



A COMPARATIVE STUDY OF CLONIDINE AS ADJUVANT TO ROPIVACAINE AND ROPIVACAINE ALONE IN EPIDURAL ANESTHESIA FOR LOWER LIMB SURGERIES

Anaesthesiology

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ABSTRACT

Introduction: Epidural anaesthesia is one of the most common regional anaesthetic techniques used for lower abdominal and lower limb surgeries. Due to similar analgesic properties, lesser motor blockade and decreased cardiotoxic tendency ropivacaine is increasingly used instead of bupivacaine now a days. Clonidine has been frequently used as an adjunct to local anesthetics because it improves the quality of anesthesia, reduces the dose requirement of the anesthetic agent and provides a more stable cardiovascular course.

Aims And Objectives:

1. To evaluate effect of ropivacaine alone in epidural anaesthesia for lower limb surgeries.
2. To evaluate effect of clonidine as adjuvant to ropivacaine in epidural anaesthesia for lower limb surgeries.
3. To compare effect of ropivacaine alone and clonidine as adjuvant to ropivacaine in epidural anaesthesia for lower limb surgeries.

Material And Method: The study was conducted in the department of Anaesthesiology, GGS Medical College, Faridkot, after approval by Hospital Ethical Committee. Written informed consent was obtained from each patient. The total of 90 patients were allocated into 2 groups of 45 patients each: 1. Group R (n=45) - 19 ml of 0.75% ropivacaine + 1 ml of normal saline (20 ml) 2. Group RC (n=45) - 19 ml of 0.75% ropivacaine + 75µg of clonidine diluted to 1 ml (20 ml). The onset time for sensory and motor block, the maximum level of sensory block, duration of analgesia and side effects were recorded. **Results:** The demographic profile were comparable in terms of age, sex, weight which was statistically non-significant in both the groups. Clonidine group (RC) had rapid onset of sensory and motor blockade (p=0.001) and prolonged duration analgesia (p=0.001). There was no statistically significant difference in HR, SBP, DBP, MAP monitored at various intervals between the two groups.

Conclusion: The use of Clonidine as an adjuvant to Ropivacaine for epidural anaesthesia produces early onset of sensory and motor blockade and prolonged the duration of analgesia as compared to ropivacaine alone, with minimal changes in haemodynamic parameters and adverse effects.

KEYWORDS

Ropivacaine, Clonidine, epidural block.

INTRODUCTION

Epidural anaesthesia is the most popular regional anaesthesia techniques used for lower limb, pelvis, perineum and lower abdominal surgeries. Epidural anaesthesia can be used as sole anaesthetic and it has the ability to maintain continuous anaesthesia after placement of an epidural catheter, thus making it suitable for procedures of long duration (1).

An ideal local anaesthetic in the epidural space should provide quick onset, sufficient motor block for surgical relaxation and good sensory block for providing post-operative analgesia with minimal central nervous system and cardiovascular toxicities (2).

Different local anaesthetics are used for epidural anaesthesia, most popular in India being Lidocaine and Bupivacaine (3). Recently Ropivacaine has been introduced and since Ropivacaine has all the advantages of bupivacaine with less cardiac toxicity, it appears that it may be an ideal local anaesthetic for epidural anaesthesia (4,5).

Ropivacaine, a long-acting amide local anesthetic, is an optically active pure S-enantiomer of propivacaine (6). Numerous comparative studies between ropivacaine and bupivacaine suggested that ropivacaine produces less cardiac as well as central nervous system toxic effects and lesser motor block (7,8). This favorable clinical profile prompted many clinicians to switch from bupivacaine to ropivacaine for the neural blockade.

Because ropivacaine has to be given in larger doses to achieve the analgesic and anaesthetic effects, the addition of adjuvants can decrease the dose requirement and permit use of more diluted solutions for better analgesia and prevent side effects associated with larger doses of ropivacaine (9,10). Recent studies have showed that reducing the concentration of ropivacaine would provide an additional margin of safety as well as reduces the incidence of the unwanted motor blockade (11).

Adjuvants are the drugs that, added to local anesthetics, enhance or

prolong their action. The most commonly used, in descending order, are the opioids (morphine, fentanyl, sufentanil, methadone), α_2 adrenergic agonists (clonidine and dexmedetomidine), ketamine and neostigmine.

The addition of adjuvants causes a reduction in the dose of local anesthetic and minimizes the hemodynamic and neurological effects (12).

Clonidine, a α_2 adrenergic agonist, acts on inhibitory α_2 adrenergic receptors to reduce central neural transmission in the spinal neurons (13). The coadministration of clonidine and local anesthetic produces better analgesia than either drug alone (14).

Clonidine augments the action of local anesthetics in regional blockades by interrupting the neural transmission of painful stimuli in A δ and C fibers as well as augments the blockade of local anesthetic agents by increasing the conductance of K⁺ ions in nerve fibers. It also exerts a vasoconstricting effect on smooth muscles, which results in a decreased absorption of the local anesthetic drug and eventually prolongs the duration of analgesia (15,16).

Addition of adjuvant to local anesthetic epidurals increases the duration of analgesia and intensity of the block with minimal stress response resulting in early ambulation and less postoperative morbidity. Although intrathecal clonidine as an adjuvant to ropivacaine has been studied extensively, there is a paucity of literature on the epidural use of ropivacaine and clonidine for lower limb surgeries.

The attempts to improve the quality of block and to enhance the postoperative analgesic effect with the addition of adjuvants is increasing in the current practice. Thus, the present study will evaluate the efficacy of epidural clonidine as an adjuvant with ropivacaine compared to ropivacaine alone in patients undergoing lower limb surgeries.

AIM AND OBJECTIVES

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MATERIAL & METHODS

After taking the permission from Thesis committee and Institutional Ethics Committee of Guru Gobind Singh Medical College, Faridkot, study was conducted on 90 selected patients undergoing lower limb surgeries under epidural anaesthesia for a period of 18 months. Written informed consent of the patient recruited in the study were taken.

Inclusion criteria for the study

1. Adult patients aged between 18 to 65 years of both sex.
2. Patients belonging to ASA class I and II posted for elective lower limb surgical procedures.

Exclusion criteria for the study

1. Patient refusal for regional anaesthesia.
2. Pregnancy and lactation.
3. Obese patient with BMI > 30.
4. Contraindication to regional anaesthesia
5. Allergy to local anaesthetics
6. Allergy to study drugs

The study population were divided into two groups with 45 patients in each group.

1. Group R (n=45) - 20 ml (19 ml of 0.75% ropivacaine + 1 ml of normal saline)
2. Group RC (n=45)- 20 ml (19 ml of 0.75% ropivacaine + 75µg of clonidine diluted to 1 ml).

A routine pre-anaesthetic examination was conducted on the evening before surgery.

The patients were premedicated with tablet alprazolam 0.5 mg and tablet ranitidine 150 mg orally at bed time on the previous night before surgery. They were kept nil orally 10 pm onwards on the previous night.

On the day of surgery, patient's basal pulse rate and blood pressure were recorded. A peripheral intravenous line with 18 gauge cannula after local anaesthesia was secured in one of the upper limbs. All the patients were preloaded with 500 ml of Ringer lactate 30 minutes prior to the epidural procedure. Multiparameter monitor was connected which recorded heart rate, non-invasive measurement of systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), continuous electrocardiogram (ECG) monitoring and oxygen saturation (SPO₂).

With the patients in sitting position under aseptic precautions, epidural space was identified by loss of resistance technique to air using 18G Tuohy needle via the midline approach at either L2-3 or L3-4 inter spinous space. An epidural catheter was threaded and fixed at 5 cms inside the epidural space. A test dose of 3 ml of 2% lignocaine with 1:200000 adrenaline was injected through the catheter after aspiration. After ruling out intrathecal and intravascular placement of the tip of the catheter, study drug was injected in increment doses. The patients were turned to supine position after 1 min.

Assessment of sensory and motor blockade was done at the end of each minute with the patient in supine position after completion of the injection of 20 ml of the study drug, which is taken as the starting time. The onset time for sensory and motor block, the maximum level of sensory block, duration of analgesia and side effects were recorded.

Onset of sensory blockade is taken as the time from the completion of the injection of the study drug till loss of sensation at T10 level. Onset of motor blockade: is taken from the completion of the injection of study drug till the patient develops Bromage scale grade 1 motor blockade. Duration of Analgesia is taken as time from onset of sensory block till the patient complains of pain at the T10 dermatome.

Side effects such as hypotension, bradycardia, headache, dry mouth, nausea, vomiting, local anaesthesia toxicity, backache, urinary retention etc were recorded.

Measurements of blood pressure, heart rate, respiratory rate and

oxygen saturation were recorded every 5 minutes till the end of 1/2 hour and then every 10 minutes till the end of surgery.

After the surgery, patients were referred to the recovery room (PACU) post anaesthesia care unit. Epidural top up was given with 8ml of 0.2% inj. ropivacaine once the patient complains of pain.

Statistical Analysis

Data was analysed using Statistical Package for the Social Sciences (SPSS version 21.00). Continuous data was presented as mean with standard deviation. Categorical data was expressed as percentages. Numerical variables were normally distributed and were compared using Chi Square test for non-parametric data and Student's 't' test for parametric data.

RESULTS

The mean age in group R was 42.69±14.00 SD and mean age in group RC was 41.29±13.28 SD. In both the groups there was predominance of male patients. The mean body weight in group R was 59.56±6.15 kg and group RC was 57.87±5.80 kg. In our study the demographic data comparing age, sex and weight shows no statistically significant difference among both the groups.

Table 1: Maximum Level Of Sensory Blockade Attained

Max dermatomal level of analgesia	Group R		Group RC		p value
	No.	%	No.	%	
T5	2	4.44	5	11.11	0.124
T6	28	62.22	34	75.56	
T8	13	28.89	5	11.11	
T10	2	4.44	1	2.22	
Total	45	100.00	45	100.00	

The maximum level of sensory blockade attained by the two groups was T5. There was no significant difference between the two groups (p=0.124).

Table 2: Mean Time For Onset Of Sensory, Motor Block And Duration Of Analgesia (minutes)

	Group R		Group RC	
	Mean	SD	Mean	SD
Sensory onset (mins)	12.41	2.51	9.86	1.51
Motor onset (mins)	22.63	3.18	18.54	4.53
Duration of analgesia (mins)	208.58	52.36	262.01	48.21

The mean time of onset of sensory blockade in group R was 12.41±2.51 mins and in group RC was 9.86±1.51 mins. There was statistical significant difference between the groups (p=0.001). The mean time taken for the onset of motor blockade was 22.63±3.18 mins in group R and 18.54±4.53 mins in group RC. There was statistical significant difference between the groups (p=0.001). The mean duration of analgesia was 208.58±52.36 mins in group R and 262.01±48.21 mins in group RC. There was statistically significant difference between the groups (p=0.001).

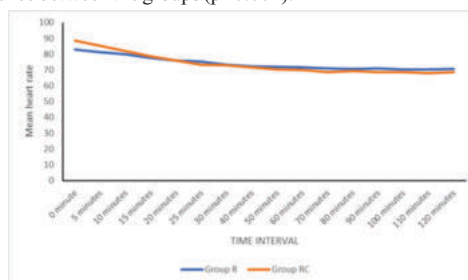


Figure 1- Mean Heart Rate (bpm) At Various Time Intervals

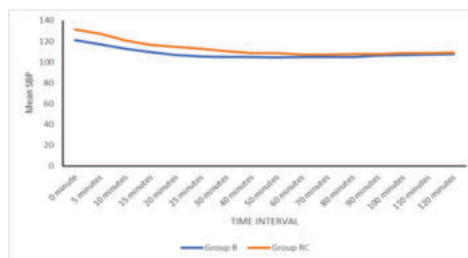


Figure 2- Mean Systolic Blood Pressure (mmhg) At Various

Intervals

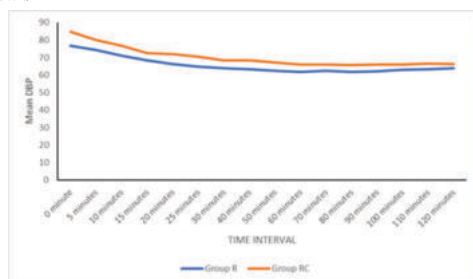


Figure 3- Mean Diastolic Blood Pressure(mmHg) At Various Time Intervals

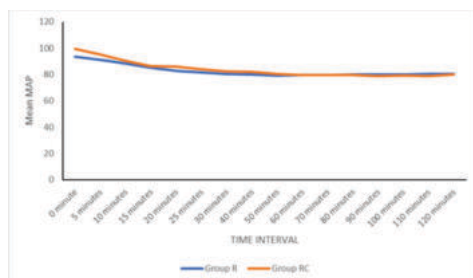


Figure 4- Mean Arterial Pressure(mmHg) At Various Time Intervals

There was no statistically significant difference in the mean heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure between groups at various intervals (Figure 1,2,3,4). 4 patients in RC group developed bradycardia which was treated with inj.atropine 0.6mg.

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 haemodynamics with reduction in cardiac morbidity, reduction in pulmonary complications due to active physiotherapy and early mobilization, reduced blood loss and decrease in thromboembolic complications following surgery (17). The addition of adjuvants like α_2 -agonists provide the rapid establishment of both sensory and motor blockade, prolonged duration of analgesia into the post-operative period, dose-sparing action of local anaesthetics and stable cardiovascular parameters makes these agents a very effective adjuvant in regional anaesthesia (18-23). Motor blockade tends to be denser with α_2 -agonists. It is also devoid of respiratory depression, pruritus, nausea, and vomiting (24).

Demographic data In our study the demographic data comparing age, sex and weight showed no statistically significant difference among both the groups. A study done by Kohli AV et al compared the demographic parameters including age, weight, height and sex of all the patients and type of surgery was also comparable. No statistical difference was observed in any group (25). In a study by Singh AK et al, the demographic profile parameters were comparable and statistically non-significant in both the groups (26).

Onset Of Sensory Blockade

In our study the mean time for onset of sensory analgesia at T10 was 12.41 ± 2.51 mins in group R and 9.86 ± 1.51 mins in group RC. This was statistically significant ($p=0.001$).

This finding was consistent with the previous observations made by Thimmappa M et al who did a comparative study of epidural ropivacaine 0.75% alone with ropivacaine plus clonidine for lower abdominal and lower limb surgeries.

This study showed the mean onset of analgesia in Group R was 12.33 ± 1.56 mins and in Group RC was 9.17 ± 1.21 mins therefore onset of anaesthesia was faster in group Group RC when compared to Group R ($p<0.001$) and this was statistically significant (27).

Kumar N et al conducted a randomised comparative study between epidural ropivacaine and ropivacaine-clonidine combination for

infraumbilical surgeries. 80 patients who underwent infraumbilical surgeries were randomly divided into two study groups comprising 40 patients in each group. This study showed the mean time for onset of sensory block was 12.90 ± 1.39 min in Group R and 8.05 ± 1.45 min in Group RC and the difference between the two groups was very highly significant ($p<0.001$) and similar to our study (28).

Bajwa SJ et al studied the qualitative and quantitative aspects of epidural block of ropivacaine 0.75% versus ropivacaine 0.75% with clonidine for elective cesarean section. They found that the onset of sensory analgesia at T10 was 11.36 ± 3.30 min in patients receiving Ropivacaine alone and 8.64 ± 2.56 min in the group RC receiving Clonidine an adjuvant and this was also associated with a faster and higher level of sensory blockade, which supported our findings (29).

Singh M et al did a comparative study of clonidine with ropivacaine versus ropivacaine alone in epidural anaesthesia for lower limb orthopedic surgery. This study showed the onset of sensory blockade was 15.43 ± 2.70 mins in group R and 10.55 ± 1.85 mins in group RC and this was statistically significant and similar to our study (30).

Kohli AV et al evaluated the effect of clonidine as adjuvants with Ropivacaine in epidural block in patients undergoing lower limb or perineal surgeries. It showed the mean time in minutes for onset of sensory block at T10 dermatome was found to be significantly decreased in RC group when compared to Group R ($p<0.001$).

The mean time of onset of sensory block was 15.67 ± 3.20 min in Group R and 12.33 ± 4.69 min in Group RC which was statistically similar to our group (25).

Onset Of Motor Blockade

The onset of motor blockade was 22.63 ± 3.18 mins in group R and 18.54 ± 4.53 mins in group RC. This was statistically significant as $p=0.001$.

Our results were in correlation with a study conducted by Singh M et al who did a comparative study of clonidine with ropivacaine versus ropivacaine alone in epidural anaesthesia for lower limb orthopedic surgery. Eighty patients were randomized to one of the two groups of forty patients each. Group 1: Received 20 ml 0.75% ropivacaine through epidural route and Group 2: Received epidural 20 ml of 0.75% ropivacaine with 75 μ g clonidine. This study showed the onset of motor blockade was 21.10 ± 2.81 mins in group R and 15.58 ± 2.02 mins in group RC and this was statistically similar to our study. The time taken for onset of motor block was significantly shorter in Group RC as compared to Group R (30).

Kumar N et al conducted a randomised comparative study between epidural ropivacaine and ropivacaine-clonidine combination for infraumbilical surgeries. 80 patients who underwent infraumbilical surgeries were divided randomly into two study groups comprising 40 patients in each group. Epidural anaesthesia was administered with 20ml of Ropivacaine 0.75% (GROUP-R) and 20 ml of epidural Ropivacaine 0.75% and Clonidine 75mcg combination (GROUP-RC).

The onset of motor block was shorter in group RC as compared to group R. The mean time for onset of motor block was 30.25 ± 2.35 min in Group R and 28.23 ± 2.91 min in Group RC and the difference between the two groups was highly significant ($p < 0.001$) and which supported our findings (28).

Maximum Level Of Sensory Blockade

In our study the maximum level of sensory blockade achieved was T5. Two patients in group R and 5 patients in group RC had T5 level of sensory blockade.

28 patients in group R and 34 patients in group RC had T6 level of sensory blockade. There was no statistically significant difference between the two groups ($p=0.124$).

In a study conducted by Kohli AV et al, maximum sensory block level was divided as T7 or higher and less than T7. Number of patients with a block level $> T7$ were 13 in Group R and 21 in Group RC. The maximum level of sensory block obtained was comparable and statistically insignificant which was similar to our study (25).

A study conducted by Kumar N et al, maximum sensory level was established at T6-T7 level, there was no statistically significant

difference in maximum level of sensory blockage in either of the group (28).

Duration Of Analgesia

In our study the duration of analgesia is longer with Ropivacaine + clonidine group compared with Ropivacaine group. It was 208.58±52.36 mins with ropivacaine group and 262.01±48.21 mins with ropivacaine + clonidine group. This was statistically significant ($p=0.001$).

Our results were in correlation with a study done by Thimmappa M et al who showed the mean duration of analgesia was 200.33±17.07 min in Group R and 261.07±17.68 min in Group RC resulting in significantly longer duration in Group RC when compared to Group R ($p<0.001$) (27).

A study done by Kohli AV et al evaluated the effect of clonidine as adjuvants with Ropivacaine in epidural block in patients undergoing lower limb or perineal surgeries. The mean duration of sensory analgesia was 161.33±21.61 min in Group R and 276.67±26.11 min in Group RC. The results of the study was consistent with our study (25).

A study conducted by Singh M et al showed the mean duration of analgesia was 243.40±11.89 min in Group R and 345±12.31 min in Group RC and this was also statistically similar to our study (30).

Singh AK et al conducted a comparative study of epidural ropivacaine (0.75%) with ropivacaine (0.75%) plus clonidine for lower abdominal and lower limb surgeries. The patients were randomly allocated into two groups; Ropivacaine ® and Ropivacaine + Clonidine (RC) and comprising of 30 patients each. Group R received 15 ml of Ropivacaine (0.75%) and group RC received 15 ml of Ropivacaine (0.75%) with Clonidine 75 µg epidurally. This study showed the duration of analgesia was 311±28.20 min in Group R and 344±24.94 minutes in Group RC when Clonidine used as an additive with Ropivacaine. The results were consistent with our study (26).

Another study by Kumar N et al showed the mean duration of sensory analgesia was 362.60±5.96 min in Group R and 451.10±13.79 min in Group RC and difference between the two groups was statistically very highly significant ($p<0.0001$) resulting in longer duration of analgesia in Group RC (28).

Side Effects

In our study 4 patients in RC group developed bradycardia which was treated with inj.atropine 0.6mg. No patients in group R developed significant bradycardia.

A study done by Kohli AV et al showed hypotension and bradycardia in insignificant number and results of this study was similar to our study (25). A study conducted by Thimmappa M et al observed Bradycardia in 13.3% of patients in Group RC whereas none of the patient in Group R had bradycardia which was similar to our study (27).

Heart Rate

There was no statistically significant difference in the heart rate between the two groups at various time intervals.

Blood Pressure

There was no statistically significant difference in SBP, DBP, MAP monitored at various intervals between the two groups. Rao KG et al in their study found that there was no event of hypotension noticed in any group thus highlighting that the adjuvant use of clonidine did not reduce the arterial pressure substantially (31).

CONCLUSION

It can be concluded that addition of 75 µg of clonidine to epidural ropivacaine produces early onset of sensory and motor blockade, prolonged duration of analgesia and less requirement of epidural top ups when compared with ropivacaine alone for lower limb surgeries with minimum changes in hemodynamic parameters and less adverse effects.

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