine dose employed in our study is 1 mcg/kg.

The volume of 0.75% bupivacaine used in hospital routinely for lower limb orthopedic surgeries under epidural anaesthesia is 17 ml after using 3 ml of 2 % lidocaine with adrenaline, the total dose being 20 ml. This is calculated as 1ml/segment upto 150 cms of height, and adding 0.1ml/segment for every 5 cms of increasing height, the mean height in our study also being 170 cms in both the groups and block upto T10 [13 segments] is required for lower limb orthopedic surgeries, total volume required would be 20 ml. Hence, in both the groups 20 ml was selected as the volume of the study drug other than the test dose.

Shalina Chandran et al.[21] in their study of epidural anaesthesia for lower extremity orthopedic surgeries compared bupivacaine 0.5 % and ropivacaine 0.75 % and used graded epidural and found that 20 ml of Ropivacaine volume is required to achieve T10 anaesthesia, as in our study.

Demographic data comparing age shows no statistically significant difference among both the groups.

In our study the mean time for onset of sensory analgesia at T10 is 12.680 ± 4.269 mins in group 1 and 9.200 ± 3.194 mins in group 2. This is statistically highly significant ($p<0.001$).

Saravia P.S.F, Sabbag AT et. al [22] in their study found no significant change in the onset time for sensory block between control and dexmedetomidine groups.

The studies conducted by Bajwa SJ, Bajwa SK, Kaur J et al[15] showed onset of sensory analgesia at T10 in ropivacaine + dexmedetomidine group was 8.52 ± 2.36 min vs 9.72 ± 3.44 min in ropivacaine + clonidine group and this is statistically significant similar to our study.

These studies have added clonidine and fentanyl to ropivacaine while comparing with ropivacaine + dexmedetomidine. That's why we got statistically highly significance compared to above studies.

In our study the maximum level of sensory block in group 1 was T6 (n=5) and in group 2 was T4. The range of block was very wide in both the groups (T12- T4).

Saravia P.S.F, Sabbag AT et al.[15] found that maximum level of sensory block at T6 between control and dexmedetomidine groups.

The studies conducted by Bajwa SJ, Bajwa SK, Kaur J et al [23] showed maximum level of sensory block at T5-6 level in group RD compared to T6-T7 in group RC which compares with our study.

In our study the time to maximum sensory block is lesser with ropivacaine + dexmedetomidine group compared with ropivacaine with clonidine group. It is 22.440 ± 4.482 mins with ropivacaine + dexmeditomidine group compared to 19.060 ± 4.326 mins with ropivacaine with clonidine group. This is statistically highly significant ($p<0.001$).

In our study, the duration of sensory block is longer with ropivacaine + dexmedetomidine group compared with ropivacaine group. It is 7.023 ± 1.276 hours with ropivacaine + dexmedetomidine group compared to 5.984 ± 1.230 hours with ropivacaine + clonidine group. This is statistically highly significant ($p<0.001$). Our study concurs with the study conducted by Bajwa SJ, Arora V, Kaur J et. al [24]who observed the mean duration of analgesia to be 366.62±24.42 mins in group RD compared to 242.16±23.86 mins with in group RF which is highly significant.

The onset of motor blockade was 15.36 ± 3.28 min in group 1 and 11.22 ± 2.61 mins in group 2. This is statistically significant. In our study motor blockade is assessed using Bromage scale and onset was taken as soon as the patient developed grade I motor blockade. Saravia P.S.F, Sabbag AT et. al [22] found that there was no sign.

In our study it was found that group 2 produced more intense motor block than group 1. 16 patients in 2 group had grade 4 motor block compared with 0 patients in group R. Also 15patients in 1 group had grade 2 motor block compared with 0 patients in group 2 group. This is statistically highly significant ($p<0.001$). Our study was found to be similar with the study conducted by Saravia P.S.F, Sabbag AT et. al.[22]

The duration of motor block in group 1 is 6.49±1.13 hours compared to 7.16 ± 1.27 hours in group 2. The duration of motor block with group 2 is more prolonged than with group 1, which is statistically highly significant (p-0.010).

In a study conducted by Saravia P.S.F, Sabbag AT et.al [22] found the duration of motor blockade was significantly higher in the dexmedetomidine group, averaging 30% higher than that observed in the control group similar to our study.

In dexmedetomidine group, 5 patients developed bradycardia which did not require any intervention and significant hypotension seen in 5 patients in group 1, 2 patients reported shivering. In group 1, 4 patient reported shivering and 6 patients reported nausea.

Conclusion

We conclude that the addition of the dexmeditomidine 1mcg/kg to 0.75% ropivacaine solution in epidural anaesthesia showed early onset of sensory and motor blockade and prolonged the duration of analgesia when compared to Ropivacaine with clonidine. There were no significant side effects. Ropivacaine and dexmedetomidine can be a safe and effective agent for epidural blockade in lower limb orthopedic surgeries.

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