Comparison of dexmedetomidine and clonidine as an adjuvant to ropivacaine for epidural anesthesia in lower abdominal and lower limb surgeries

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ABSTRACT

Background: The quality and duration of analgesia is improved when a local anesthetic is combined with alpha 2 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. The aim of our study is to compare the effect of clonidine and dexmedetomidine when used as an adjuvant to epidural ropivacaine in lower abdominal and lower limb surgeries. **Materials and Methods:** Patients were randomized into two groups-group ropivacaine with clonidine (RC) received 15 ml of 0.75% ropivacaine with 1 μg/kg clonidine and group ropivacaine with dexmedetomidine (RD) received 15 ml of 0.75% ropivacaine with 1 μg/kg dexmedetomidine epidurally. Onset of sensory analgesia using cold swab, onset of motor blockade using Bromage scale, time to 2 dermatome regression of sensory level, time to first demand for analgesia, sedation using Ramsay sedation scale, intra operative hemodynamic parameters and complications were assessed. **Results:** The onset (RD-8.53 ± 1.81, RC-11.93 ± 1.96) and duration of sensory blockade (RD-316 ± 31.5, RC-281 ± 37, sedation were found to be significantly better in the dexmedetomidine group. No significant difference was found in terms of onset of motor blockade and hemodynamic changes. **Conclusion:** Dexmedetomidine at doses of 1 μg/kg is an effective adjuvant to ropivacaine for epidural anesthesia, which is comparable to clonidine.

Key words: *Clonidine, dexmedetomidine, epidural, ropivacaine*

INTRODUCTION

Epidural anesthesia is a versatile technique used both for providing anesthesia and postoperative analgesia. It contributes to intra operative hemodynamic stability and has shown to reduce perioperative stress response thereby causing a decrease in complications and improving patient outcome. It helps in early mobilization by relieving postoperative pain, which decreases the incidence of thromboembolic events.[1-5]

Ropivacaine is being increasingly used in comparison to bupivacaine due to similar analgesic properties, reduced

cardio toxicity and lesser motor blockade. A slightly larger dose of ropivacaine may be required, but the addition of an adjuvant helps in the reduction of total required dose of local anesthetic and enhances the efficacy thereby providing increased duration and intensity of blockade.[6-8]

The quality and duration of analgesia is improved when a local anesthetic is combined with alpha 2 adrenergic agonist. Both clonidine and dexmedetomidine are alpha 2 adrenergic agonists, which have analgesic properties and potentiate local anesthetic effects.[9-11] Neuraxial clonidine, enhances the action of local anesthetics, increases the intensity and duration of analgesia. It is known to have sedative properties and the side effects are hypotension and bradycardia.[12-15] Dexmedetomidine is about 8 times more selective towards the alpha 2 adrenoreceptor than clonidine and hence allows the use of higher doses with less α_1 effect. It has been found to have hemodynamic stability, sedative, anxiolytic, analgesic, neuroprotective and anesthetic sparing effect. It causes more intense motor blockade and co-operative sedation without increasing the incidence of side effects.[16-18]

There are limited studies in the Indian population demonstrating the effects of dexmedetomidine when given epidurally with local anesthetics. The aim of our study was to compare the effect of clonidine and dexmedetomidine when given as an adjuvant to ropivacaine in epidural anesthesia.

MATERIALS AND METHODS

This randomized double-blinded study was carried out in 60 patients undergoing lower abdominal and lower limb surgeries. After getting approval from the Hospital Ethics and Research Committee, patients of both genders, aged 18-60 years of physical status American Society of Anesthesiologists I or II satisfying inclusion criteria, were recruited. During preanesthetic visit the patients were explained about the study purpose, merits and demerits of the procedure and instructed to demand analgesia as per need and informed written consent was obtained. Patients were fasted for 8 h and premedicated with tablet ranitidine 150 mg and tablet alprazolam 0.5 mg in the night, the day before and in the morning of the day of surgery. All patients were preloaded with 10 ml/kg of ringer lactate, and baseline reading of the study parameters were recorded.

Patients were randomized into two groups ropivacaine with clonidine (RC) and ropivacaine with dexmedetomidine (RD) by computer generated numbers. Group RC received 15 ml of 0.75% ropivacaine with 1 μg/kg clonidine, and group RD received 15 ml of 0.75% ropivacaine with 1 μg/kg dexmedetomidine epidurally. Blinding was achieved by making total volume to 16 ml in both groups. Resident who was preparing the study drug was not involved in the study.

In the operation theater after connecting standard monitoring, the epidural space was identified and confirmed using loss of resistance to air. A test dose of 3 ml of 2% lignocaine with 1:200,000 adrenaline was administered following which 16 ml of the study drug was administered epidurally as per randomization.

Onset of sensory block was evaluated by using cold swab along the midline at every minute till onset of block at T10. The degree of motor block was assessed using the Bromage motor scale: 0-Free movement of legs and feet, 1-able to flex knee with free movement of feet, 2-unable to flex knees, but movement of feet, 3-unable to move legs or feet. The assessment for motor block was done every 5 min after administration of study drug till a block of Bromage grade 3 motor blockade was achieved. The level of sedation was assessed 10 min after grade 3 motor

blockade and at the end of surgery based on the Ramsay sedation scale.

Hemodynamic parameters were monitored every 5 min for the first 30 min, every 10 min thereafter till the end of surgery. Patients received inj. Atropine 0.6 mg when the heart rate (HR) fell below 20% of baseline (bradycardia) and injection mephentermine in titrated boluses when there was hypotension (fall below 20% of baseline). Any side-effects seen after administration of study drug was noted and treated appropriately.

Onset of sensory analgesia was defined as the time taken to achieve loss of cold sensation at T10 dermatome level from the end of injection of the study drug. Duration of analgesia was defined as the time taken from the onset of sensory block at T10 to the time of pain sensation at the surgical site with a visual analog scale score of >3. Peak sensory level was defined as the highest dermatome level of sensory blockade achieved after administration of study drug. Time to two dermatome regression was defined as the time interval from the sensory block at the highest dermatome to the regression of sensory blockade by two dermatomes. The sensory level was assessed every 15 min after 2 h of epidural bolus injection till 2 dermatome regression of sensory level was observed. The time to motor blockade was defined as the time interval from the administration of epidural study drug to the achievement of grade 3 motor blockade in the lower limbs. The assessment for motor block was done every 5 min after administration of study drug till a block of Bromage grade 3 motor blockade was achieved.

The data were analyzed using SPSS version 19 and Microsoft Excel 2011 (IBM). The following statistical tests were used for analysis. Demographic data: ANOVAs test, onset of sensory block and motor block: Unpaired Student's *t*-test, sedation: Chi-square test, hemodynamic variation: Unpaired Student's *t*-test, complications: Chi-square test.

RESULTS

The two groups were comparable as there was no significant difference between the two groups in respect to age and sex distribution, height and weight characteristics. The distribution of the type of surgery and the duration of surgery were also found to be comparable [Table 1]. Both groups had patients undergoing hernioplasty, vaginal hysterectomies and lower limb surgeries.

There is a significant difference in the block characteristics between the two [Figure 1]. We found no significant difference found between the two groups in terms of onset
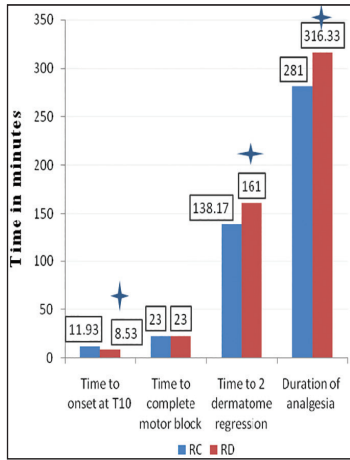
Figure 1: Block characteristics between the two groups: ✦ Shows significantly earlier onset and prolonged duration of sensory block with no difference in motor blockade
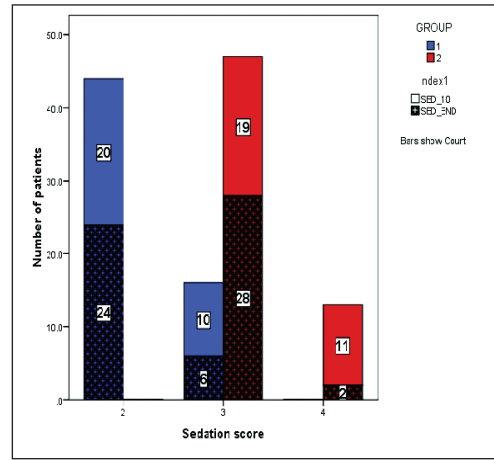

Figure 2: Sedation scores 10 min after motor blockade and at the end of surgery

Table 1: Demogrphic data with mean duration of surgery

Parameters	Mean ± SD		P
	Group RC	Group RD	
Age (years)	40.60±9.7	45.10±9.0	>0.05
Gender (male:female)	22:8	18:12	>0.05
Height (in cm)	160.30±6.45	160.63±5.93	>0.05
Weight (in kg)	60±9.10	57.50±7.96	>0.05
Mean duration of surgery	88.33±23.64	95.33±23.99	>0.05

SD: Standard deviation; RC: Ropivacaine with clonidine; RD: Ropivacaine with dexmedetomidine

of motor blockade. The difference in the sedation between the two groups was found to be statistically significant ($P = 0.000$) [Figure 2]. There was a significant fall in HR by 20% between 30 and 50 min of epidural injection in both groups; however there was no significant difference in the fall of HR between the two groups ($P = 0.592$) [Figure 3]. We also found significant fall in mean arterial pressure by 25% between 40 and 50 min in both groups, however there was no significant difference in the occurrence of hypotension between the two groups ($P = 0.796$).

DISCUSSION

Epidural anesthesia is considered as a gold standard technique as it provides complete and dynamic anesthesia. The benefits include suppression of stress response by sympatholysis, stable hemodynamics 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.[1,2,5]

Chandran *et al.*[6] compared the characteristics of 0.75% ropivacaine and 0.5% bupivacaine and concluded that

ropivacaine and bupivacaine at these doses produced equally effective anesthesia. 0.75% ropivacaine produces adequate intensity of motor and sensory blockade and is comparable to 0.5% bupivacaine with reduced side-effects. Hence, we used 0.75% ropivacaine to provide epidural anesthesia. Dexmedetomidine is known to have 8 times more affinity than clonidine for alpha adrenergic receptors; however there are no studies documenting the equivalent doses of epidural dexmedetomidine and clonidine.[17,19,20]

There are no studies indicating the equipotent doses of epidural dexmedetomidine and clonidine. A number of studies have used epidural clonidine at doses of 1-4 μg/kg and it has been suggested that epidural clonidine at a dose of 1 μg/kg prolongs analgesia without producing unwanted side effects. Epidural dexmedetomidine has been studied at doses ranging from 1 to 2 μg/kg and it was observed that at doses <1 μg/kg dexmedetomidine does not prolong the block of ropivacaine. Hence in our study, we have used equal and low concentrations of 1 μg/kg of clonidine and dexmedetomidine as an adjunct to ropivacaine in epidural anesthesia.

Our study showed significantly earlier onset of sensory blockade in the patients receiving dexmedetomidine (8.53 ± 1.81 min) when compared to the patients receiving clonidine (11.93 ± 1.96 min). There was a significantly higher dermatomal spread in group RD. This finding was consistent with the previous observations made by Bajwa *et al.*,[10] who found that the onset of sensory analgesia at T10 was faster in the group receiving dexmedetomidine (8.52 ± 2.36 min) when compared to the patients receiving clonidine (9.72 ± 3.44 min) and this was also associated with a faster and higher level of sensory blockade. It has been observed that when the dexmedetomidine is administered epidurally it reaches a maximum concentration in the cerebrospinal fluid within 5 min with a distribution half-life
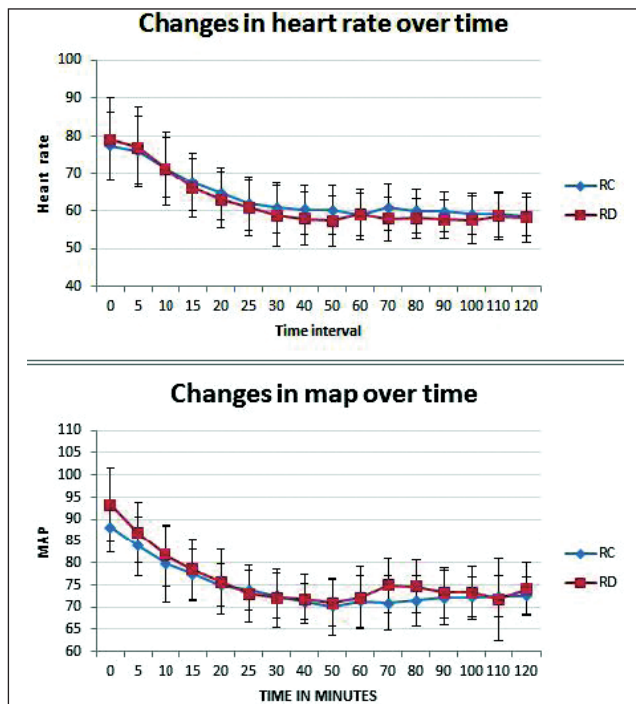
Figure 3: Hemodynamic changes between two groups represented as line diagram. There was a significant fall in HR by 20% and mean arterial pressure by 25% between 30 and 50 min in both groups, however there was no significant difference between the two groups ($P = 0.796$)

of 0.7 min. There is a dose dependent anti nociceptive effect of epidural dexmedetomidine, which has been associated with its affinity for the alpha 2 receptors on the spinal cord. Dexmedetomidine also has higher lipid solubility in comparison to clonidine.

In this study, we found that the duration of sensory analgesia was more in group RD (316 ± 31.15 min) than group RC (281 ± 37 min). This was found to be consistent with the study done by Bajwa *et al.*[10] where they found a significantly longer time to first rescue top up in the dexmedetomidine group (342.88 ± 29.16 min) than the clonidine group (310.76 ± 23.76 min). This may be because they had also used onset of incisional pain to indicate analgesia time, however the higher doses of dexmedetomidine (1.5 μg/kg) and clonidine (2 μg/kg) may be considered to explain the prolonged duration in comparison to our study. Neogi *et al.*[21] studied the characteristics of clonidine (1 μg/kg) and dexmedetomidine (1 μg/kg) with 0.25% ropivacaine when given caudally for postoperative analgesia in children and found that the mean duration of analgesia was not significantly prolonged between the groups receiving clonidine (13.17 ± 0.68 h) and dexmedetomidine (13.17 ± 0.68 h). In their study caudal analgesia was given as an adjuvant to general anesthesia and CRIES score of 4 and above was used to denote the duration of analgesia.

We found no statistically significant time to complete motor blockade between the two groups, group RD in 23.00 ± 4.27 min and group RC in 23.07 ± 4.63 min. Bajwa *et al.*[10] found that patients receiving dexmedetomidine (17.24 ± 5.16 min) achieved grade 3 motor blockade in less time than those receiving clonidine (19.52 ± 4.06) as an adjuvant. This may be attributed to the larger doses of dexmedetomidine (1.5 μg/kg) and clonidine (2 μg/kg) used in their study.

We found significantly better sedation in the patients who received dexmedetomidine than those who received clonidine at both 10 min and at the end of surgery. In a similar study conducted by Oriol-Lopez *et al.*[23] assessing the anxiolytic and sedative property of epidural dexmedetomidine in patients undergoing abdominal surgeries, dexmedetomidine was given at a dose of 1 μg/kg. Following the injection, Ramsay sedation score was used for assessment of sedation. They found that 90% of the patients receiving dexmedetomidine were sedated to a score of 3-4 for 90 min after drug administration. The findings of Bajwa *et al.*[10] also showed a significantly higher level of sedation in the patients who received dexmedetomidine in comparison to clonidine. These findings from the studies mentioned above concur with the findings from our study, showing that dexmedetomidine causes significantly higher sedation than clonidine when given epidurally.

We found that the HR significantly fell in both the groups by 20% in 30-50 min after the epidural injection. Blood pressure decreased by 25% in 30-50 min following epidural injection. However, this change was not statistically significant ($P > 0.05$). Similar observations were observed by Bajwa *et al.*[10] and Schnaider *et al.*[22] where a 15% fall of HR and blood pressure from the baseline which was not statistically significant. We observed similar hemodynamic changes in both the study groups. We found no significant difference in the atropine and mephentermine requirement as rescue in both the groups. Findings were similar to studies done by Bajwa *et al.*[10] and Swami *et al.*[11] who also found no significant differences in terms of hypotension and bradycardia between the patients receiving dexmedetomidine or clonidine. We had two patients in group RC and one patient in group RD who had dry mouth. The study conducted by Bajwa *et al.*[10] showed a higher incidence of nausea and dry mouth during the postoperative period.

The limitations of our study was that as different surgeries were taken up in this study, therefore onset of pain at surgical incisional site may not give an accurate duration of analgesia. There is also need for larger studies, using different concentrations of both drugs to find equipotent doses of epidural dexmedetomidine and clonidine. There

is a further requirement to assess the long term safety and effects of epidural dexmedetomidine as most studies only determine the short terms effects.

CONCLUSION

Based on the results and methodology employed, dexmedetomidine is found to be an effective adjuvant to ropivacaine for epidural anesthesia when compared to clonidine at doses of 1 μg/kg as it provides faster onset, prolonged duration of action with better sedation.

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