*Original Research Article*

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# Ultrasound Guided Caudal Epidural: A Comparative Study of Ropivacaine Clonidine versus Ropivacaine Dex Medetomidine for Perioperative Analgesia in Spine Surgery

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**Abstract**

*Background:* Caudal epidural is a proven technique for providing analgesia for lower spinal surgeries. Prolonged pain relief with no motor blockade is desired for early mobilization. Now, with ultrasound, we can visualize the caudal space and can see both the needle position and the injection. This has made the technique much more reliable.

*Aim:* To compare the analgesic and sedative effects Clonidine and dexemedetomidine a selective α2-agonist drugs when used caudal epidurally as an adjuvant to ropivacaine and also to evaluate the feasibility of ultrasound guided caudal block in patients undergoing lumbar spine surgery.

*Settings and Design:* A Comparative, Prospective randomized, controlled two group's clinical study of 60 adults undergoing lumbosacral surgeries.

*Materials and Methods:* 60 patients were allocated into any one of two groups of 30 patients each, by means of computer-generated randomization: *Group RD:* Patients receiving caudal block with injected Ropivacaine 0.2% 20 ml+1µg/kg of injdexmedetomidine. *Group RC:* Patients receiving Ropivacaine 0.2% 20 ml + 2µg/kg clonidine.

*Statistical Methods:* Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups, Non-parametric setting for Qualitative data analysis. Fisher exact test used when cell samples are very small.

*Results:* The duration of postoperative analgesia was more in RD GROUP compared Patients in RC GROUP, which is statistically significant P=0.005**.

Significant lower mean VAS score at 480min [P < 0.001] and 720 min [P 0.010] in RD group compared to RC group with minimal sedation score and hemodynamic disturbances.

*Conclusion:* Dexmedetomidine is a better neuraxial adjuvant to ropivacaine when compared to clonidine for providing prolonged post-operative analgesia with lower pain score and stable cardiorespiratory parameters.

**Keywords:** Analgesia; Caudal Epidural; Ultrasound.

## Introduction

Administration of analgesic medication, before the actual onset of painful stimulus, is more effective than that after the onset of painful stimulus. This is the principle of preemptive analgesia.[1,2] Caudal epidural blockade is particularly popular in pediatric practice, even in the adult population, the caudal

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approach to the epidural space is generally easily accomplished and can be used to provide effective analgesia.[3] Caudal epidural is a proven technique for providing analgesia for spinal surgeries. Prolonged pain relief with no motor blockade is desired for early mobilization. Postoperative pain following lumbosacral spine surgeries can be alleviated by caudal analgesia using local anesthetics, duration of analgesia can further be prolonged by adding adjuvants to local anesthetics.[3,4] Single shot caudal block provides analgesia for 2-4 hours, but this can be further prolonged by adding adjuvants like opioids, ketamine, alpha 2 agonists, adrenaline, etc. Clonidine and dexemedetomidine a selective α2-agonist with safe pharmacokinetic profile is a good neuraxial adjuvant.[5]

Alpha 2 adrenergic agonists have both analgesic and sedative properties when used as an adjuvant in regional anesthesia.[6,7] The anesthetic and the analgesic requirement get reduced to a huge extent by the use of α 2 adrenergic agonists because of their analgesic properties and augmenttion of local anesthetic effects as they cause hyperpolarization of nerve issues by altering transmembrane potential and ion conductance at locus coeruleus in the brainstem.[8,9] The stable hemodynamics and the decreased oxygen demand due to enhanced sympathoadrenal stability make them very useful pharmacologic agents.[10] Now, with ultrasound, we can visualize the caudal space and can see both the needle position and the injection. This has made the technique much more reliable. Aims and objectives of this study are to compare the analgesic and sedative effects of both these drugs when used caudal epidurally as an adjuvant to ropivacaine, and also to evaluate the feasibility of ultrasound guided caudal block.

*Methodology*

The study design was a prospective, double-blinded, and randomized controlled trial. Sixty patients physical status American Society of Anesthesiologists (ASA) Classes I and II between the age of 18 and 65 years who underwent lumbosacral surgeries were included in the study. Written informed consent was taken. They were allocated into any one of two groups of 30 patients each, by means of computer-generated randomization:

- Group RD: Patients receiving caudal block with injected ropivacaine 0.2% 20 ml+1μg/kg of injdexmedetomidine.
- Group RC: Patients receiving ropivacaine 0.2% 20 ml + 2μg/kg clonidine.

Patients with cardiac conductive disorders, hepatic insufficiency, renal impairment, psychiatric disorders, those with contraindications for a caudal block (skin infection at the injection site, bleeding diathesis, neurological disorders, and sacral anomalies) and a history of allergy to any of the study medications were excluded from the study. Patients who had undergone previous back surgeries were also excluded from the study. In the preoperative visit, the numerical visual rating scale for pain was explained to all patients, which ranges from 0 = no pain to 10 = worst imaginable pain.[11] The demographic data (age, weight, and ASA status, type of operation, and duration of surgery) and hemodynamic parameters such as heart rate (HR) and mean blood pressure (MBP) were recorded before the block which was considered as the baseline and at regular intervals intraoperative and postoperatively using standard monitoring such as pulse oximeter, HR, noninvasive blood pressure, electrocardiogram, and oxygen saturation. After securing appropriate gauge IV cannula, anesthesia was induced with injection fentanyl 2 μg/kg, injection propofol 2 mg/kg, and endotracheal intubation facilitated by injection vecuronium 0.1 mg/kg and then turned prone for the surgery. Under strict aseptic precautions, sacral hiatus was identified by ultrasound. Twenty gauge IV cannula needle was used to locate caudal space under ultrasound guidance. After negative aspiration for blood and cerebrospinal fluid, the study drugs were introduced into the caudal space according to allocation. The anesthetist blinded to the contents of the syringe injected into the epidural space. Patients in the RD Group were given 1ug/kg dexmedetomidine with 20 ml of 0.2% ropivacaine and patients in Group RC were given 2μg/kg of injection clonidine with 0.2% injection ropivacaine. Moreover, surgeon was asked to wait for 15 min to put incision. IV paracetamol 1 g was given to all patients intraoperatively and the same was continued eight hourly for the first 24 h. Intraoperatively, HR and MBP were recorded. A fall of systolic blood pressure to <20% baseline was considered as hypotension. Bradycardia was considered when HR dropped to <60/min or <20% of baseline pulse and was treated with IV atropine sulfate 0.6 mg. Response for incision managed either by opioids i.e. fentanyl 1ug/kg or by increase in isoflurane. All patients were observed in the post anesthesia care unit for the next 6 h. All patients were catheterized before starting of surgery as a routine protocol of neurosurgeons and were kept for 12 h. At the end of the operation, patients were placed back in the supine position and the trachea

was extubated after reversal of the muscle relaxant by administration of mixed neostigmine 40 µg/kg with glycopyrrolate 10 µg/kg intravenously. Total opioid requirement recorded at the end of surgery .Visual analog scale (VAS)[11] was used for the assessment of postoperative pain relief at immediate postoperatively, 30 min, 1, 2, 4, 8, 12, and 24 h by a trained nurse. At VAS score of ≥4, rescue analgesia was given in the form of injection tramadol 50 mg IV. Duration of analgesia is defined as the time taken from the time of caudal anesthesia to the first request of rescue analgesia. Sedation score was assessed on a four point categorical scale as 0 = awake, alert; 1 = drowsy, not sleeping; 2 = asleep, arousable by verbal contact; 3 = asleep, not arousable by verbal contact. Side-effects such as nausea, vomiting, respiratory depression, motor blockade (Bromage scale >1), deep sedation (Ramsay sedation scale [RSS] >3), shivering and hypotension, duration of surgery, and parameters were recorded.

*Statistical Methods:* Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance. The following assumptions on data is made, Assumptions: 1.Dependent variables should be normally distributed, 2.Samples drawn from the population should be random, Cases of the samples should be independent.

Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters. Leven`s test for homogeneity of variance has been performed to assess the homogeneity of variance.

Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups, Non-parametric setting for Qualitative data analysis. Fisher exact test used when cell samples are very small.

*Statistical software:* The Statistical software namely SPSS 22.0, and R environment ver. 3.2.2 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, Fs etc.

## Results

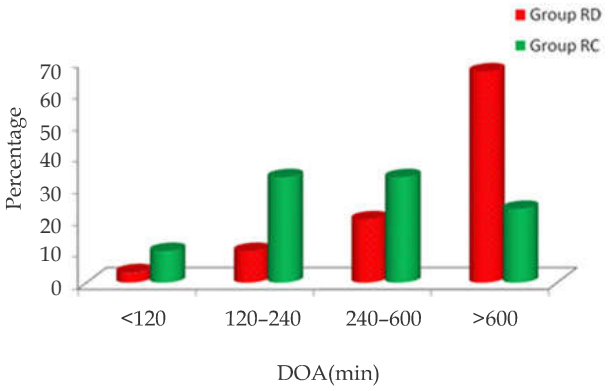
The demographic profile of our patients was comparable with respect to mean age, body weight, body mass index, ASA grade and duration of surgery two groups were comparable in age, weight, sex distribution (Table 1,2,3) and baseline HR and MAP. The duration of surgery and duration of anesthesia were also comparable in the two groups. The caudal block was successful in all the patients included in the study. None of the patients in either group required intraoperative extra opioid [fentanyl] analgesia. All patients remained vitally stable throughout the procedure and intraoperative hemodynamic parameters were comparable in the two groups.

The duration of postoperative analgesia was more than 600 min (10 hr) in twenty (20) patients in RD group compared to seven (7) Patients in RC GROUP, which is statistically significant P=0.005** [Fig. 1].

**Table 1:** Age distribution of patients studied.

| Age in years | Group RD | Group RC | Total |
|---|---|---|---|
| 21-30 | 6(20%) | 8(26.7%) | 14(23.3%) |
| 31-40 | 11(36.7%) | 3(10%) | 14(23.3%) |
| 41-50 | 6(20%) | 11(36.7%) | 17(28.3%) |
| 51-60 | 7(23.3%) | 2(6.7%) | 9(15%) |
| >60 | 0(0%) | 6(20%) | 6(10%) |
| Total | 30(100%) | 30(100%) | 60(100%) |
| Mean ± SD | 40.87±10.03 | 43.80±14.24 | 42.33±12.30 |

Samples are age matched with P=0.360, student t test




P=0.005**, Significant, Fisher Exact Test

**Fig. 1:** Duration of Analgesia [DOA] (min) distribution in two groups of patients studied.

**Table 2:** Gender distribution of patients studied.

| Gender | Group RD | Group RC | Total |
|---|---|---|---|
| Female | 12(40%) | 15(50%) | 27(45%) |
| Male | 18(60%) | 15(50%) | 33(55%) |
| Total | 30(100%) | 30(100%) | 60(100%) |

Samples are gender matched with P=0.436, Chi-Square test.

**Table 3:** Weight (kg) distribution in two groups of patients studied.

| Weight (kg) | Group RD | Group RC | Total |
|---|---|---|---|
| <50 | 4(13.3%) | 0 | 4(6.7%) |
| 50-60 | 17(56.7%) | 26(86.7%) | 43(71.7%) |
| 61-70 | 9(30.0%) | 4(13-.3%) | 13(21.7%) |
| Total | 30(100.0%) | 30(100.0%) | 60(100.0%) |
| Mean ± SD | 56.80±9.92 | 59.40±3.15 | 5810±7.60 |

Samples are weight matched P=0.189, student t test.

Rescue analgesic requirement was in required eight patients in group RD compared with eighteen patients in group RC, which is statistically significant P=0.009**. (Table 4).

**Table 4:** Rescue Analgesia distribution in two groups of patients studied.

| Rescue A | Group RD | Group RC | Total |
|---|---|---|---|
| No | 22(73.3%) | 12(40%) | 34(56.7%) |
| Yes | 8(26.7%) | 18(60%) | 26(43.3%) |
| Total | 30(100%) | 30(100%) | 60(100%) |

P=0.009**, Significant, Chi-Square Test.

There was a significant difference between the groups in the VAS score (Fig. 2) measured 4th hourly in the postoperative period. Group RC patients achieved significantly higher VAS score compared with Group RD patients, where 15 out of 30 patient achieved a VAS score of more than 4 at 480min compared with 4 patients in Group RD, which is statistically significant P < 0.001 and 21 patients in RC group compared with 9 patients in RD group at 720 min, which is statistically significant P 0.010. (Table 5).

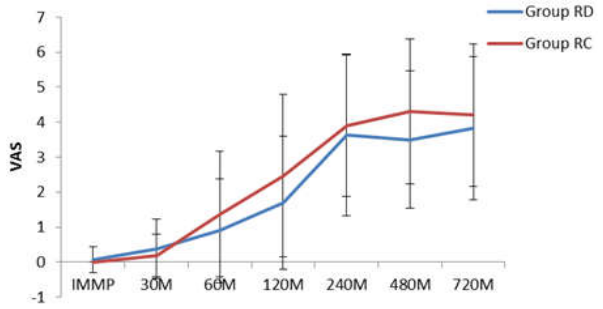



**Fig. 2:** VAS- A comparison in two groups of patients studied.

Both the groups showed gradual decreasing trends in mean heart rate from the pre-operative baseline intraoperatively, which may be attributable to caudal dexemedetomidine/clonidine (Fig. 3). No increase in heart rate during incision in both groups. Changes in mean arterial pressure (MAP) in both the groups are comparable and statistically insignificant (P > 0.05) (Fig. 4). Both the groups showed gradual decreasing trends in MAP from the pre-operative baseline value, which may be attributable to caudal dexemedetomidine/clonidine. No increase in MAP during incision in both the group. No statistical significant in HR and MAP postoperatively in both Group RD and Group RC (Fig. 5,6). Both groups showed comparable modified Bromage scale scores at all the set time points, none of the patients in the two groups had residual motor block. Difference of mean sedation score between both the groups was not statistically significant. 7 patients had sedation score of 1 in RC group compared to 6 patients in RD group whereas 7 patients in RC had sedation score of 2, compared to 9 patients in RD group. Overall, none of the patient in either groups had profound deep sedation (sedation score>3).The incidence of other side effects like nausea, vomiting, headache, shivering and dizziness were comparable in both the groups and statistically non-significant. We did not observe the respiratory depression in any patient from either group.

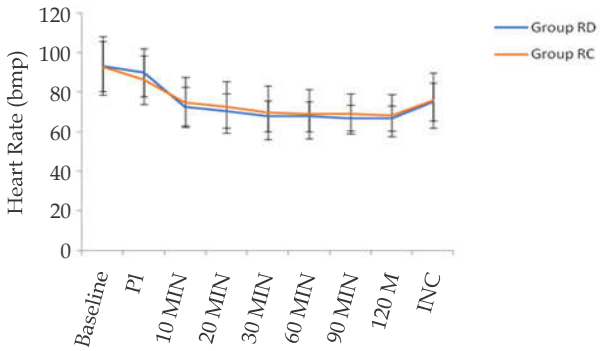



**Fig. 3:** Heart Rate (bpm) - a comparison in two groups of patients studied.

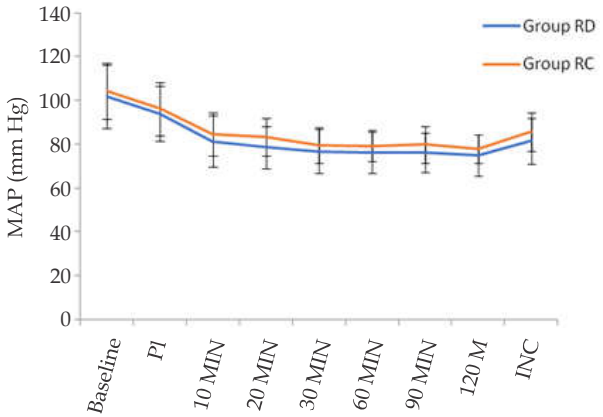



**Fig. 4:** MAP (mm Hg)-a comparison in two groups of patients studied.**Table 5:** VAS- A comparison in two groups of patients studied.

**Table 5:** VAS- A comparison in two groups of patients studied.

| VAS | Group RD | Group RC | Total | P value |
|---|---|---|---|---|
| IMMP | 0.07±0.37 | 0.00±0.00 | 0.03±0.26 | 0.321 |
| 30M | 0.37±0.85 | 0.20±0.61 | 0.28±0.74 | 0.387 |
| 60M | 0.90±1.49 | 1.37±1.79 | 1.13±1.65 | 0.278 |
| 120M | 1.70±1.90 | 2.47±2.32 | 2.08±2.13 | 0.166 |

| | | | | |
|---|---|---|---|---|
| 240M | 3.63±2.31 | 3.90±2.02 | 3.73±2.25 | 0.178 |
| 480M | 3.50±1.96 | 4.30±2.07 | 3.90±2.04 | 0.130 |
| 720M | 3.83±2.04 | 4.20±2.04 | 4.02±2.03 | 0.489 |
| 1440M | 2.83±1.51 | 3.14±1.25 | 2.98±1.38 | 0.402 |

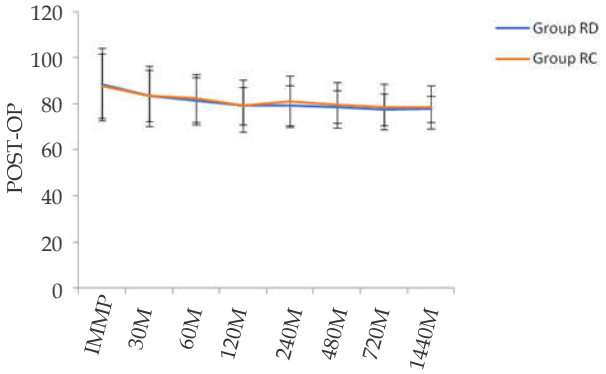



**Fig. 5:** PostoperativeHeart Rate (bpm) - a comparison in two groups of patients studied.

**Table 6:** QOP [Quality of Picture]-distribution in two groups of patients studied.

| QOP | Group RD | Group RC | Total |
|---|---|---|---|
| Good | 23(76.7%) | 25(83.3%) | 48(80%) |
| Interme | 7(23.3%) | 5(16.7%) | 12(20%) |
| Total | 30(100%) | 30(100%) | 60(100%) |

P=0.519, Not Significant, Chi-Square Test.

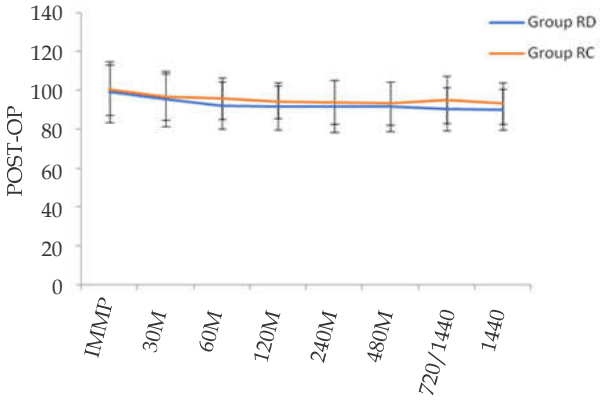
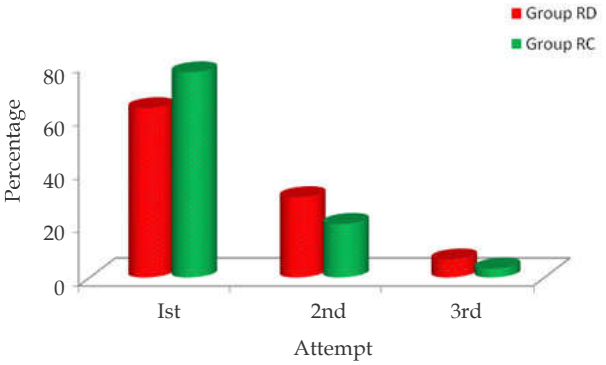
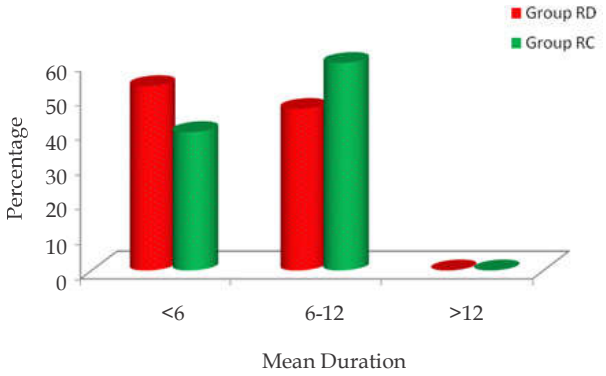



**Fig. 6:** Postoperative MAP (mm Hg - a comparison in two groups of patients studied.




P=0.526, Not Significant, Fisher Exact Test

**Fig. 7:** Attempt-distribution in two groups of patients studied.




P=0.365, Not Significant, Fisher Exact Test

**Fig. 8:** Mean Duration-distribution in two groups of patients studied.

*Feasebility of Usage of Ultrasound*

The US-guided blocks were performed by residents in 78.33% of case and in 21.67% by senior practitioners. The quality of the picture was judged "good" by the practitioner in 80% of cases, "intermediate" in 18.49%, and was never considered "bad" pictures (Table 6). Localization of the tip of the needle was possible for all blocks: directly in 73.3% of punctures or indirectly, by the movement of adjacent anatomic structures, in 26.7% of cases. The spread of local anesthetic was visualized in all cases. For blocks among 60 patients, in 42 patients (70%) a single attempt was successful. A second attempt was required in 15 patients [25%] and more than 2 attempts needed in 3 patients [5%] (maximum 3 attempts) (Fig. 7]. The mean duration of the technique from ultrasonographic identification of anatomical structures to withdrawal of the needle was <6 min in 46.7% and 6 to 12 min in 53.3%) (Fig. 8). Only one side effect was noted (blood during aspiration test), no injection was performed. The needle was relocated and injection of the local anesthetic was completed.

## Discussion

Caudal epidural block is a simple and effective means of relieving pain after lumbosacral spine surgeries. Relieving pain might enhance restoration of function by allowing the Patient to breathe, cough and to be easily ambulant.[12] The pharmacologic properties of α-2 agonists have been employed clinically to achieve the desired effects in regional anesthesia.[13,14,15] Caudal Epidural administration of these drugs is associated with sedation, analgesia, anxiolytic, hypnosis and sympatholytic. . Further,

addition of these two adjuvants promotes faster onset compared to established time of onset of sensory analgesia with ropivacaine alone.[16,17]

Clonidine has been used successfully used over the last decade for the said purpose and the introduction of dexmedetomidine has further widened the scope of α-2 agonists in regional anesthesia.[18] The faster onset of action of local anesthesia, rapid establishment of both sensory and motor blockade, prolonged duration of analgesia into the post-operative period, dose-sparing action of local anesthesia and stable cardiovascular parameters makes these agents a very effective adjuvant in regional anesthesia.[19-21] Scope of ultrasound for caudal epidural in prone position, is easy to use, is radiation free and can provide real-time images in guiding the caudal epidural needle into caudal space. Ultrasound may therefore be used as an adjuvant tool in caudal needle placement.[22]

The results of the study has shown that the addition of either 1. µg/ kg dexmedetomidine or 2 µg/kg clonidine as adjuvant to epidural ropivacaine not only prolongs the duration of analgesiaalso provide good hemodynamic stability. Duration of block was prolonged in RD group than in RC group. Saravana Babu MS et al.,[23] compared epidural ropivacaine and dexmedetomedine 1µg/ kg with ropivacine and clonidine 2µg/kg in 60 patients for spine surgeries given postoperatively and found dexmedetomedine as neuraxial adjuvant is better for prolonging duration of analgesia and for cardio respiratory stability. Fawzi MH et al., also used same dose with good results.[24] These properties of dexmedetomidine are mostly due to their increased affinity to α2 receptors (8 times more than clonidine). This affinity is when the drug is used in IV route. The affinity for epidural route is not known.[25,26,27]

The 11 point linear Visual Analogue Scale (VAS) being a reliable validated score for assessing acute postoperative pain was used in our study. The mean VAS score at postoperative 4 hour, 8 hour and 12 hour were statistically lower in RD group compared to RC group. The time to first rescue analgesic was prolonged in the RD group compared to the RC group and it was statistically significant. Even Bajwa, et al[28] noticed that rescue analgesia was comparatively shorter (310.76 ± 23.75 min) in the patients who were administered clonidine ($P < 0.05$), compared with dexmedetomedine.

In our study heart rate and blood pressures were in a clinically acceptable range. Hemodynamic parameters, the cardio-respiratory parameters remained stable throughout the study period, which reaffirms the established effects of α2 agonists in providing a hemodynamically stable post-operative analgesia.[29] The use of alpha-2 agonists for regional neural blockade in combination with local anaesthetic results in increased duration of sensory blockade.[30,20]

Eighty six percent of the patients remained awake but calm in Clonidine group compared to Eighty five percent in dexmedetomidine group who were equally cooperative and calm. Overall none of the patient in either groups had profound deep sedation (sedation score>3) or motor blockade and respiratory depression.[30] This can be attributed to lower concentrations of ropivacaine and the α2 agonists properties of sedation with no respiratory depression.

The results of this prospective descriptive study show that the performance of real-time US-guided caudal nerve block is feasible and easy under general anesthesia. As noted by our anesthesiologist team, the technique is easy to learn because the puncture site using the US-guided approach was sensibly unchanged in comparison with landmark technique.

## Conclusion

Dexmedetomidine is a better neuraxial adjuvant to ropivacaine when compared to clonidine for providing low pain score and prolonged post-operative analgesia and stable cardiorespiratory parameters.

## Reference

1. Kundra P1, Gurnani A, Bhattacharya A. Preemptive epidural morphine for postoperative pain relief after lumbar laminectomy.AnesthAnalg. 1997 Jul; 85(1):135-8.
2. Sekar C, Rajasekaran S, Kannan R, Reddy S, Shetty TA, Pithwa YK. Pre-emptive analgesia for postoperative pain relief in lumbosacral spine surgeries. Spine J. 2004; 4(3):26.
3. Schloss B, Jayanthi VR, Bhalla T, Tobias JD. Caudal epidural blockade in adolescents. Saudi J Anaesth. 2016; 7:57-60.
4. Bajwa SJ, Kaur J, Bajwa SK, Bakshi G, Singh K, Panda A. Caudal ropivacaine-clonidine: A better post-operative analgesic approach. Indian J Anaesth 2010; 54(3): 226-30.
5. Sukhwinder Kaur Bajwa, 1 et al. Dexmedetomidine and clonidine in epiduralanaesthesia: A comparative evaluation. Indian J Anaesth 2011; 55:116-21.

6. Mauro VA, Brandão ST. Clonidine and dexmedetomidine through epidural route for post-operative analgesia and sedation in a colecistectomy. Rev Bras Anestesiol 2004; 4:1-10.
7. Fukushima K, Nishimi Y, Mori K. The effect of epidural administered dexmedetomidine on central and peripheral nervous system in man. AnesthAnalg 1997; 84:S292.
8. Correa-Sales C. A hypnotic response to dexmedetomidine, an alpha-2 agonist, is mediated in the locus coeruleus in rats. Anesthesiology 1992; 76:948-52.
9. Taittonen MT, Kirvelä OA, Aantaa R, Kanto JH. Effect of clonidine and dexmedetomidine premedication on perioperative oxygen consumption and haemodynamic state.Br J Anaesth 1997; 78:400-6.
10. Buerkle H. Peripheral anti-nociceptive action of alpha2- adrenoceptor agonists. Baillière's Clin Anaesth 2000; 14:411-8.
11. Jensen MP, Turner JA, Romano JM. What is the maximum number of levels in pain intensity measurement? Pain 1994; 58:387–392.
12. Sandhya Kalappa, Raghavendra Biligiri Sridhara, Saraswathi Kumaraswamy. Dexmedetomidine as an Adjuvant to Pre-Emptive Caudal Epidural Ropivacaine for Lumbosacral Spine Surgeries Journal of Clinical and Diagnostic Research. 2016 ;10(1): 22-24.
13. Kamibayashi T, Maze M. Clinical uses of alpha-2 adrenergic agonists. Anaesthesiology 2000; 93: 1345-9.
14. Hall JE, Uhrich TD, Ebert TJ. Sedative, analgesic and cognitive effects of clonidine infusions in humans. Br J Anaesth 2001; 86:5-11.
15. Hall JE, Uhrich TD, Barney JA, Arain SR, Ebert TJ. Sedative, amnesic, and analgesic properties of small-dose dexmedetomidine infusions. Anesth Analg 2000; 90:699-705.
16. Ogun CO, Kirgiz EN, Duman A, Kara I, Okesli S. The comparison of intrathecal isobaric ropivacaine and isobaric ropivacaineclonidine for caesarean delivery. Internet J Anesthesiol 2007; 15:1.
17. El Saied AH, Steyn MP, Ansermino JM. Clonidine prolongs the effect of ropivacaine for axillary brachial plexus blockade. Can J Anaesth 2000; 47:962-7.
18. Gertler R, Brown HC, Mitchell DH, Silvius EN. Dexmedetomidine: A novel sedative-analgesic agent. Proc (BaylUniv Med Cent) 2001; 14:13-21.
19. Coskuner I, Tekin M, Kati I. Effects of dexmedetomidine on the duration of anaesthesia and wakefulness in bupivacaine epidural block. Eur J Anaesthesiol 2007; 24:535-40.
20. El-Hennawy AM, Abd-Elwahab AM, Abd-Elmaksoud AM, and El-Ozairy HS, Boulis SR. Addition of clonidine or dexmedetomidine to bupivacaine prolongs caudal analgesia in children. Br J Anaesth 2009; 103:268-74.
21. Aantaa R, Kanto J, Scheinin M, Kallio A, Scheinin H. Dexmedetomidine, an alpha 2-adrenoceptor agonist, reduces anesthetic requirements for patients undergoing minor gynaecologic surgery. Anesthesiology 1990; 73:230-5.
22. Chen CP, Tang SF, Hsu TC, et al. Ultrasound guidance in caudal epidural needle placement. Anesthesiology. 2004; 101(1):181-184.
23. Saravana Babu MS, Verma AK, Agarwal A, Tyagi CM, Upadhyay M, Tripathi S. A comparative study in the postoperative spine surgeries: Epidural ropivacaine with dexmedetomidine and ropivacaine with clonidine for Postoperative analgesia. Indian J Anaesth. 2013; 57:371-76.
24. Fawzi HM, Almarakbi WA. Effects of pre-emptive caudal dexmedetomedine-bupivacaine mixture in adult patients undergoing single level lumbar laminectomy: A prospective randomized study. Ain Shams Journal of Anaesthesiology. 2012; 5: 223-28.
25. Aryan HE, Box KW, Ibrahim D, Desiraju U, Ames CP. Safety and efficacy of dexmedetomidine in neurosurgical patients. Brain Inj 2006; 20:791-8.
26. Swami SS, Keniya VM, Ladi SD, Rao R. Comparison of dexmedetomidine and clonidine (α2 agonist drugs) as an adjuvant to local anaesthesia in supraclavicular brachial plexus block: A randomised double-blind prospective study. Indian J Anaesth 2012; 56:243-9.
27. Schnaider TB, Vieira AM, Brandão AC, Lobo MV. Intraoperative analgesic effect of epidural ketamine, clonidine or dexmedetomidine for upper abdominal surgery. Rev Bras Anestesiol 2005; 55:525-31.
28. Bajwa SJ, Bajwa SK, Kaur J, Singh G, Arora V, Gupta S, et al. Dexmedetomidine and clonidine in epidural anaesthesia: A comparative evaluation. Indian J Anaesth 2011; 55:116-21.
29. Pichot C, Longrois D, Ghignone M, Quintin L. Dexmedetomidine and clonidine: A review of their pharmacodynamy to define their role for sedation in intensive care patients. Ann Fr Anest Reanim 2012; 31:876-96.
30. Kanazi GE, Aouad MT, Jabbour-Khoury SI, Al Jazzar MD, Alameddine MM, Al-Yaman R, et al. Effect of low-dose dexmedetomidine or clonidine on the characteristics of bupivacaine spinal block. Acta Anaesthesiol Scand 2006; 50:222-7.