Research Article

Comparative study of hemodynamic profile in intraoperative period and side effects of epidural ropivacaine with clonidine and dexmedetomidine for lower limb surgeries

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Abstract

Background: Epidural anesthesia gained great popularity by virtue of its distinct advantages over spinal anesthesia, such as provision of extended anesthesia in prolonged surgeries; early ambulation of patients, which reduces the hospital stay; and reduced incidence of postsurgical complications such as deep vein thrombosis.

Objective: To study ropivacaine with clonidine and dexmedetomidine in epidural anesthesia for lower limb surgeries with respect to hemodynamic profile in intraoperative period and their side effects.

Materials and Methods: Sixty patients of either sex of ASA grades I and II aged between 20 and 60 years were included in the study and randomly divided in two groups: group RC, patient received ropivacaine (0.75% 20 mL) with clonidine (2 μg/kg; *n* = 30); group RD, patient received ropivacaine (0.75% 20 mL) with dexmedetomidine (1.5 μg/kg; *n* = 30). The hemodynamic parameters recorded were mean heart rate, mean systolic blood pressure, mean diastolic blood pressure (DBP), and mean arterial pressure (MAP), respiratory rate, and oxygen saturation. These parameters were recorded preoperatively and then at 5-min intervals during intraoperative period till the end of the surgery. The study was carried out in the Department of Anesthesia, Grant Medical College Hospital, Indore, Madhya Pradesh, and Sir J.J. Group of Hospitals, Mumbai, Maharashtra, India.

Results: Heart rate was lower in group RD compared with group RC from 10 to 40 min intraoperatively, although it remained stable throughout the intraoperative period in both the groups. DBP was lower in group RD compared with group RC from 15 to 20 min intraoperatively. MAP was lower in group RD compared with group RC from 10 to 20 min intraoperatively, although it remained stable throughout the intraoperative period in both the groups. Oxygen saturation and respiratory rate showed no statistically significant differences and remained stable throughout the intraoperative period in both the groups. The incidence of side effects such as nausea, vomiting, dizziness, headache, and respiratory depression was nil in both the groups, while the incidence of dry mouth in both the groups was equal 36.33%, and the difference was not significant.

Conclusion: Hemodynamic parameters such as heart rate, blood pressure, oxygen saturation, and respiratory rate remained stable throughout the intraoperative period with both dexmedetomidine and clonidine.

KEY-WORDS: Ropivacaine, clonidine, dexmedetomidine, hemodynamic parameters, side effects

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Introduction

Pain is by far one of the most common and distressing effects of disease, and all medical persons regard its relief as one of their main duties. An acute pain service must act as a research vehicle, while anesthesiologists remain crucial contributors in the fascinating field of pain management. If pain is agony, then relieving pain is ecstasy.

For decades, central neuraxial blockade, both spinal and epidural, has served as one of the major modalities for pain relief in perioperative period. Of them, epidural anesthesia gained great popularity by virtue of its distinct advantages over spinal anesthesia, namely:

- Provision of extended anesthesia in prolonged surgeries.
- Fewer hemodynamic disturbances.
- Ability to provide postoperative analgesia via epidural catheter.
- Early ambulation of patients, which reduces the hospital stay.
- Reduced incidence of postsurgical complications such as deep vein thrombosis.

Various additives have been used for extending duration of spinal and epidural block to prolong the effect of local anesthetic agents. They include drugs such as opioids, ketamine, midazolam, and neostigmine. The α2 agonists, namely, clonidine and dexmedetomidine, have been recently added to the armamentarium of the anesthetists' additives in regional blocks.

The α2-adrenergic agonists produce clinical effect by binding to α-adrenergic receptors. Analgesic and anesthetic requirements get reduced to a large extent by use of these two adjuvants because of their analgesic properties. They also augment local anesthetic effect by causing hyperpolarization of nerve tissue by altering transmembrane potential and ion conductance at the locus ceruleus in the brainstem. The stable hemodynamic and decreased O_2 demand owing to enhanced sympathoadrenal stability make them very useful pharmacologic agents.[1]

In this study, the hemodynamic profile in the intraoperative period and side effects of both these drugs, dexmedetomidine and clonidine, as adjuvants to ropivacaine in epidural anesthesia in patients undergoing lower limb surgeries have been studied and compared.

Material and Methods

After institutional ethics committee approval, 60 patients of either sex of ASA grades I and II aged between 20 and 60 years were included in the study and randomly divided in two groups.

The inclusion criteria were

1. ASA grade I or II;
2. age between 20 and 60 years;
3. weight between 40 and 70 kg;
4. patients of either sex;
5. patients who gave consent; and
6. patients without history of any drug or substance allergy.

The exclusion criteria were

- Patients with history of
  1. diabetes or hypertension;
  2. coagulation disorders;
  3. anticoagulation therapy;
  4. kidney disease;
  5. psychiatric disorder;
  6. drug abuse;
  7. allergy to amide local anesthetics;
  8. drug interactions with injection ropivacaine, clonidine, and dexmedetomidine; and
- Patients not ready to give a written consent.

All the patients underwent complete preanesthesia checkup that included detailed history and general and systemic physical examination and investigations as per the pro forma. A written informed consent was obtained from every patient.

Patients were randomly allocated to one of the following two groups:

Group RC: patient received ropivacaine (0.75% 20 mL) with clonidine (2 μg/kg; $n = 30$);

Group RD: patient received ropivacaine (0.75% 20 mL) with dexmedetomidine (1.5 μg/kg; $n = 30$).

On arrival in the operation theatre, NBM status and consent were checked and confirmed. Monitoring of heart rate (HR), blood pressure (BP), oxygen saturation, and respiratory rate (RR) was initiated. The baseline readings of this parameter were recorded. An IV access was secured with 18G cannula, and an infusion of Ringer lactate was started at 8–10 mL/kg.

The 18G epidural catheter was inserted in L_{2-3} or L_{1-2} intervertebral space using Tuohy needle under all aseptic precautions in sitting position; 5 cm of the catheter length was kept in epidural space and test dose of 3 mL of 2% lignocaine hydrochloride solution containing adrenaline 1:2,00,000 was injected.

After 3–5 min of administering test dose and confirming its correct placement, patients in group RC were given 20 mL of 0.75% ropivacaine[2,3] and 2 μg/kg clonidine[4,5] in supine position by epidural route. Patients in group RD were given 20 mL solution of 0.75% ropivacaine and 1.5 μg/kg dexmedetomidine.[6–8] HRs, BP, SPO_2, and RR were recorded at every 5-min interval throughout the surgery.

The pinprick method was used to evaluate and check sensory level, while Bromage scale was used to measure motor blockade effect at 5, 10, 15, 20, 25, and 30 min after epidural administration of drug. Sensory block by pinprick method was graded as: grade 0, sharp pin felt; grade 1, analgesia, dull sensation felt; grade 2, anesthesia, no sensation felt. Bromage scale for motor blockage was 0, no block; 1, inability to raise extended leg; 2, inability to flex knee; and 3, inability to flex ankle and foot.

If there was persistent pain in the pinprick method after about 25–30 min of epidural administration of drug, the block was deemed unsuccessful and the patient excluded from the study.

Patient was given surgical position 25–30 min after epidural administration of drugs after confirming complete establishment of sensory and motor blockade.

Following block characteristics were observed and recorded:

1. Time of onset of sensory blockade.
2. Highest dermatomal level of sensory blockade.

3. Time of onset of motor blockade.
4. Complete establishment of motor blockade.
5. Time for two segment regression of sensory blockade.
6. Time of rescue analgesia.

Grading of sedation was evaluated by 5-point scale: 1, alert and wide awake; 2, arousable to verbal command; 3, arousable with gentle tactile stimulation; 4, arousable with vigorous shaking; and 5, unarousable.

Sedation score was recorded just before initiation of surgery and every 5 min thereafter throughout the surgical procedure. Analgesia and sedation were evaluated hourly for initial 6 h and then 6 hourly for next 18 h in postoperative period. After surgery, patients were shifted to postanesthetic care unit (PACU) where they remained for at least 6 h. Analgesia was evaluated by visual analog scale (VAS) ranging from 0 = lack of pain to 10 = worst imaginable pain.

Hypotension was defined as systolic pressure falling more than 20% and was treated first with fluid challenge and then with injection mephentermine (3–6 mg IV bolus). HR < 50 beats/min was treated with 0.6 mg injection atropine IV. Intravenous fluids were given as per body weight and operative loss requirement.

During surgical procedure, adverse events such as anxiety, nausea, vomiting, pruritus, shivering, and so on were noted. Nausea and vomiting was treated with injection ondansetron (4 mg IV). All the vitals and hemodynamic parameters were recorded in the recovery room at 5, 10, 15, 20, 25, and 30 min. Rescue analgesia was given with top-up dose of 8 mL of 0.2% ropivacaine in postoperative period if the VAS score was more than 3. Time for rescue analgesia was noted.

Results

A comparison was studied between:

1. The hemodynamic parameters (mean HR, mean SBP, mean DBP, MAP, RR, and SPO_2) in groups RC and RD. These parameters were recorded preoperatively and then at 5-min intervals during intraoperative period till the end of surgery.
2. The side effects in group RC and group RD.

To test whether there was any significant difference in between the two groups with reference to the study variables, unpaired t test and Mann–Whitney test were used at appropriate places as a statistical test. The *p*-value <0.05 was considered significant.

In groups RC and RD, there was no incidence of nausea, vomiting, shivering, headache, dizziness, and respiratory depression. Eleven of the 30 patients (36.33%) in each group experienced dry mouth either intraoperatively or postoperatively, and there was no difference in incidence in both the groups. This was not statistically significant ($p = 1.000$).

Discussion

This study was done in 60 patients of either sex of ASA grades I and II, aged 20–60 years, and of weight 40–70 kg undergoing lower limb surgery.

Demographic Data

The demographic data with respect to age, weight, and gender was comparable in both the groups as shown in Table 1. The mean age in group RC was 38.17 ± 11.86 years and in group RD was 38.10 ± 12.44 years. By applying unpaired *t* test ($p = 0.965$), difference in the age was not significant.

The mean weight in group RC was 58.07 ± 5.29 kg and in group RD was 55.80 ± 10.38 kg, which was not significant (unpaired *t* test, $p = 0.443$). The gender distribution was similar in both the groups: women, 5 (16.7%), and men, 25 (83.3%). The Pearson χ^2 test showed that difference in gender distribution was not significant (p = 1.000).

Duration of Surgery

As shown in Table 1, the mean duration of surgery in group RC was 103.50 ± 30.60 min and in group RD, 50 ± 25.92 min. Thus the two groups were comparable with respect to duration of surgery. By applying unpaired *t* test, the difference between the duration of surgery in the two groups was not significant ($p = 0.892$).

Hemodynamic Parameters

The hemodynamic parameters recorded were mean HR, mean SBP, mean DBP, MAP, RR, and SPO_2. These parameters were recorded preoperatively and then at 5-min intervals during intraoperative period till the end of the surgery.

Heart Rate

As shown in Table 2, there was a significant decrease in mean HR in group RD compared with group RC from 10 to 40 min intraoperatively, which was statistically significant. From 45 min onward till the end of the surgery, mean HR in

Table 1: Distribution of age, weight, and duration of surgery

Variables	Group RC		Group RD		Unpaired *t* test		
	Mean	SD	Mean	SD	*t*	*p*	Difference
Age (years)	38.17	11.86	38.10	12.44	–0.044	0.965	Not significant
Weight (kg)	58.07	5.29	55.80	10.38	–0.767	0.443	Not significant
Duration of surgery (min)	103.50	30.60	102.50	25.92	0.137	0.892	Not significant

$p < 0.05$: significant (unpaired *t* test).

Table 2: Comparison of mean HR in groups RC and RD

Heart rate (/min)	Group RC		Group RD		Mann–Whitney test		
	Mean	SD	Mean	SD	*z*	*p*	Difference
Preoperative	79.27	9.60	80.43	6.99	–1.210	0.226	Not Significant
0 min	78.13	8.78	80.50	6.98	–1.907	0.056	Not Significant
5 min	79.80	8.68	78.67	9.62	–0.424	0.672	Not Significant
10 min	78.83	7.61	73.57	12.01	–2.489	0.013	**Significant**
15 min	75.67	8.89	69.97	11.44	–2.453	0.014	**Significant**
20 min	74.63	7.54	66.10	10.79	–3.762	0.00017	**Significant**
25 min	71.67	6.62	63.90	9.72	–4.118	0.005	**Significant**
30 min	69.43	6.52	63.37	10.00	–3.996	0.005	**Significant**
35 min	68.23	5.90	65.87	13.56	–2.530	0.011	**Significant**
40 min	66.37	6.67	66.50	15.97	–1.998	0.046	**Significant**
45 min	65.10	7.08	68.13	17.73	–1.103	0.270	Not Significant

$p < 0.05$: significant (Mann–Whitney test).

Table 3: Comparison of mean SBP in groups RC and RD

SBP (mm Hg)	Group RC		Group RD		Unpaired *t* test		
	Mean	SD	Mean	SD	*t*	*p*	Difference
Preoperative	120.90	9.51	120.77	10.54	–0.328	0.743	Not Significant
0 min	121.80	9.10	120.77	10.61	–0.774	0.439	Not Significant
5 min	120.73	8.73	116.17	11.34	–1.859	0.063	Not Significant
10 min	117.07	9.77	109.67	12.96	–2.502	0.012	**Significant**
15 min	113.00	10.60	104.50	11.01	3.046	0.0035	**Significant**
20 min	108.83	9.58	102.77	10.48	2.340	0.0227	**Significant**
25 min	106.97	8.97	101.90	9.51	2.123	0.038	**Significant**
30 min	106.63	7.09	102.10	10.06	–2.008	0.045	**Significant**
35 min	104.70	7.92	103.90	11.14	0.321	0.750	Not Significant
40 min	101.97	7.97	106.23	9.23	–1.916	0.060	Not Significant
45 min	101.60	6.90	105.87	7.94	–1.222	0.632	Not Significant

$p < 0.05$: significant (unpaired *t* test).

group RC and RD was statistically not significant. In 2011, Bajwa et al.[9] studied the comparison of ropivacaine (0.75%) of dexmedetomidine and clonidine in epidural anesthesia, in which hemodynamic parameters in perioperative and postoperative period in both the groups were compared. There was a decrease in mean HR in both the groups. Thus, this study was in concurrence with the study by Bajwa et al.

Mean SBP

As shown in Table 3, from 10 to 30 min, intraoperatively, mean SBP in group RD was lower than mean SBP in group RC, which was statistically significant as per unpaired *t* test. From 35 min onward till the end of the surgery, the mean SBP in groups RC and RD was statistically not significant as per unpaired *t* test. In the study by Bajwa et al.,[9] there was a decrease in SBP in both the groups studied, which was in concurrence with this study.

Diastolic Blood Pressure

As shown in Table 4, DBP was comparable in both the groups. From 15 to 20 min, intraoperatively, mean DBP in group RD was lower than mean DBP in group RC, which was statistically significant as per unpaired *t* test. From 25 min onward till the end of the surgery, the difference was not statistically significant as per Mann–Whitney test. In the study by Bajwa et al.,[9] there was decrease in DBP in both the groups studied, similar to the result in this study.

Mean Arterial Pressure

As shown in Table 5, MAP was comparable in both the groups. At 10, 15, and 20 min intraoperatively, the mean of MAP in group RD was lower than in group RC, which was statistically significant as per Mann–Whitney test ($p \leq 0.05$). From 25 min onward till the end of the surgery, the difference was statistically not significant as per Mann–Whitney test ($p \geq 0.05$). In Bajwa et al.,[9] there was decrease in MAP in both the groups. Thus, this study was in concurrence with the study by Bajwa et al.

Respiratory Rate

As shown in Table 6, intraoperatively, the difference in mean RR of groups RC and RD at various time intervals

Table 4: Comparison of mean DBP in groups RC and RD

DBP (mmHg)	Group RC		Group RD		Unpaired *t* test		
	Mean	SD	Mean	SD	*t*	*p*	Difference
Preoperative	78.07	5.66	78.60	7.64	–0.218	0.828	Not Significant
0 min	78.23	5.67	77.70	8.72	–0.127	0.899	Not Significant
5 min	76.37	6.48	73.57	9.88	–1.298	0.194	Not Significant
10 min	73.23	6.85	70.23	11.26	–1.615	0.106	Not Significant
15 min	70.07	7.45	65.13	9.30	2.269	0.027	**Significant**
20 min	67.87	7.82	63.53	8.77	2.021	0.048	**Significant**
25 min	65.03	7.36	62.77	8.66	–1.253	0.210	Not Significant
30 min	61.83	7.53	63.07	8.34	–0.601	0.550	Not Significant

$p < 0.05$: significant (unpaired *t* test).

Table 5: Comparison of mean MAP in groups RC and RD

MAP (mm Hg)	Group RC		Group RD		Unpaired *t* test		
	Mean	SD	Mean	SD	*t*	*p*	Difference
Preoperative	92.34	6.36	92.65	8.24	–0.059	0.953	Not Significant
0 min	92.76	6.27	92.06	8.95	–0.356	0.722	Not Significant
5 min	91.16	6.54	87.77	9.87	1.568	0.122	Not Significant
10 min	87.84	7.26	83.38	11.50	–2.174	0.030	**Significant**
15 min	84.38	8.13	78.26	9.63	2.660	0.010	**Significant**
20 min	81.52	7.98	76.61	9.00	2.236	0.029	**Significant**
25 min	79.01	7.48	75.81	8.32	1.566	0.123	Not Significant
30 min	76.77	6.86	76.08	8.19	0.353	0.725	Not Significant

$p < 0.05$: significant (unpaired *t* test).

Table 6: Comparison of mean RR in groups RC and RD

Respiratory rate	Group RC		Group RD		Unpaired *t* test		
	Mean	SD	Mean	SD	*t*	*p*	Difference
Preoperative	15.37	3.77	16.60	2.36	–1.164	0.435	Not Significant
0 min	14.90	1.67	15.50	2.61	–1.061	0.293	Not Significant
5 min	15.80	2.17	`16.03	3.07	–0.164	0.870	Not Significant
10 min	15.40	2.55	14.70	3.59	–1.115	0.265	Not Significant
15 min	15.20	3.43	16.20	3.48	–0.850	0.395	Not Significant
20 min	14.63	4.10	16.97	3.16	–1.298	0.172	Not Significant
25 min	14.93	4.48	16.37	4.08	–1.308	0.191	Not Significant
30 min	16.67	4.17	17.30	4.04	–0.528	0.598	Not Significant

$p < 0.05$: significant (unpaired *t* test).

was not significant statistically as per Mann–Whitney test ($p > 0.05$). In the study by Bajwa et al.,[9] the difference in mean RR was statistically not significant ($p \geq 0.05$), similar to this study.

Oxygen Saturation

In Table 7, the SPO_2 recordings in both the groups showed that there was no fall in saturation intraoperatively.

Side Effects

Table 8 shows that, in groups RC and RD, there was no incidence of nausea, vomiting, shivering, headache, dizziness, and respiratory depression. Eleven of the 30 patients (36.33%) in each group experienced dry mouth either intraoperatively or postoperatively. Thus, the incidence of dry mouth in groups RC and RD was statistically not significant ($p = 1.000$), which was similar to the study by Bajwa et al. They found that the incidence of dry mouth was significantly higher in both the groups RC and RD but it was not statistically significant on comparison ($p > 0.05$). The incidence of other side effects such as nausea, vomiting, headache, shivering, and dizziness were comparable in both the groups and statistically not significant. The study did not observe respiratory depression in any patient from either group.[9] Thus, the results of the above-mentioned study were in concurrence with this study.

Table 7: Comparison of SPO_2 in groups RC and RD

SPO_2	Group RC		Group RD		Mann–Whitney test		
	Mean	SD	Mean	SD	*z*	*p*	Difference
Preoperative	100	0.00	100	0.00	0.000	1.000	Not Significant
0 min	100	0.00	100	0.00	0.000	1.000	Not Significant
5 min	99.87	0.43	99.97	0.18	–1.043	0.297	Not Significant
10 min	99.93	0.25	99.97	0.18	–0.587	0.557	Not Significant
15 min	99.90	0.31	100	0.00	–1.762	0.078	Not Significant
20 min	99.80	0.48	99.97	0.18	–1.720	0.085	Not Significant
25 min	99.83	0.38	100	0.00	–1.431	0.121	Not Significant
30 min	99.90	0.31	99.93	0.25	–0.463	0.643	Not Significant

$p < 0.05$: significant (Mann–Whitney test).

Table 8: Side effects in groups RC and RD

Side effects	Group RC	Group RD
Nausea	0	0
Vomiting	0	0
Shivering	0	0
Headache	0	0
Dizziness	0	0
Dry mouth	11 (36.33%)	11 (36.33%)
Respiratory depression	0	0

Conclusion

This study included 60 patients who were randomly assigned to any of the two groups: group RC, patient received ropivacaine (0.75% 20 mL) with clonidine (2 μg/kg; *n* = 30), epidurally; group RD, patient received ropivacaine (0.75% 20 mL) with dexmedetomidine (1.5 μg/kg; *n* = 30), epidurally. All the patients in both the groups were comparable with regard to age, gender, weight, and duration of surgery.

All patients received epidural anesthesia through lumbar epidural space using 18G Tuohy needle and catheter. Catheter was fixed at 5 cm within the epidural space.

Duration of analgesia in group RD was longer (288.50 ± 21.90 min) compared with group RC (202.17 ± 35.03 min), and the difference was statistically significant. The incidence of side effects such as nausea, vomiting, dizziness, headache, and respiratory depression was nil in both the groups, while incidence of dry mouth in both groups was equal 36.33%, and the difference was not significant.

HR was lower in group RD compared with group RC from 10 to 40 min intraoperatively, although it remained stable throughout the intraoperative period in both the groups. MAP was lower in group RD compared with group RC from 10 to 20 min intraoperatively, although it remained stable throughout the intraoperative period in both the groups. Oxygen saturation and RR showed no statistically significant differences and remained stable throughout the intraoperative period in both the groups.

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