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The comparison of clonidine and dexmedetomidine as an adjuvant to 0.5% bupivacaine in epidural anaesthesia for lower limb surgeries

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Abstract

Background and Objectives: Epidural anesthesia is a popular technique for providing anesthesia for lower limb surgeries. Dexmedetomidine and Clonidine are known to enhance the effect of local anaesthetics. The purpose of this study was to compare the impact of dexmedetomidine and clonidine on the onset and duration of epidural anaesthesia using bupivacaine.

Methods: After IEC approval, a prospective, randomized, double blinded study was conducted on 60 ASA I and II adult patients undergoing lower limb surgeries under epidural anaesthesia. Patients were randomly divided into Group A receiving 0.5% isobaric bupivacaine 15 ml with dexmedetomidine 1 µg/kg and Group B receiving 0.5% isobaric bupivacaine 15 ml with clonidine 2 µg/kg epidurally. Onset and duration of sensory and motor blocks, duration of analgesia, sedation, and adverse effects were assessed.

Results: The onset of sensory and motor block was significantly faster in Gr A compared to Gr B ($p < 0.05$). The duration of sensory and motor block was significantly more in Gr D compared to Gr M. Mean arterial pressures were comparable between the groups in the intraoperative period. However, sedation scores with dexmedetomidine were better than clonidine. No other adverse event was observed.

Conclusion: Dexmedetomidine in combination with 15 ml bupivacaine (0.5%) hastened onset of sensory and motor block, and prolonged the duration of sensory and motor block when used for epidural, without producing any adverse events.

Keywords: Lower limb surgeries, epidural, bupivacaine, clonidine, dexmedetomidine

1. Introduction

Epidural anesthesia is the most commonly used technique for providing not only peri-operative surgical anesthesia but postoperative analgesia in lower limb surgeries [1]. It also contributes to reduced hospital stay and less financial implications while avoiding the side effects of general anesthesia. Many techniques and drug regimens, with partial or greater success, have been tried from time to time to calm the patients and to eliminate the anxiety component during regional anesthesia [2, 3, 4]. Many a time for achieving desired effect, invariably large volumes of local anesthetics are used with deleterious consequences or the impulsive use of large doses of sedation or even general anesthesia defeats the novel purpose of regional anesthesia [5]. To overcome these problems there is an ongoing effort to find a better adjuvant in regional anesthesia.

Alpha 2-adrenergic receptor agonists have been the focus of interest for their sedative, analgesic, peri-operative sympatholytic, anesthetic-sparing, and hemodynamic-stabilizing properties [6]. Dexmedetomidine is a highly selective α -2 adrenergic agonist with an affinity eight times greater than that of clonidine [7].

The present double-blind prospective randomized study aims at comparing the hemodynamic, sedative, and analgesia potentiating effects of epidurally administered clonidine and dexmedetomidine when combined with bupivacaine.

2. Materials and Methods

Ethical statement: The study was approved by the Institutional Ethics Committee, IGIMS, Patna, Bihar, India. Written consent was obtained after informing the participants about the nature, scope and risks related to the study.

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Methods: This study was conducted at IGIMS, Patna, India between April 2019 and November 2020. Sixty consenting adult patients were included in this double blind, randomized, controlled study. The sampling type was randomized cluster sampling.

Inclusion criteria

Patients of either sex,
ASA I and II physical status,
Between 18 and 60 years of age,
Scheduled for surgery on lower extremity under epidural anaesthesia

Exclusion criteria

1. Patient refusal.
2. Known contraindications to regional anaesthesia (coagulopathy, local infection).
3. Known allergy to bupivacaine, clonidine or dexmedetomidine.
4. Concomitant use of analgesics or sedatives.
5. ASA III / IV patients.
6. History of significant systemic illness.
7. Failed brachial plexus block.

Preanaesthesia

Preanaesthetic evaluation of all the patients was performed before admission to the ward. All patients were premedicated with oral ranitidine 150 mg and alprazolam 0.25 mg on the night before surgery and were kept fasting for 6 hours prior to surgery.

Intervention plan

On arrival in the operation theatre, routine monitoring in the form of ECG, NIBP, SPO₂ and respiration were instituted and baseline values were noted. Intravenous access was established with 18G intravenous catheter on the dorsum of the non operative hand and infusion of plasmalyte was started.

By use of computer generated random numbers, patients were allocated to one of two groups;

- Gr A: Patients received epidural anesthesia with 15 ml Bupivacaine 0.5% and 1mcg/kg dexmedetomidine
- Gr B: Patients received epidural anesthesia with 15 ml Bupivacaine 0.5% and dexmedetomidine. 2mcg/kg of clonidine.

Oxygen through face mask was administered @ 4L/min to all the patients. Patients were positioned for epidural anesthesia. After aseptic preparation of the area, Patients were administered epidural block with 18 gauge Tuohy Needle - Portex Continuous Epidural (Smith Med. Inc.) and catheter was secured 3-4 cm into the epidural space. The catheter was then anchored in place on the back of the patient using adhesive tape and a test dose of 3 ml of 2% lignocaine hydrochloride solution containing adrenaline 1:200,000 was injected. After 4-6 min of administering the test dose, patients were received study drugs.

Blinding

The study drugs were prepared by an independent clinician not involved in the study. The anaesthesiologist performing the block and observing the patient was blinded to the treatment group. Neither the patient nor the attending anaesthesiologist who also collected the data was aware of the group allocation.

Parameters of observation

Block characteristics

1. **Onset of motor block:** Time from bupivacaine administration to when a modified Bromage score for lower limb of 3 was achieved.
2. **Onset of sensory block:** Time from bupivacaine administration to when there was complete lack of cold sensation at T 10 dermatome level.
3. **Duration of motor block:** Time interval between onset of motor block to complete regression of the block (Bromage score 0).
4. **Duration of sensory block:** Time interval between onsets of sensory block to restoration of cold sensation. Motor block was assessed by modified Bromage scale for the lower limb; modified Bromage scale (0 = No block, 1 = Inability to raise extended leg, 2 = Inability to flex knee and 3 = Inability to flex ankle and foot).

The regression of block was assessed every thirty minutes till complete recovery from motor and sensory block.

The time taken for onset of sensory block at T10; the highest dermatomal level of sensory analgesia; the complete establishment of motor blockade (Bromage 3), the time to two segment regression of analgesic level, regression of analgesic level to S1 dermatome using pin-prick method. sedation was evaluated by Ramsay sedation scale. Sedation scores were recorded just before the initiation of surgery and thereafter every 20 min during the surgical procedure.

Other parameters

Heart rate and Mean arterial pressure: Baseline values were noted and thereafter at every 10min interval. During the surgical procedure and postoperative period adverse event like anxiety, nausea, vomiting, pruritis, shivering, dry mouth, respiratory depression etc., were recorded. Nausea and vomiting were treated with 0.1 mg/kg of IV ondansetron. Shivering was treated with injection tramadol 25 mg IV. All the vital and hemodynamic parameters were recorded in the recovery room also at 1, 5, 10, 20 and 30 min interval.

Postoperatively block characteristics were assessed at 30 min intervals till 6 h.

Postoperative pain were assessed by 10-point Numerical rating scale (NRS), in which 0 represented no pain and 10 represented worst possible pain. NRS was measured every 30 min postoperatively. If patient complained of pain (defined as NRS >4), injection tramadol 100 mg was administered. Duration of analgesia (starting from epidural drug administration to once the patient asks for additional epidural analgesia with NRS >4).

Rescue interventions

Rescue interventions were planned for bradycardia, hypotension and pain;

- Bradycardia (<50 BPM): atropine
- Hypotension (<20% of baseline value): mephentermine.
- Pain: Intravenous tramadol as rescue analgesic.

Statistical methods

Power analysis

The primary outcome variable was the duration of the sensory and motor block. The secondary outcome variables included haemodynamic parameters. PASS version 11 software was used for calculation of sample size, with results of prior study^[8]. With power of study 80% and alpha

error 5%, the sample size came to 24 for each group. Considering drop outs, 30 patients in each group were recruited.

Statistical software

The data was compiled and subjected to statistical analysis using Statistical Package for Social Sciences [SPSS Inc, Version 20.0.Chicago, IL, USA)

Statistical tests

Statistical tests employed were Student's t-test for age, weight, onset and duration of motor and sensory blocks and haemodynamic parameters. Gender and ASA grade data were subjected to Chi-square test. Data is presented as

mean \pm SD. P-value < 0.05 was considered to indicate statistical significance.

3. Result

Sixty five patients were assessed for eligibility. Three patients did not give consent for participation and two was not included due to presence of chronic kidney disease. Sixty patients were enrolled and randomized to either of the two groups; 30 each in the intervention and the comparator groups. Finally, 27 patients in Group M and 26 patients in Group D were analyzed, the rest being excluded due to failed block [Figure 1]

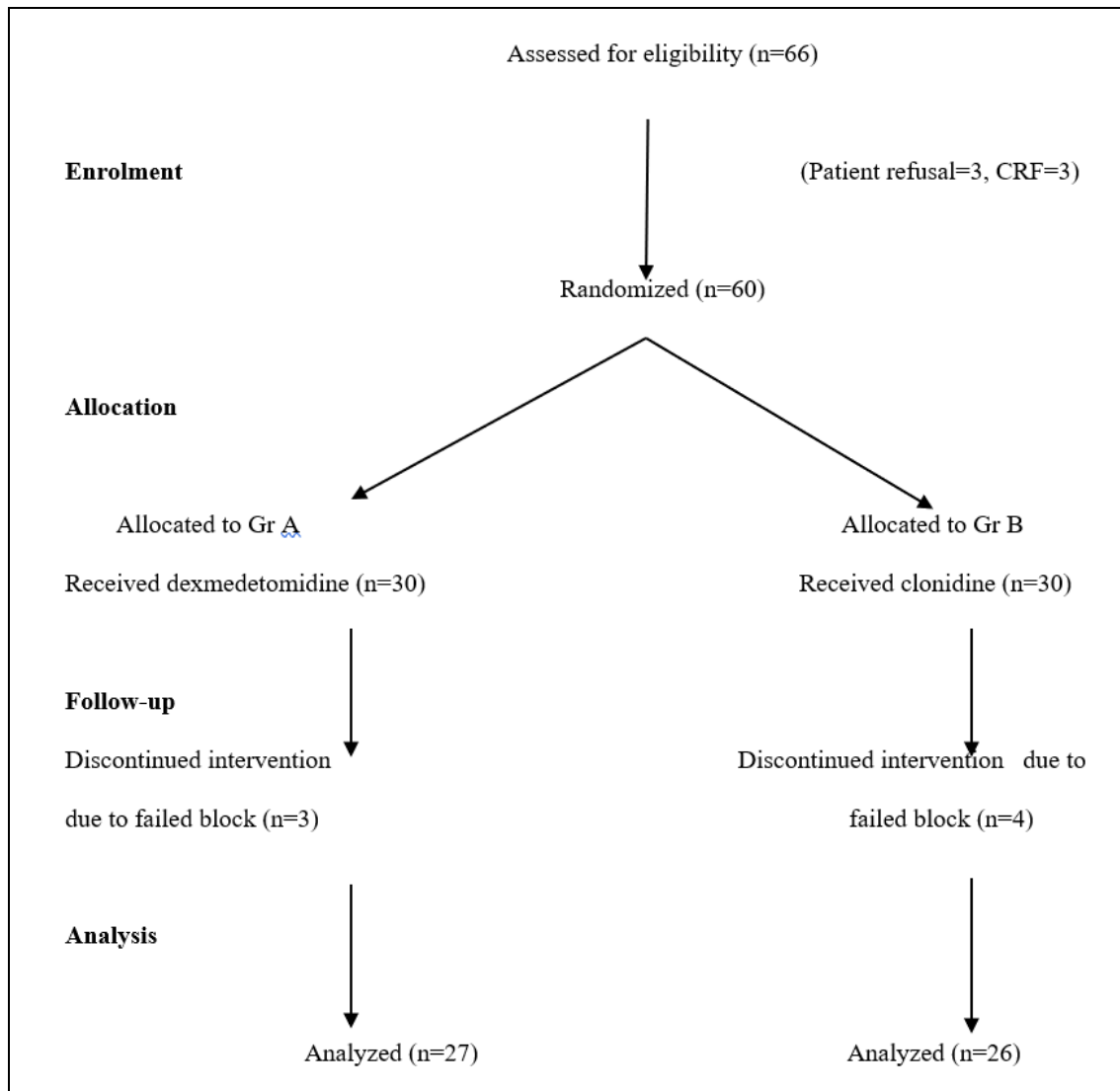


Fig 1: CONSORT flow diagram of study participants

There was no statistically significant difference between the patients in the two groups with respect to age, gender, body weight and ASA physical status [Table 1]. There were 13

male patients in group A whereas group B comprised of 14 males. Eight patients belonged to ASA II status in group M and 6 in group D.

Table 1: Demographic characteristics

	Group A (n=27) Mean \pm SD	Group B (n=26) Mean \pm SD	p-value
Age (Years)	44.3 \pm 13.6	39.8 \pm 12.3	0.201
Gender (M/F)	14 / 13	12 / 14	0.678
Weight (Kg)	59.7 \pm 7.0	56.8 \pm 8.4	0.347
ASA grade (I/II)	20 / 7	18 / 8	0.589

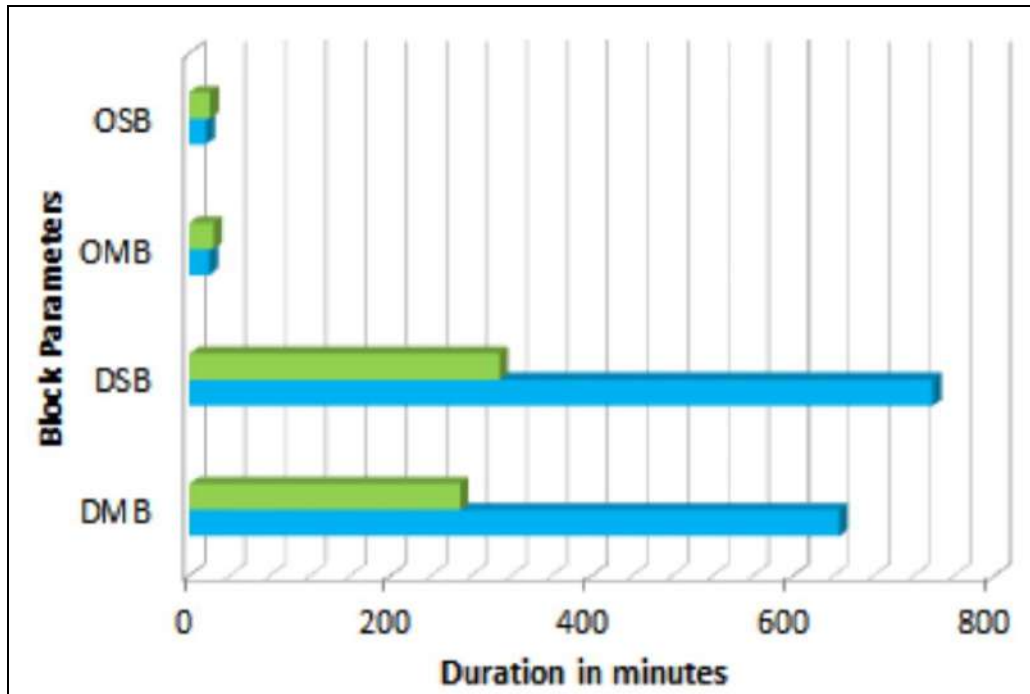
Demographic variables like age, sex, weight and ASA grading were comparable in both groups

Addition of dexmedetomidine as an adjuvant to epidural bupivacaine resulted in an earlier onset of sensory analgesia at T10 when compared to the addition of clonidine. Dexmedetomidine not only provided earlier onset, but also

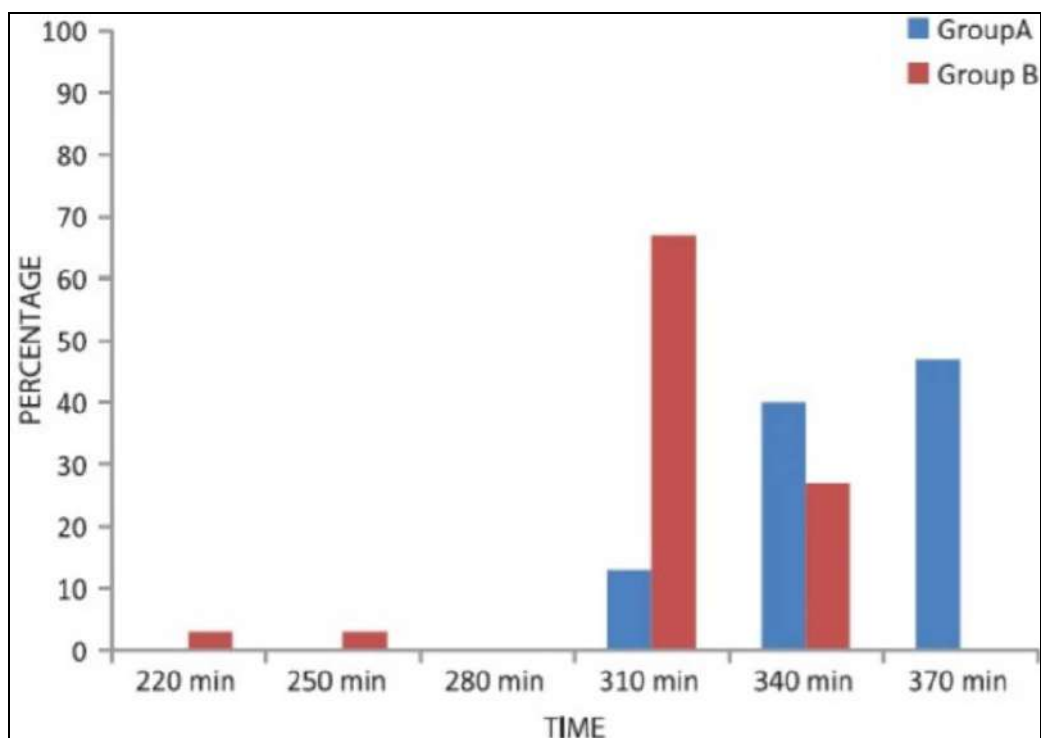
helped in achieving the maximum analgesic level in a shorter period compared to clonidine group. There was no statistically significant difference in the dermatomal spread among two groups. Motor block of Bromage 3 was achieved earlier in patients from the dexmedetomidine group than of the clonidine group.

Table 2: Block characteristics

	Group M (n=27) Mean \pm SD	Group D (n=26) Mean \pm SD	p-value
Onset time sensory block (min)	20.8 \pm 1.7	18.6 \pm 1.9	<0.001
Onset time motor block (min)	24.6 \pm 1.4	18.5 \pm 2.7	<0.001
Duration time sensory block (min)	317.7 \pm 46.7	638.4 \pm 66.3	<0.001
Duration time motor block (min)	368.8 \pm 32.7	615.0 \pm 106.0	<0.001



Graph 1: Block Characteristics (Blue: Group A & Green: Group B)



Graph 2: The requirement of rescue analgesia among Group A and Group B

In Group A time to “rescue analgesia” was prolonged compared to Group B. In both groups, the NRS followed a decreasing trend from 0 to 15 min after epidural administration. From 15 to 220 min (4 h) scores were stable and this period totally pain free. The mean NRS score was higher in the clonidine group at each time interval after 220 min ($P = 0.0001$). In Group A 13% patients needed rescue analgesia at 310 min, 40% at 340 min and 47% at 370 min ($P = 0.0057$). In Group B, 3% patients needed analgesia at 220 min, 3% at 250 min, 67% at 310 min and 27% patients at 340 min. The duration of analgesia also prolonged in the dexmedetomidine group compared to clonidine group.

Haemodynamic parameters i.e. heart rate and mean arterial pressure in both the groups were compared at an interval of 10 minutes during sedative infusion [Table 3, 4]. The baseline values of mean heart rate were comparable in both the groups and remained so during initial infusion of the sedatives and up to ten minutes thereafter. The mean heart rate values were found to be significantly lower [$p < 0.05$] in the dexmedetomidine group after 20 minutes of infusion till the end of the infusion [Table 3].

Table 3: Mean heart rate values during the procedure

	Group A	Group B	P value
B	83.30 ± 8.25	84.19 ± 10.07	0.725
10	80.89 ± 7.06	78.96 ± 11.14	0.458
20	78.81 ± 7.16	71.65 ± 9.87	0.004*
30	79.19 ± 8.01	71.92 ± 11.78	0.012*
40	80.15 ± 7.75	73.31 ± 12.78	0.024*
50	79.19 ± 8.48	71.85 ± 10.47	0.007*
60	80.78 ± 7.16	74.69 ± 9.08	0.010*
70	81.89 ± 6.93	74.38 ± 8.11	0.001*
80	84.70 ± 7.29	73.4 ± 6.50	0.000*
90	88.63 ± 3.11	71.92 ± 5.53	0.000*
100	85.11 ± 4.31	74.14 ± 10.55	0.034*
110	92.33 ± 5.13	71.45 ± 2.82	0.004*
120		70	

HRB – Baseline heart rate

HR 10 to HR 120 – Heart rate after every 10 minute interval till 120 minutes

Group A – Dexmedetomidine group Group B- Clonidine group

* P value statistically significant

The baseline value of mean arterial pressure was comparable in both the groups [$p > 0.05$] and remained so till the end of the infusion [Table 4].

Table 4: Mean arterial pressure values during the procedure

	Group A	Group B	P value
B	100.19 ± 4.61	98.27 ± 9.62	0.063
10	99.52 ± 5.61	94.88 ± 11.62	0.075
20	97.96 ± 5.94	95.73 ± 13.34	0.440
30	96.56 ± 4.25	94.77 ± 12.09	0.482
40	97.67 ± 5.03	96.62 ± 15.74	0.748
50	97.26 ± 5.71	93.50 ± 14.34	0.222
60	98.81 ± 5.02	95.62 ± 14.46	0.294
70	98.70 ± 5.44	94.36 ± 12.21	0.112
80	99.61 ± 5.87	97.30 ± 9.25	0.344
90	99.88 ± 5.21	96.92 ± 11.30	0.414
100	96.33 ± 3.67	98.29 ± 15.25	0.751
110	97.00 ± 2.00	95.00 ± 1.41	0.285
120		97.00	

MAPB – Baseline mean arterial pressure

MAP 10 to MAP 120 – Mean arterial pressure after every 10 min interval till 120 minutes

Group A – Dexmedetomidine group Group B- Clonidine group

Bradycardia was observed in one patient in dexmedetomidine group that was treated with injection atropine 0.3mg. Hypotension necessitating administration of injection mephentermine 3mg was also observed in one patient in group D [Table 5].

No episode of nausea, vomiting, hypoxemia or respiratory depression was observed in any patient.

Table 5: Adverse events

	Group A (n=26)	Group D (n=27)
Bradycardia	1	0
Hypotension	1	0

4. Discussion

Selection of the exclusive epidural route during this study was done deliberately to avoid the spinal anesthesia induced sudden hypotension, to provide the post-operative pain relief and to compare the analgesic, anesthetic potency, safety of the dexmedetomidine and clonidine. Hence in this study we compared block characteristics and duration of analgesia between epidural dexmedetomidine and clonidine to Bupivacaine.

To provide sedation, stable hemodynamics and prolonged postoperative analgesia are the main desirable qualities of an adjuvant used in epidural anesthesia^[9]. The demographic profile in the present study was comparable to other studies and did not show any statistical difference.

In the present study, the dexmedetomidine showed an earlier onset of sensory and motor blockade. Postoperatively number of the top ups were less with the bupivacaine dexmedetomidine group as compared to bupivacaine clonidine group.

Sukhminder Bajwa *et al.*^[10] also found the early onset of analgesia and motor blockade in epidural dexmedetomidine when used with ropivacaine.

Gupta *et al.*^[11] found similar results with epidural dexmedetomidine when used with levobupivacaine in doses comparable to our study.

Sedation score was 2 on Ramsey sedation scale throughout the surgery and up to 2 h in post-operative room with the dexmedetomidine group, whereas in group I patients were given midazolam for the same effects. All these results show the analgesic, anesthetic and sedative properties of the dexmedetomidine.

In the present study, baseline heart rate was between 80 and 90/min. Heart rate dropped down to 56 and 70/min in six patients in epidural dexmedetomidine group. None of the patients needed atropine. Similarly, mean arterial pressure decreased from baseline in both the groups and comparable, but it never went below 70 mm of Hg. The decrease in the heart rate caused by alpha-two agonist can be explained on the basis of their central action where they decrease the sympathetic outflow and nor epinephrine release^[8, 12, 13]. The stable hemodynamics can possibly be explained on the basis of lower volumes of the local anesthetic agent used, the lower doses of the adjuvant used.

Hypotension and bradycardia were observed in one patient from dexmedetomidine which was managed by mephentermine and atropine. None of the patients in the present study had episodes of the respiratory depression.

5. Conclusion

Dexmedetomidine is better epidural adjuvant to clonidine as it provides comparable stable hemodynamics, early onset

and establishment of sensory and motor anesthesia, prolonged postoperative analgesia and superior sedation levels.

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