

Comparative Study of Ropivacaine with Dexmedetomidine 1µg/Kg and Ropivacaine with Clonidine 1µg/Kg by Epidural Route in Patients Undergoing Lower Abdominal and Lower Limb Surgeries

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Abstract:

INTRODUCTION: Regional anaesthesia is safe, cost-effective approach wherever feasible and also it is the technique of choice for providing excellent postoperative analgesia. Spinal anaesthesia, regional anaesthetic technique, the early-onset and sure success of the method, ease in technique but duration of anaesthesia and analgesia is limited.

Epidural anaesthesia, has many advantages for a prolonged duration with frequent top-ups for delivering excellent postoperative analgesia. It contributes to intraoperative hemodynamic stability reduce perioperative stress response, decrease in complications and improving patient outcome by relieving postoperative pain, decreases the incidence of thromboembolic events.

AIMS AND OBJECTIVES OF THE STUDY:

To evaluate the efficacy of dexmedetomidine and clonidine, adjuvant to ropivacaine in epidural anaesthesia for lower abdominal and lower limb surgeries. Compare Onset and duration of sensory blockade, motor blockade, duration of analgesia, haemodynamic changes and side effects.

MATERIALS AND METHODS:

60 patients aged between 18 and 60 belonging to ASA I and II divided into two groups, each group consist of 30 patients.

Group RC: Receives 15ml of 0.75 % ropivacaine with 1 µg/kg clonidine.

Group RD: Receives 15ml of 0.75 % ropivacaine with 1 µg/kg dexmedetomidine.

Injected epidurally undergoing lower abdominal and lower limb surgeries. All patients are managed similarly and the effect of onset, duration of sensory, motor blockade, haemodynamic and complications are evaluated. Results obtained were tabulated and analysed.

RESULTS:

The onset and duration of sensory blockade were faster in group RD than group RC which was statistically significant. The onset and duration of Motor blockade is more intense and Sedation score is greater in RD group than RC group which is highly significant. Side effects are more with RD group than RC which are treatable.

CONCLUSION:

The addition of Dexmedetomidine to Ropivacaine for epidurally to shorten the onset of block and prolong the duration of block. The dosage of 1µg/kg used in the study significantly increase the duration of the analgesia.

Key Words: Analgesia, chlonidine, dexmedetomidine, epidural, ropivacaine, side effects.

Date of Submission: 14-04-2021

Date of Acceptance: 28-04-2021

I. Introduction

HISTORY:

Regional anaesthesia is safe, cost-effective technique of choice for providing excellent postoperative analgesia. Spinal anaesthesia is the preferred regional anaesthetic technique, technical ease, early-onset, sure success of the method, and the duration of anaesthesia and analgesia is limited.

Epidural anaesthesia, providing prolonged duration with frequent top-ups is the preferred method of choice for delivering excellent postoperative analgesia, intraoperative hemodynamic stability, reduce perioperative stress response, decrease in complications, improving patient outcome and decreases the incidence of thromboembolic events.

To combat a lot of patient apprehension and anxiety, due to surgery and unfamiliar environment of the operation theatre and noise of sophisticated equipments, sedative drugs added as adjuvants to local anaesthetics, α -2 agonists like clonidine, dexmedetomidine provide the prolonged duration of anaesthesia and analgesia and excellent sedation, amnesia and decreased anxiety to the patient with excellent hemodynamic stability.

The α -2 adrenergic agonists have both analgesic and sedative properties when used as an adjuvant in regional anaesthesia^{1,4}. Dexmedetomidine is a highly selective α -2 adrenergic agonist with an affinity of 8 times greater than clonidine. These adjuvants, because of their analgesic properties and augmentation of local anaesthetic effects, reduce the requirement of anaesthetic agents. Stable hemodynamics and decreased oxygen demand due to enhanced sympathoadrenal stability make them very useful pharmacologic agents.^{5,6}

ANATOMY OF THE EPIDURAL SPACE

The space between the spinal dura and the periosteum lining the vertebral canal is the epidural space^{18,19,20,21} average diameter is 0.5cms.

Structures encountered from skin to the epidural space by the advancing epidural needle via the midline approach are:

1. Skin
2. Subcutaneous tissue
3. Supraspinous ligament
4. Interspinous ligament
5. Ligamentum flavum

Boundaries of the epidural space:

1. **Superior:** The foramen magnum. The two layers of the dura mater are attached to the margins of the foramen magnum.
2. **Inferior:** Sacral hiatus and the sacrococcygeal membrane.
3. **Lateral:** Periosteum of the pedicles and the intervertebral foramina.
4. **Anterior:** Posterior longitudinal ligament covers the vertebral bodies and the intervertebral discs.
5. **Posterior:** The anterior surfaces of the laminae and their connecting ligaments, roots of the vertebral spines and the ligamentum flavum.

Contents of the epidural space:

- Dural sac and the spinal nerve roots.
- Epidural plexus of veins.
- Epidural fat.
- Lymphatics.
- Spinal arteries.

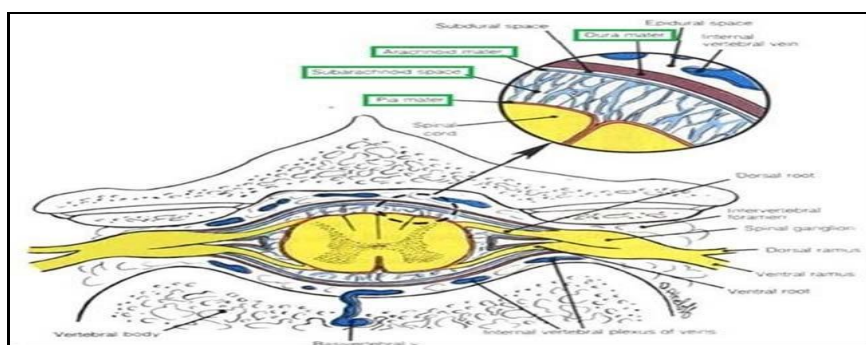


Figure No.1: Epidural space

Pharmacology of Ropivacaine:

Ropivacaine is a long acting regional anesthetic that is structurally related to Bupivacaine. It is a pure s(-)enantiomer developed for the purpose of reducing potential toxicity and improving relative sensory and motor block profile. Ropivacaine is an optically pure s(-) enantiomeric form of the parent chiral molecule propivacaine. It belongs to the group of local anesthetics the pipercoloxylidides and has a propyl group on the piperidine nitrogen atom compared to bupivacaine which has a butyl group.

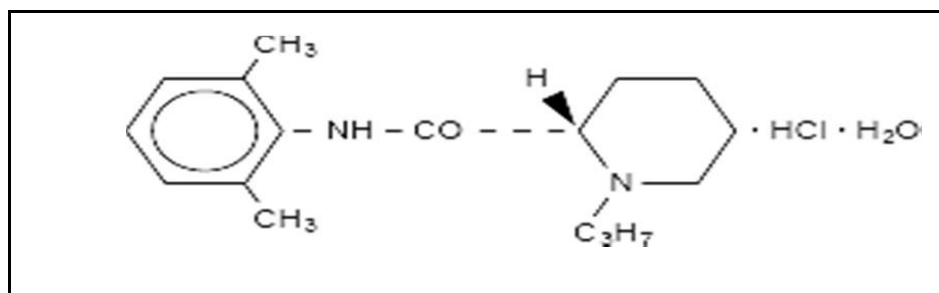


Figure No.2 : Structure of Ropivacaine

DEXMEDETOMIDINE:

Dexmedetomidine is a highly selective α_2 -adrenergic agonist. The effects of dexmedetomidine can be reversed with α_2 -antagonist drugs.

Physicochemical Characteristics:

Dexmedetomidine is the active S-enantiomer of medetomidine, a highly selective α_2 adrenergic agonist and imidazole derivative that is used in veterinary medicine. Dexmedetomidine is water soluble and available as a parenteral formulation.

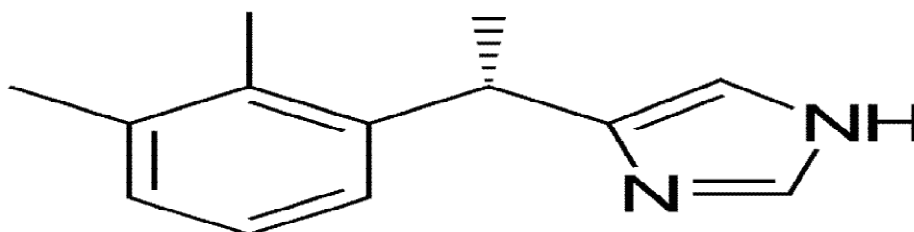


FIGURE NO 3: STRUCTURE OF DEXMEDETOMIDINE

Pharmacodynamics:

Dexmedetomidine produces its effects through activation of CNS α_2 -receptors. It seems to decrease perioperative opioid consumption and improve pain scores, but analgesic benefit has not been shown in all settings. Specifically, it may be beneficial for prevention of emergence delirium after paediatric anaesthesia. At the other extreme of age, dexmedetomidine may be superior to propofol for reducing delirium in elderly patients requiring sedation after cardiac or non-cardiac surgery.

CLONIDINE

Mechanism of action:

Clonidine stimulates pre-synaptic α_2 receptors and inhibits norepinephrine release from both central and peripheral adrenergic terminals. It also has some and in high oral doses may cause paradoxical hypertension by stimulating vascular alpha 1 receptors²³ due to α_1 agonist activity. sedative effect reflects the inhibition of the nucleus in the pontine locus coeruleus.²²

II. Material And Methods

The study was carried out on patients of Department of Anaesthesiology, Siddhartha Medical College/General Hospital Vijayawada, Andhra Pradesh. A total 60 patients of either sex between 18 and 60 years of age under physical status ASA 1 and ASA 2 scheduled for elective lower abdominal and lower limb surgeries were included after obtaining ethical clearance from the institution and informed written consent from the patients.

INCLUSION CRITERIA:

- ASA physical status class I and II.
- Age between 18 -60 years.

EXCLUSION CRITERIA:

- Psychiatric Diseases.
- History of Drug abuse and allergy to local anaesthetics of the amide type.
- ASA III and IV
- Contraindications of epidural anaesthesia
- Spine abnormalities.
- Hematological disorders.
- Bleeding or coagulation test abnormalities.
- Local skin infection.
- Hemodynamically unstable patients such as bradycardia, orthostatic hypotension, atrioventricular block.

Preanesthetic checkup done one day prior to the surgery premedicated with Tab. Ranitidine 150 mg and Tab. Alprazolam 0.5mg in the night the day before surgery, Patients were randomized into 2 groups ropivacaine with clonidine (RC) and ropivacaine with dexmedetomidine (RD) by computer generated numbers, blinding was achieved by resident who was preparing the study drug was not involved in study.

PROCEDURE: On the morning of the surgery, everything kept ready for emergency intubation and emergency drugs. After shifting the patient to operation theatre non-invasive minimum mandatory monitors were attached and the baseline pulse rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, ECG (lead II) and oxygen saturation were noted down. A wide bore I.V. cannula was secured. After taking aseptic precautions of the back (lumbar region) epidural space was identified by Loss of resistance method (Syringe technique), Negative pressure technique (Hanging drop sign).



Figure 4: drugs trays with epidural kit

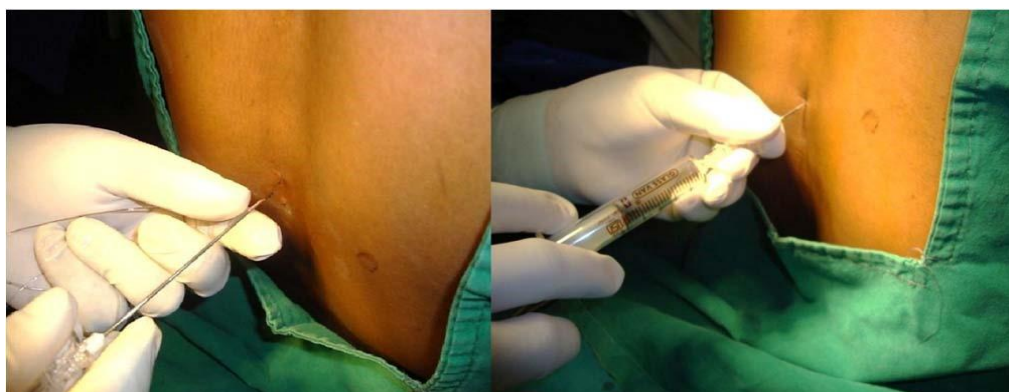


Figure 5: Epidural needle insertion

Figure 6: Loss of resistance method

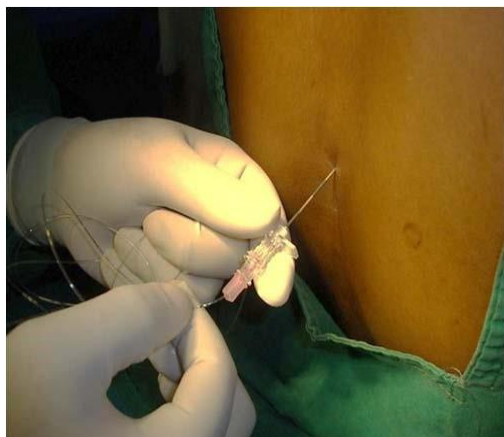


Figure 7: Epidural catheter insertion



Figure 8: Drug injection

A test dose of 3ml of 2% lignocaine hydrochloride solution comprising adrenaline 1:2,00,000 was injected. Later the thesis drug is administered as follow

- Group RC: Receives 15ml of 0.75 % ropivacaine with 1 µg/kg clonidine
- Group RD: Receives 15ml of 0.75 % ropivacaine with 1 µg/kg dexmedetomidine

The bilateral pin-prick method to evaluate and check the sensory level & modified Bromage scale for motor block.

MODIFIED BROMAGE SCALE

- 0 – No motorblock
- 1 – Inability to raise extended legs, able to move knees and feet
- 2 – Inability to flex knee, able to move feet
- 3 – Inability to flex ankle & foot, complete motor block
- Time of onset of sensory block level at T10, highest sensory block level, motor block level, intensity of motor block and duration of analgesia were recorded.
- Ramsay sedation scale was used for assessment of sedation score.
 1. Patient is anxious and agitated or restless.
 2. Patient is cooperative, oriented and tranquil.
 3. Patient responds to verbal commands only.
 4. Patient asleep with brisk response to a light glabellar tap or loud auditory stimulus.
 5. Patient asleep with sluggish response to light glabellar tap or loud auditory stimulus.
 6. Patient does't respond to painful stimulus.
- Heart rate (HR), blood pressure (BP), O2 saturation (SPO2) were monitored continuously and recordings were made every 5 mins for 10mins interval, thereafter at 10mins interval for 30 mins, thereafter at 15mins interval for 60 mins and finally at 20mins up to 120mins.
- Any side effects like hypotension (defined as systolic arterial pressure falling more than 20% mmHg) was noted and treated with inj. Mephentermine 6mg in bolus doses and bradycardia (heart rate <50 bpm) was noted and treated with 0.6mg with inj. Atropine.
- Statistical analysis was done by applying Chi-square test, Anova test and students 't' test to analyze the data, p value was determined. Microsoft word and Excel have been used to create tables, charts etc. P > 0.05 is not significant, P < 0.05 is significant, P < 0.001 is highly significant.

III. Observation And Results

Table 1: Demographic data

PARAMETER	GROUP – RC	GROUP – RD	P VALUE
Number of patients	30	30	
Age	39.60 ± 10.46	40.23 ± 12.07	0.829
Weight	59.60 ± 8.96	59.27 ± 11.01	0.898

Patients participated in this study were in the age group of 18-60 years. On statistical comparison the two groups were comparable and statistically not significant. The weight of the patients in group RC & group RD are comparable and statistically not significant. The mean weight in group RC is 59.6 kgs and group RD is 59.27 kgs.

Table 2: ASA grade in two groups

ASA grade	Group – RC		Group – RD	
	Number	Percentage (%)	Number	Percentage (%)
ASA	19	63.3	16	53.3
ASA II	11	36.7	14	46.7
Total	30	100	30	100

In this study 63.3 % of patients in the RC group and 53.3 % of patients in the RD group belong to ASA I. 36.7 % patients in RC group and 46.7 % in RD group belongs to ASA II. Distribution of ASA grade is statistically not significant in two groups with P = 0.30.

Table 3: Surgeries in two groups of patients studied

Surgeries	Group – RC		Group – RD	
	Number	Percentage (%)	Number	Percentage (%)
Hernioplasty	4	13.33	3	10
CRIF/ORIF with PFN	10	33.33	11	36.66
ORIF with ILN	3	10	5	16.66
DHS	3	10	1	3.33
TAH	10	33.33	10	33.33
Total	30	100	30	100

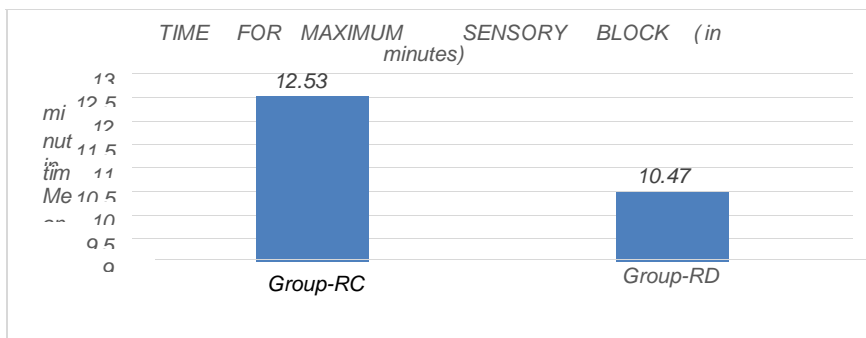
Table 4: comparison of time for onset of sensory and motor block

Variables	Group – RC	Group – RD	P value
Time from injection to sensory level T10 (in min)	6.63 ± 2.49	5.30 ± 2.07	0.028
Time for maximum sensory block (in minutes)	12.53 ± 3.70	10.47 ± 2.89	0.019
Onset time for Bromage 3 (in minutes)	21.73 ± 5.15	19.17 ± 6.50	0.096



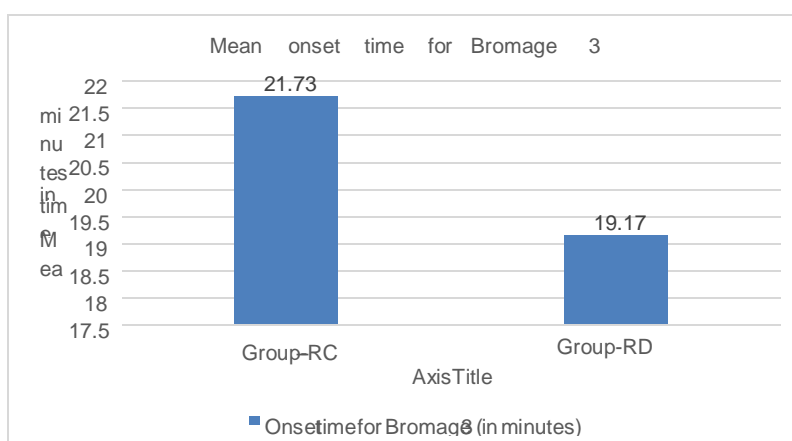
Graph 1: Time from injection to T10 sensory level

Onset of sensory blockade in both groups is comparable and the distribution of patients was statistically significant, onset is delayed in group RC.



Graph 2: Time from injection to maximum sensory block

Time for maximum sensory blockade is comparable and the distribution of patients was Statistically significant. onset is delayed in group RC.



Graph 3: Time from injection to Bromage 3

Onset time for Bromage 3 is compared in both groups, which are statistically not Significant. The systolic blood pressure in 2 groups was compared at 1,20,30,45,90 and 120 min statistically significant. The mean diastolic blood pressure is compared between 2 groups at 1,20,45 and 60 were statistically significant. The mean arterial blood pressure in 2 groups are compared and at 1,20,45,60 min. The study is statistically significant. (P < 0.05). The heart rate is compared between 2 groups at 20,60,90 the study is statistically significant. (P < 0.05).

Table 5: Comparison of side effects in two groups

Side effects	Group – RC		Group – RD	
	Number	Percentage (%)	Number	Percentage (%)
Dry mouth	0	0	2	6.66
Hypotension	11	36.66	23	76.66
Bradycardia	8	26.66	19	63.33

In this study side effects of 2 groups were compared, 6.66 % patients of RD group had experienced dry mouth, 76.66 % developed hypotension, 63.33 % developed bradycardia. In RC group 36.66 % developed hypotension and 26.66 % developed bradycardia.

Table 6: Comparison of Ramsay sedation scale in both the groups

RSS	Group - RC	Group - RD	P value
1 min	1.00 ± 0	1.00 ± 0	<0.001
5 min	1.00 ± 0	1.00 ± 0	<0.001
10 min	1.13 ± 0.35	1.97 ± 0.18	<0.001

20 min	1.90 ± 0.55	2.73 ± 0.45	<0.001
30 min	2.00 ± 0.53	2.97 ± 0.18	<0.001
45 min	2.3 ± 0.65	3.0 ± 0	<0.001
60 min	2.43 ± 0.51	3.0 ± 0	<0.001
90 min	2.5 ± 0.51	3.0 ± 0	<0.001
120 min	2.62 ± 0.49	3.0 ± 0	<0.001

Ramsay sedation score was compared in both groups, RSS score is more in group RD So RD group was more sedative action. Statistically both groups were highly significant. (p value <0.001). Duration of time for 2 segment regression, time for Bromage grade 1, time for sensory regression to S 1, time for 1st epidural top up all were comparable and all were statistically highly significant (p value <0.001).

IV. Discussion

Epidural anaesthesia is considered as a gold standard technique as it provides complete and dynamic anaesthesia. The benefits include suppression of stress response by sympatholysis, stable hemodynamics with reduction in cardiac mortality, reduction in pulmonary complications due to active physiotherapy and early mobilization, reduced blood loss and decrease in thromboembolic complications following surgery.

Epidural anaesthesia provides adequate anaesthesia, it does not decrease apprehension induced by fear of surgery and unfamiliar environment of operation theatre. In order to overcome this draw backs there always has been a search for drugs with sedative properties to be added as adjuvants to local anaesthetics.

α-2 agonists to local anaesthetics in epidural anaesthesia having its own pharmacology profile and its side effects.

The main aim of postoperative analgesia is to provide subjective comfort, in addition to inhibiting nociceptive impulse caused by surgical trauma and to blunt somatic as well as autonomic reflexes in response to pain.

The epidural administration of these drugs is associated with sedation, anxiolysis, analgesia, hypnosis and sympatholysis.^{3,4} The faster onset of action of local anaesthetic, rapid establishment of both sensory and motor blockade, prolonged postoperative analgesia, dose sparing action of local anaesthetic and stable cardiorespiratory parameters make these agents very effective adjuvants in neuraxial anaesthesia.⁷⁻¹²

The present study was performed to compare the clonidine and dexmedetomidine in their efficacy as adjuvants in epidural anaesthesia.

The two groups were comparable and the mean values of age with standard deviation are 39.60 ± 10.46, 40.23 ± 12.07 in RC and RD groups respectively. There was no statistically significant difference between these two groups, P = 0.829 and 0.898 respectively.

Anand VG,¹⁴ et al (2011) used 0.25 % ropivacaine caudally, Chandran²⁴ et al (2014) also used 0.75 % epidurally, MausumiNeogi,¹⁵ et al (2011) also used 0.25 % caudally, Salgado,¹⁶ et al (2008) used 0.75 % epidurally, Arunkumar, V.R. Hemanth kumar,¹³ et al (2015) used 0.75% epidurally, Bajwa SJ.¹² (2011) et al (2011) used 0.75 % epidurally.

0.75 % Ropivacaine produce adequate intensity of motor and sensory blockade and is comparable to 0.5 % bupivacaine with reduced side effects and less cardiotoxicity compared to clonidine and also mean onset time of sensory block was shorter in 0.75 % Ropivacaine group when compared to 0.5 % Bupivacaine group. Hence for present study the dose selected is similar as in the study conducted by Sruthi Arunkumar,¹³ et al.

In present study the mean time for onset of sensory analgesia at T 10 is 6.63 ± 2.49 mins

In group RC and 5.30 ± 2.07 mins in group RD. This is statistically significant (p < 0.05)

and the onset is faster in RD group compared to RC group. Saravia P.S.F, Sabbag AT et al²⁵ found no significant change in the onset time for sensory block between control and dexmedetomidine groups.

In present study the duration of sensory block is longer with Ropivacaine + Dexmedetomidine group compared to Ropivacaine + Clonidine group. It is 429.60 ± 46.20 mins in Ropivacaine + Dexmedetomidine group compared to 367.67 ± 49.02 mins in Ropivacaine + Clonidine group. This is statistically highly significant. (P < 0.001)

V, Kaur J¹⁷ et al who observed the mean duration of analgesia to be 366.62±24.42 mins in group ropivacaine with dexmedetomidine compared to 242.16±23.86 mins with in group ropivacaine with fentanyl which is highly significant. Present study also concords with study conducted by Sruthi Arunkumar, V.R. Hemanth kumar, N. Krishnaveni, M.

In the present study, the onset of motor blockade was 12.53 ± 3.70 mins in group RC and 10.47 ± 2.89 mins in group RD. This is not significant statistically. Motor block was assessed using modified Bromage scale. **Saravia P.S.F, Sabbag AT et al**²⁵ found no significant change in the onset time for motor block between control and Dexmedetomidine group.

Brockway M S et al²⁶, who conducted a study comparing 0.5 %, 0.75 % and 1 % ropivacaine with 0.5 % and 0.75 % Bupivacaine found no significant differences in the onset of motor block.

Finucane B T et al²⁷, found no clinical difference in the onset of motor block, when comparing 0.5 %, 0.75 % and 1 % ropivacaine with 0.5 % Bupivacaine for epidural anaesthesia in patients undergoing abdominal hysterectomy.

The duration of motor block in present study in group RD is 390.33 ± 45.37 mins compared to 348.50 ± 40.15 in group RC. The duration of motor block with group RD group is more prolonged than with group RC, which is statistically highly significant. ($P < 0.001$).

Brockway M S et al²⁶, compared 0.5 %, 0.75 % and 1 % ropivacaine 15ml with 0.5 % and 0.75 % Bupivacaine 15ml in 110 patients and found no significant difference in onset, spread or duration of motor block when similar concentrations were compared. However, Ropivacaine produced a slower onset, shorter duration and less intense block than Bupivacaine.

Wolff A.P et al²⁸ studied 126 patients undergoing elective hip surgery; they received 20ml of 0.5 %, 0.75 % and 1 % ropivacaine or 0.5 % Bupivacaine extradurally in a double-blind study. Return of motor function was earlier with Ropivacaine compared to Bupivacaine.

In present study, the sedation scores were higher in RD group patients. This is statistically highly significant. ($P < 0.001$) Similar results were also observed by **Bajwa SJ, Arora V, Kaur J¹² et al**. Mean sedation scores were significantly higher in dexmedetomidine group compared to clonidine group ($P < 0.001$).

Bajwa SJ, Bajwa SK, Kaur J, Singh G, Arora V, Gupta S, et al¹² reported that sedation score was more in dexmedetomidine group when compared with clonidine group which was statistically significant ($p < 0.05$). In present study, sedation score was more in group RD (dexmedetomidine) when compared with group RC (clonidine) which is statistically highly significant ($p < 0.001$). Present study results are similar to **Bajwa sj et al¹²** study.

The study conducted by **Sruthi Arunkumar, V.R. Hemanthkumar, N. Krishnaveni, M. Ravishankar, Velrajaya, and M. Aruoli. Et al¹³**(2015) were found significant good sedation in the patients who received dexmedetomidine than those who received clonidine.

V. Conclusion

The α -2 against Dexmedetomidine given epidurally with Ropivacaine produces synergistic effect of profound and prolonged motor blockade and also a prolonged duration of sensory blockade and provide good sedation. Even though the side effects are more with dexmedetomidine group, they were treatable. So Ropivacaine + Dexmedetomidine can be safe and effective agent for epidural blockade in lower abdominal and lower limb surgeries.

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