Original Research Article

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A Comparative Study of Epidural Dexmedetomidine and Clonidine as Adjuvant to 0.2% Isobaric Ropivacaine for Post Operative Analgesia in Lower Limb Orthopaedic Surgeries

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Abstract

Background: Various adjuvants are being used with local anesthetics for prolongation of analgesia like opioids, but the onset and duration of analgesia is improved when a local anesthetic is combined with alpha2 adrenergic agonist. Though, the effects of clonidine on local anesthetics have been extensively studied, there are limited studies demonstrating the effects of epidural dexmedetomidine on local anesthetics. *Aims and objectives:* To compare the efficacy, onset and duration of postoperative analgesia and side effects of clonidine and dexmedetomidine when used epidurally as an adjuvant to ropivacaine in patients undergoing lower limb orthopedic surgeries. *Settings and Design:* This study was designed to compare the efficacy, onset and duration of postoperative analgesia and side effects of clonidine and dexmedetomidine when used epidurally as an adjuvant to ropivacaine in patients undergoing lower limb orthopedic surgeries. *Methods and Material:* Patients were randomized into two groups- group ropivacaine with dexmedetomidine (RD) received 20 ml of 0.2% ropivacaine with 1 μg/kg dexmedetomidine epidurally and group ropivacaine with clonidine (RC) received 20 ml of 0.2% ropivacaine with 2 μg/kg clonidine. Onset and duration of analgesia and Ramsay sedation score and hemodynamic parameters were monitored and side effects if any noted. *Statistical analysis used:* mean±standard deviation for quantitative continuous data and compared by unpaired *t*-test. *Result:* The onset of analgesia (RD-4.4±0.67min, RC-6.3±0.74min) and duration of analgesia (RD-665.16±29.8min, RC-462.16±29.8min) were found to be significantly better in dexmedetomidine group. Better sedation score was seen in dexmedetomidine group. *Conclusion:* Epidural dexmedetomidine (1mcg/kg) and clonidine (2mcg/kg) with ropivacaine 0.2% had good efficacy however the dexmedetomidine provided faster and prolonged duration of postoperative analgesia and good sedation compared to clonidine.

Keywords: Epidural; Analgesia; Ropivacaine; Clonidine; Dexmedetomidine.

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Introduction

Epidural anesthesia is the most commonly used technique for providing not only intraoperative surgical anesthesia but also post-op analgesia in orthopedic lower limb surgeries [1]. It helps in early postoperative mobilization and rehabilitation with minimally associated pain and discomfort is the most desirable feature in modern orthopaedic surgery [2].

Ropivacaine, a new amide local anaesthetic, 's' enantiomer of bupivacaine with less toxicity. It has minimal cardiovascular and central nervous system toxicity as well as lesser propensity of motor block during postoperative epidural analgesia [3]. The duration of analgesia is 4 to 5 hours.

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Various adjuvants are being used with local anesthetics for prolongation of analgesia like opioids, but there is always a possibility of side effects like nausea, respiratory depression, pruritus and urinary retention [4]. Alpha 2 adrenergic agonists provide both analgesic and sedative properties when used as adjuvants in regional anaesthesia [5].

Clonidine, An alpha2 adrenoceptor agonist, acts by stimulating alpha2 receptor in the brain and blocks A-delta and C fibers as a consequence of an increase in potassium conductance in isolated neurons, thus intensifying local anesthetic conduction block [6]. Clonidine decreasing local anesthetic spread due to the action on postsynaptic alpha 2 receptors and cause local vasoconstriction, thus provides prolonged analgesia [7,8].

Dexmedetomidine, a new addition to the class of alpha-2 agonist which has eight fold greater affinity to alpha 2 agonists than clonidine with numerous beneficial effects [9]. It acts on both pre and post synaptic sympathetic nerve terminal and central nervous system and highly selective to alpha 2a receptors than alpha 1, thereby causing sedative, hypnotic, anti-anxiety, analgesic, and sympatholytic effects [10].

This study was designed to compare the efficacy, onset and duration of postoperative analgesia and side effects of clonidine and dexmedetomidine when used epidurally as an adjuvant to ropivacaine in patients undergoing lower limb orthopedic surgeries.

Methodology

Institute Ethics Committee (ICE) clearance was obtained and 60 patients belongs to ASA I and II, aged between 18 to 60 years; undergoing elective lower limb orthopedic surgeries under standard regional anesthesia were selected randomly. Patients belong to ASA III or more, suspected coagulopathy, known allergy to any of the study drugs and any signs of infection at the site of epidural block were excluded.

Sample Size: 60 cases

Sample size was calculated by using Winpepi statistical package at significance level of 5% with power of 80% using the inputs given below-

According to the study conducted by MS Saravana Babu, Anil Kumar Verma et al. in 2013 [15], on comparison of epidural route administration of inj clonidine (2mcg/kg) and inj dexmedetomidine (1mcg/kg) as an adjuvant to 0.2% ropivacaine (20 ml) in patients undergoing spine surgeries. We took the following inputs-

Parameter	Dexmedetomidine	Clonidine
Duration of analgesia (in minutes)	407 ± 47 (mean ± SD)	345 ± 35.09 (mean ± SD)

SD of duration of analgesia for dexmedetomidine – 47, SD of duration of analgesia for clonidine – 35.09 and difference in mean duration of analgesia between two groups was 62,we arrived at a minimal sample size of 16patients.

Hence we enrolled 30 patients in each group to account for potential dropouts or protocol violations.

Patients were divided into group RC and group RD. After obtaining informed consent, thorough pre-operative evaluation was done for all patients. In the operation theater, an intravenous access was secured and ECG, pulse oxymeter, NIBP monitors attached and baseline parameters like the pulse rate (PR), mean arterial pressure (MAP), and peripheral oxygen saturation (SpO_2) were observed and recorded. In sitting position under all aseptic precaution Lumbar epidural catheter was put at L2-L3 intervertebral space with 18 gauze tuhoy needle. Location of epidural space was confirmed by loss of resistance technique and epidural catheter was secured 3-5 cm into the epidural space.

Subarachnoid block was then given in L3-L4 space using 26G Quincke's needle and 3 ml of 0.5% heavy bupivacaine was injected. Surgery was performed under spinal anaesthesia. On being shifted to recovery room, the study was started once the patient in the post-operative room was noted to have pain (VAS>4). A test dose of 3ml lignocaine with adrenaline (1:200,000) was given epidurally and the patients were randomly allocated to one of the following two groups in a double-blinded fashion.

Group RD: Received ropivacaine 0.2% 20ml and dexmedetomidine 1 mcg/kg.

Group RC: Received ropivacaine 0.2% 20 ml plus clonidine 2 mcg/kg.

After giving epidural dexmedetomidine or clonidine; heart rate, blood pressure (SBP, DBP and MAP), onset and duration of analgesia and Ramsay sedation score and side effects (nausea, dry mouth, bradycardia and hypotension) were recorded at 0 min, 30 min, 60 min, 90 min, 120 min and 6 hours and noted. Once the patient asked for additional epidural analgesia (VAS>4) for pain relief, the study ended and rescue analgesia with inj. Diclofenac 75mg IV given. Assessment of pain was done by using visual analogue score (VAS score).

Results were statistically analysed, Variables were presented as mean±standard deviation for quantitative continuous data such as onset and duration of analgesia and compared using unpaired *t*-test. p value < 0.05 is considered significant.

Ramsay Sedation Score [18]

1. Patient anxious or agitated or both.
2. Patient cooperative, oriented and tranquil. Patient response to commands only.
3. A brisk response to light glabellar tap.
4. A sluggish response to a light glabellar tap.
5. No response.

Results

All the enrolled 6o patients (30 patients in each group) completed the study. The demographic profile of two groups was similar in age, gender distribution, weight, height and ASA grading.

With regards to HR statistical difference existed between Group RD and Group RC. There was a fall in heart rate at 30, 60, 90 and 120min, which was statistically significant (p<0.05) (Figure 1) but not clinically.

MAP was significantly lower in Group RD than Group RC at 30, 60, 90, 120min and 6 hours after giving drug from baseline (Figure 2), which was statistically significant, but not clinically.

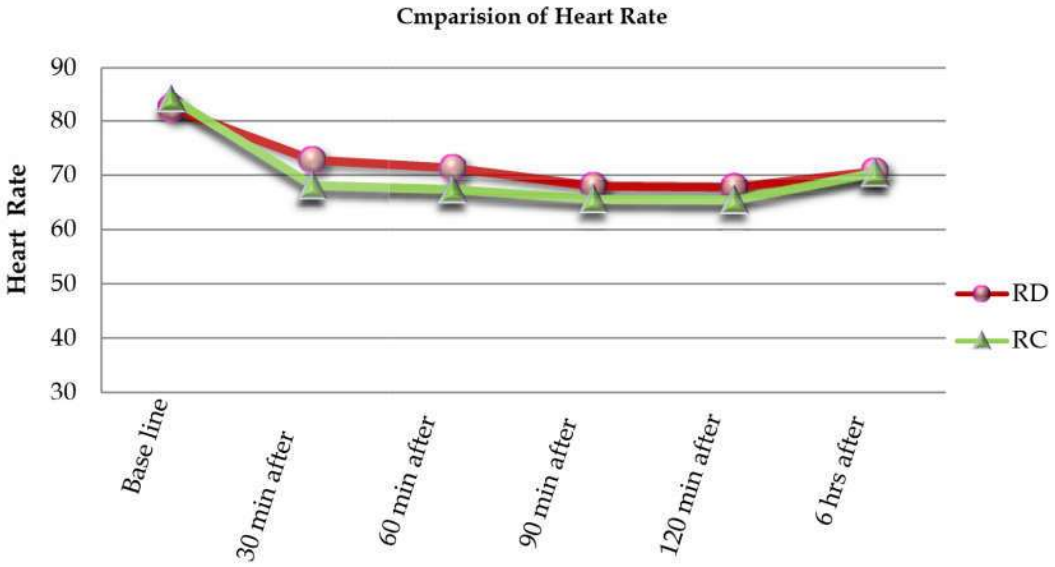

Fig. 1: Line diagram showing comparison of heart rate in study groups

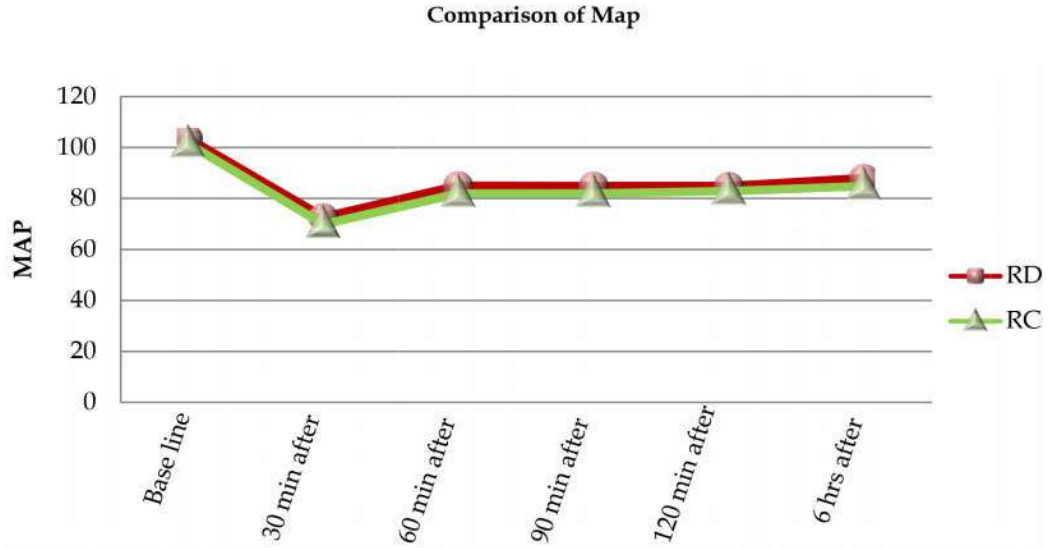

Fig. 2: Line diagram showing comparison of MAP in study groups

In group 'RD' majority of patients had onset of analgesia in 4.4±0.67 minutes, however in RC majority of patients had onset of analgesia in 6.3±0.74 minutes and the difference was statistically significant (p<0.0001) (Figure 3). In group RD duration of analgesia was 665.16±29.81 minutes where as in group RC duration of analgesia was 462.16±36.19 minutes, which was statistically significant (p<0.0001) (Figure 4) (Table 1).

The sedation score was analyzed quantitatively within groups for each stage from baseline to 6hrs. This was statistically significant at 30 min, 60 min and 90 min (p< 0.05). The sedation score was relatively lower in Group RD, which was statistically not significant at 120 min and 6hrs (p>0.05) (Figure 5) (Table 2).

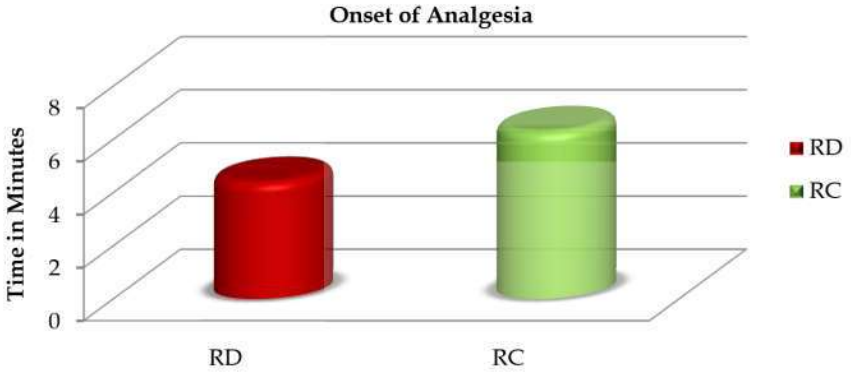

Fig. 3: Bar diagram showing the comparison of onset of analgesia in study groups

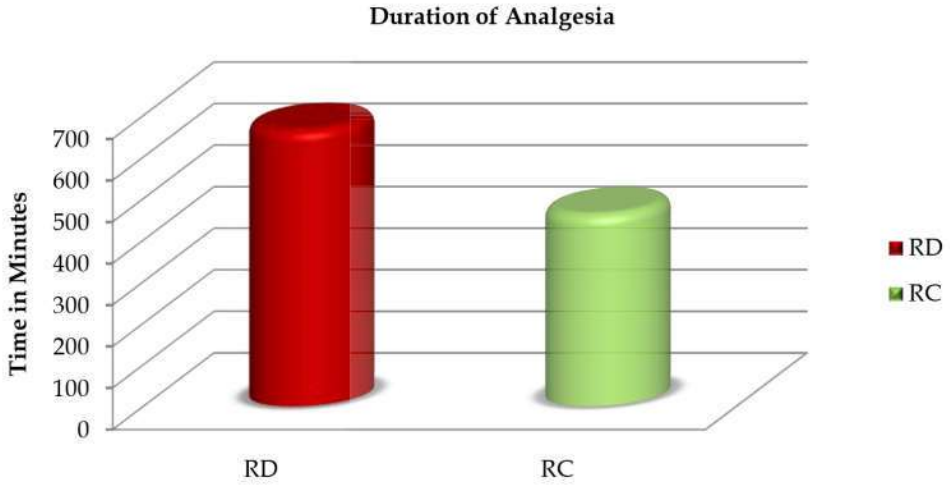

Fig. 4: Bar diagram showing the comparison of duration of analgesia in study groups

Table 1: Comparison of onset and duration of analgesia in study groups

Analgesic Characteristics	Group RD (N= 30)	Group RC (N= 30)	P Value	Significance
Onset of Analgesia	4.4 ± 0.67	6.3 ± 0.74	0.00	Significant
Duration of Analgesia	665.16 ± 9.8	462.16 ± 36.19	0.00	Significant

Table 2: Comparison of sedation score in study groups

Sedation Score	Group RD	Group RC	P Value	Significance
Base Line	1.1 ± 0.30	1.06 ± 0.25	0.6	Not Significant
After 30 Min	2.9 ± 0.3	2.3 ± 0.46	0.00	Significant
After 60 Min	2.73 ± 0.44	2.3 ± 0.46	0.00	Significant
After 90 Min	2.46 ± 0.5	2.1 ± 0.30	0.00	Significant
After 120 Min	2.03 ± 0.18	2.13 ± 0.3	0.16	Not Significant
After 6 Hrs	2.06 ± 0.25	2.1 ± 0.30	0.64	Not Significant

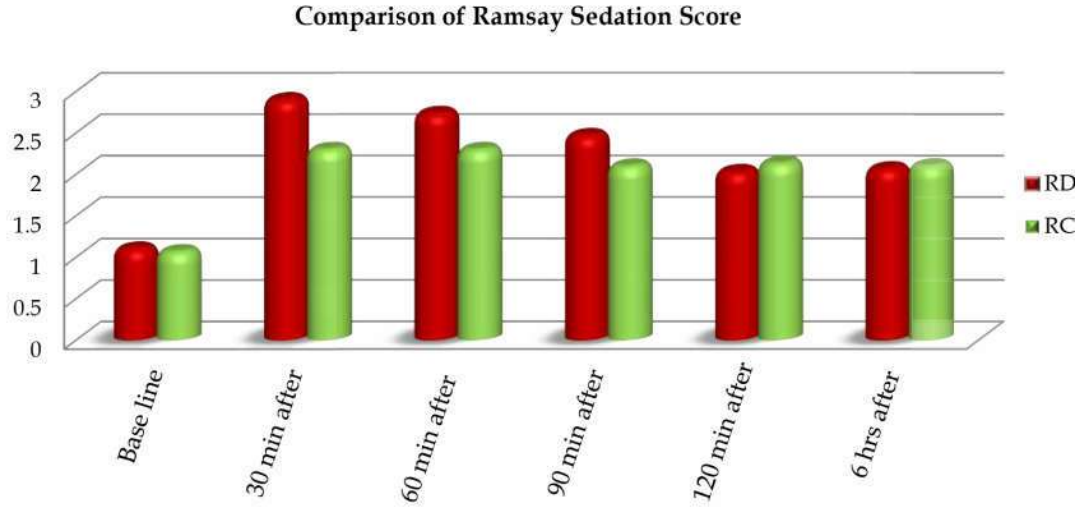

Fig. 5: Bar diagram showing the comparison of ramsay sedation score in study groups

Table 3: Comparison of side effects in study groups

Side Effect	Group RD (N=30)	Group RC (N=30)	P Value
Nausea	3	3	>0.05
Dry mouth	1	2	>0.05
Bradycardia	3	2	>0.05

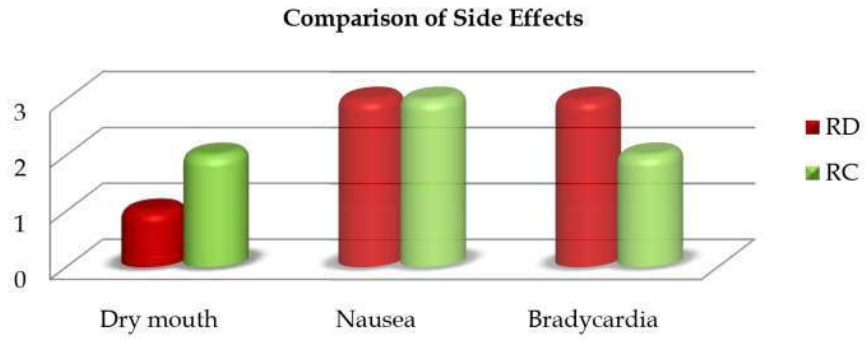

Fig. 6: Bar diagram showing Comparison of side effects in study groups

The above Table 3 and Figure 6 was showing the side effects in both the groups. Bradycardia was treated immediately by inj. Atropine (0.6 mg) IV.

Discussion

Epidural anaesthesia is a safe and inexpensive technique with advantages of providing surgical anaesthesia and prolonged postoperative pain relief. Various adjuvants are being used with local anaesthetics to prolong the duration of intraoperative and postoperative analgesia. Epidural administration of alpha$_2$ agonist is associated with sedation, analgesia, anxiolysis, and sympatholysis. It also causes rapid establishment of both sensory and motor blockade, prolonged duration of analgesia in the postoperative period, dose-sparing action of local anaesthetics and stable cardiovascular parameters makes these agents a very effective adjuvant in regional anaesthesia [11].

The analgesic action of intrathecal or epidural clonidine was first demonstrated clinically in 1984 [12]. On the other hand, dexmedetomidine has been administered epidurally for postoperative analgesia in humans in clinical trials [13,14]. The main aim of our study was to evaluate the efficacy, onset and duration of analgesia of epidural dexmedetomidine over epidural clonidine when combined with the 0.2% ropivacaine.

In our study the mean time of onset of analgesia in group RD was 4.4±0.67 min and in group RC was 6.3±0.74 min. The duration of analgesia in group RD was 665.16±29.8 min and in group RC was 462.16±29.8 min. Similar results was found by MS Saravana Babu, Anil Kumar Verma et al in 2013 [15], who studied 60 patients of age 18 to 65 years undergoing spine surgeries, compared the epidural route administration of inj clonidine (2mcg/kg) and inj dexmedetomidine (1mcg/kg) as an adjuvant to 0.2% ropivacaine (20 ml) and found that addition of dexmedetomidine to ropivacaine as an adjuvant resulted in earlier onset of analgesia (7.33± 1.76 min) as compared to clonidine (8.40±1.6 min) and duration of analgesia was prolonged with dexmedetomidine (407±47 min) compared to clonidine (345.0±35.09). Better sedation score was seen with dexmedetomidine group at different intervals as compared to clonidine.

The cardio-respiratory parameters, as is evident from figure 1 and 2, a slight decrease in heart rate and mean arterial pressure was observed in both the groups, which was not significant clinically. The side effect profile of both these drugs was quite favorable as none of the patient in either group had profound deep sedation or respiratory depression which correlates very well with other studies [8,16,17].

Conclusion

We conclude that epidural dexmedetomidine (1mcg/kg) and clonidine (2mcg/kg) with ropivacaine 0.2% had good efficacy however the dexmedetomidine provided faster and prolonged duration of postoperative analgesia and good sedation compared to clonidine. Overall the experience with dexmedetomidine was quite satisfactory as compared to clonidine under regional anaesthesia.

Key Message

Epidural dexmedetomidine and clonidine with ropivacaine 0.2 % had good efficacy, however the dexmedetomidine provided faster and prolonged duration of postoperative analgesia and can be practiced routinely.

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