A COMPARATIVE STUDY OF DEXMEDETOMIDINE AND CLONIDINE IN EPIDURAL ANAESTHESIA WITH ROPIVACAINE FOR LOWER ABDOMINAL AND LOWER LIMB SURGERY

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ABSTRACT

BACKGROUND

Epidural anaesthesia using Inj. Ropivacaine results in an effective anaesthesia and postoperative analgesia and addition of adjuvants would be advantageous. Clonidine and dexmedetomidine are α_2-agonists used as adjuvants in epidural anaesthesia. Aim of our study was to compare Inj. Dexmedetomidine and Inj. Clonidine added to epidural ropivacaine with respect haemodynamic parameters- heart rate, systolic blood pressure, diastolic blood pressure, motor blockade and sedations scores in patients undergoing lower abdominal and lower limb surgeries.

MATERIALS AND METHODS

This prospective, randomized, double blind study involved 60 patients of ASA-I, II who were categorized into two groups- Group-RD (n=30) received 1µ/kg Inj. Dexmedetomidine and Group-RC (n=30) received 1 µg/kg Inj. Clonidine. Patients in both groups received 17 ml of Inj. Ropivacaine epidurally. Patients were assessed for sensory block of T_{10} level, heart rate, systolic blood pressure and diastolic blood pressure, motor blockade using modified Bromage score and sedation score using Ramsay sedation scale.

RESULTS

Epidural anaesthesia using ropivacaine and adjuvants either clonidine or dexmedetomidine resulted in good sensory analgesia. Haemodynamic parameters with respect to heart rate, systolic blood pressure and diastolic blood pressure were similar between the two groups and were statistically not significant ($p > 0.05$). Sedation scores and modified Bromage scores were statistically significant ($p < 0.05$) for brief intervals of time.

CONCLUSION

Clonidine and Dexmedetomidine when used as adjuvants to epidural ropivacaine result in stable haemodynamics. Their sedation and motor blockade effects are comparable without significant adverse effects.

KEYWORDS

Clonidine, Dexmedetomidine, Epidural Anaesthesia, Ropivacaine.

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BACKGROUND

Epidural anaesthesia has been used for decades to facilitate surgery having the additional advantage of its use in postoperative period for analgesia. Ropivacaine is a long acting amide local anaesthetic which produces effects similar to other local anaesthetics by reversible inhibition of sodium ion influx into the nerve fibres.[1,2] It is less cardiotoxic[3] and neurotoxic[4] than bupivacaine. It has been extensively used by epidural route.

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Clonidine and Dexmedetomidine are α_2-agonists which have been used perioperatively as sedatives, analgesics and to decrease pressor response to laryngoscopy and endotracheal intubation.[5] Affinity for α_2-receptors when compared to α_1-receptors, for Dexmedetomidine is 1620 whereas for clonidine it is 220.[6] Hence, Dexmedetomidine is more α_2 receptor specific than Clonidine. Use of adjuvant along with a local anaesthetic would be beneficial in epidural anaesthesia resulting in more effective analgesia and, sensory and motor blockade.[7] Clonidine and Dexmedetomidine have been used as adjuvant medications in addition to local anaesthetics in epidural anaesthesia and analgesia.[5] In our study we compared Dexmedetomidine and Clonidine in dose of 1µ/kg epidurally along with Ropivacaine.

Aims and Objectives

1. To compare heart rate, systolic blood pressure and diastolic blood pressure changes associated with-

Dexmedetomidine+Ropivacaine and Clonidine+ Ropivacaine administered by epidural route.
2. To compare their effect on motor blockade as assessed by modified Bromage scale.
3. To compare the sedative effect of two drugs given during the study.
4. To observe and compare the adverse effects between the two study drugs during intraoperative and perioperative period.

MATERIALS AND METHODS

This was a prospective, randomized, double blinded study involving 60 American Society of Anaesthesiologists (ASA) grade I, II patients which was undertaken after obtaining approval from Institutional Ethics Committee. Patients who were scheduled for elective lower abdominal and lower limb surgeries necessitating epidural anaesthesia were included in the study after obtaining written and informed consent. Exclusion criteria were patients' refusal to participate in the study, weight >120 kgs, height <150 cms, history of diabetes mellitus, hypertension, history of cardiac illness e.g. Ischemic heart disease, valvular heart disease, history of respiratory disease e.g. bronchial asthma, COPD, history of central nervous system problems e.g. stroke, TIA, psychiatric illness, patients with ECG changes suggestive of heart block, patients on β-blockers and α_2-antagonists, patients with coagulation abnormality, known allergy to any of the medications used in the study. Patients who were pregnant or those who were lactating were also excluded from the study. Patients with contraindication for epidural anaesthesia were also excluded from the study.

After obtaining written and informed consent from the patients, patients were randomized by envelope method and allocated into 2 equal groups namely Group-RD and Group-RC. Patients in Group-RD (n=25) received 17 ml of 0.75% Inj. Ropivacaine and 1 µg/kg of Inj. Dexmedetomidine whereas those in Group-RC (n=25) received 17 ml of 0.75% Inj. Ropivacaine and 1 µg/kg of Inj. Clonidine.

Preanaesthetic evaluation was done for all patients well in advance before the scheduled surgery by history taking, general physical examination, recording vital signs, systemic examination, examination of airway and spine. Laboratory investigations included complete haemogram, blood urea and serum creatinine, serum electrolytes, electrocardiogram (ECG). Any other investigations if necessary were performed according to the patients' assessment.

Nil per oral for 8 hours for solids and 2 hours for water were obtained for all patients prior to institution of anaesthesia. Preoperative anxiolysis was achieved using Tab. Diazepam 10 mg night before surgery. In addition, all patients received Tab. Ranitidine 150 mg and Tab. Ondansetron 4 mg with sips of water on night before surgery and 2 hours prior to institution of anaesthesia. Venous access was secured using a 18G I.V. cannula. On the day of surgery patients were reassessed by systemic examination and baseline vitals were recorded. Patients were preloaded using 10 ml/kg of crystalloids Ringers' lactate or 0.9% saline over 20 minutes.

Within the operating room, monitoring the patients included continuous 5-lead electrocardiogram (ECG), non-invasive blood pressure (NIBP), plethysmography (SpO_2). Baseline vital signs were recorded, and patients were positioned appropriately for institution of epidural anaesthesia. Under strict aseptic precautions lumbar spine was felt and skin infiltrated using 2 ml of 2% Inj. Lignocaine in L_4-L_5 space. Epidural space was approached by loss of resistance technique to air using 18G Touhy needle and a 18G epidural catheter was threaded 5 cms into the epidural space and secured appropriately. Test dose of 3 ml 2% Inj. Lignocaine with adrenaline (5µ/ml) was administered epidurally to rule out intravascular or subarachnoid placement of epidural catheter. Study drug preparation was injected after administration of test dose. Patients were monitored for heart rate, blood pressure, respiratory rate and SpO_2 every 5 minutes. All patients received oxygen by face mask at rate of 5 litres/min. Hypotension was treated (drop in mean arterial pressure of more than 20% from baseline) Inj. Ephedrine 6 mg I.V. and bradycardia (HR <50/min) was treated with Inj. Atropine 0.6 mg i.v. Respiratory depression (RR <8/min or SpO_2 <90%) was managed with intermittent positive pressure ventilation using 100% oxygen. Nausea and vomiting were treated using 4 mg Inj. Ondansetron intravenously. Sensory blockade was assessed bilaterally using pin prick method from distal to proximal dermatome level. Motor blockade was assessed using Modified Bromage Scale and sedation was assessed using Ramsay Sedation Scale.

The following details were observed and recorded:

1. Time to attain sensory block of T_{10} level.
2. Peak sensory level.
3. Systolic and diastolic blood pressure changes.
4. Motor blockade as assessed by modified Bromage scale.
5. Sedation score using Ramsay sedation scoring system.

Adverse effects namely nausea, vomiting, shivering, dryness of mouth, urinary retention and respiratory depression were monitored, recorded and treated accordingly. Surgery was performed after confirmation of sensory blockade till T_{10} level and complete motor blockade was achieved. After completion of surgical procedure patients were shifted to recovery room followed by post-operative room. Patients were educated and instructed to inform to postoperative staff nurse for any discomfort at surgical incision site who was also blinded to the study. Duration of analgesia was recorded from the onset of sensory blockade to the time of discomfort at the surgical site as reported by the patient. Study was ended with the onset of discomfort or pain at the surgical site incision.

Statistical Methods

The information collected from all the patients were recorded in a master chart. Statistical analysis was performed using SPSS 18.0.2 software and Kruskul Wallis

chi-square test was used to test the significance of difference between quantitative and variables and Yate's chi square test was used for qualitative variables. A 'p' value of <0.05 was considered to be significant.

RESULTS

All patients who were included in the study continued to stay in their study group till the end and none of the patients were excluded later for any reason. Patients in either group did not vary significantly with respect to age, gender, height and weight (Table-1). Although male predominance was noted in both the groups, it was just a coincidence and it was not statistically significant (Table-1). Patients did not vary significantly with respect to ASA grading (p=0.486) and duration of surgery (p=0.327).

Parameters	Group-RC	Group-RD	'p' value
Age distribution (years)	45.70 ± 22.19	43.93 ± 18.09	0.266 (ns)
Gender distribution Male:Female	21:9	24: 6	0.371 (ns)
Height (cms)	156.97 ± 5.85	159.10 ± 6.94	0.203 (ns)
Weight (kgs)	56.40 ± 8.81	54.07 ± 8.29	0.295 (ns)
ASA grade (I:II)	19:11	24: 6	0.486 (ns)
Duration of surgery (minutes)	112.67 ± 32.16	134.00 ± 23.58	0.327 (ns)

Table 1. Demographic Data Other Parameters Expressed As Mean ± SD

ns= statistically not significant, p <0.05 is significant.

Sedation Score	Group RC	Group RD	'p' value
5 min	1.00 ± 0.00	1.00 ± 0.00	1.000
10	1.63 ± 0.49	1.70 ± 0.47	0.591
15	2.13 ± 0.73	2.60 ± 0.67	0.213
20	2.67 ± 0.84	3.03 ± 0.61	0.059
25	2.77 ± 0.82	3.57 ± 0.68	<0.001
30	2.83 ± 0.83	3.80 ± 0.48	<0.001
40	2.57 ± 0.86	3.40 ± 1.22	0.003
60	2.60 ± 1.00	2.90 ± 1.32	0.326
80	2.33 ± 0.99	2.50 ± 1.48	0.618
100	2.00 ± 0.91	1.82 ± 1.18	0.533
120	1.62 ± 0.75	1.18 ± 0.53	0.043
140	1.20 ± 0.41	1.09 ± 0.30	0.466
160	1.00 ± 0.00	1.00 ± 0.00	-
180	1.00 ± 0.00	1.00 ± 0.00	-

Table 2. Sedation Scores (Ramsay Sedation Score)- Comparison Between 2 Groups

Patients' sedation score was also monitored, and they were comparable in mean sedation score at baseline. Most patients were sedated to a score between 2 to 4 in both the groups between 15 minutes to 90 minutes. Sedation in Group-RD was statistically significant when compared to Group-RC between 25 minutes to 60 minutes (p <0.05) (Table-2). However, it was statistically not significant beyond 60 minutes (p >0.05) between the two groups (Table-2).

Motor blockade (Bromage)	Group RC	Group RD	'p' value
5 min	1.00 ± 0.26	1.00 ± 0.00	1.000
10	1.47 ± 0.51	2.00 ± 0.00	<0.001
15	1.97 ± 0.18	2.20 ± 0.61	0.049
20	2.80 ± 0.89	3.73 ± 0.69	<0.001
25	3.47 ± 0.90	3.93 ± 0.37	0.011
30	3.73 ± 0.69	4.00 ± 0.00	0.039
40	3.93 ± 0.37	4.00 ± 0.00	0.321
60	3.97 ± 0.18	4.00 ± 0.00	0.321
80	4.00 ± 0.00	4.00 ± 0.00	-
100	4.00 ± 0.00	4.00 ± 0.00	-
120	4.00 ± 0.00	4.00 ± 0.00	-
140	3.88 ± 0.50	4.00 ± 0.00	0.397
160	3.78 ± 0.67	4.00 ± 0.00	0.662
180	-	-	-

Table 3. Motor Blockade (Bromage)- A Comparison in Two Groups

p < 0.05 is significant.

Motor blockade was assessed by using Modified Bromage scale. A score of 2 was achieved by 10 minutes in Group-RD and at 15 minutes in Group-RC and in majority of patients between 10 to 20 minutes. A score of 4 was achieved by 40 minutes in Group-RD and by 80 minutes in Group-RC in all patients (Table-3). The mean Bromage score was statistically significant from 5 minutes to 35 minutes (p <0.05). After 40 minutes it was statistically not significant (p >0.05) (Table-3).

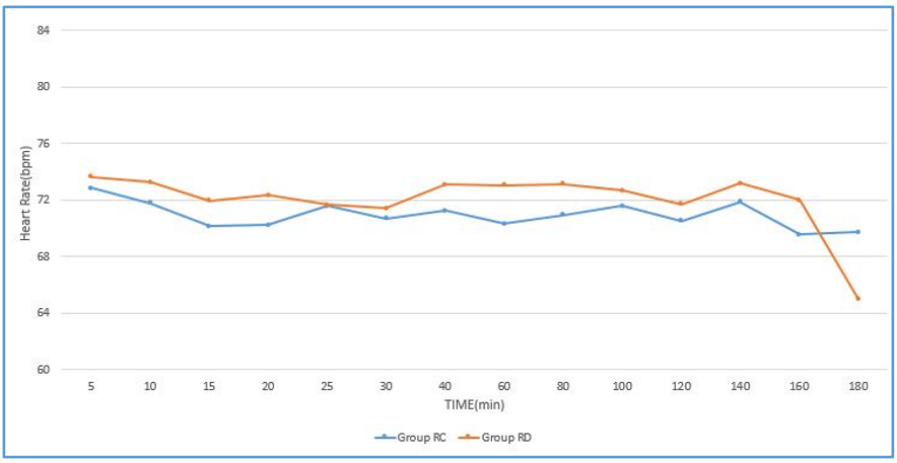

Figure 1. Comparison of Mean Heart Rate between the Two Groups

Heart rate was monitored every 5 minutes and their mean were comparable between the two groups across all intervals of time and it was statistical not significant (p >0.05) throughout the procedure (Figure-1). We did not notice any patient developing bradycardia necessitating administration of Inj. Atropine.

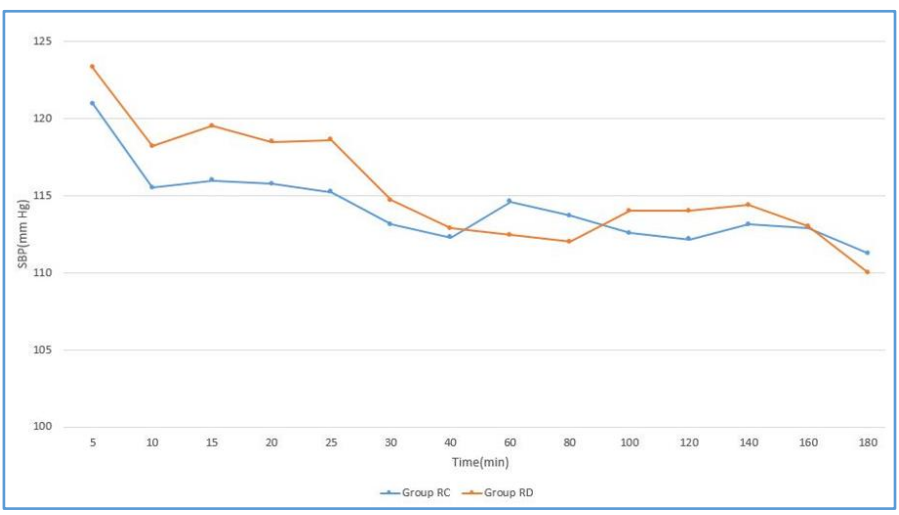

Figure 2. Comparison of Mean Systolic Blood Pressure between the Two Groups

Systolic blood pressure was recorded every 5 minutes in both the groups. There was no significant drop in systolic blood pressure from the baseline and it remained close to baseline values throughout the procedure (Figure-2). The mean systolic blood pressure was comparable between the two groups and it was statistically insignificant between the two groups (p >0.05) across all intervals of time.

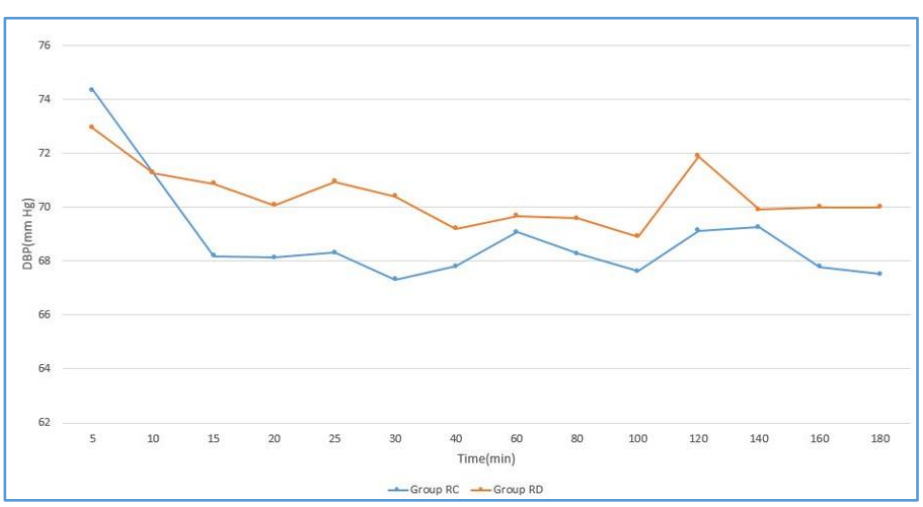

Figure 3. Comparison of Mean Diastolic Blood Pressure between the Two Groups

Diastolic blood pressure was also recorded every 5 minutes and there was no significant drop from the baseline values (Figure-3). Both the groups were comparable with respect to diastolic blood pressure and it was statistically not significant ($p > 0.05$) across all intervals of time.

DISCUSSION

Epidural anaesthesia has been a technique of choice for lower abdominal and lower limb surgeries especially when surgery is anticipated to be longer or as a technique for achieving postoperative pain relief.[7] Ropivacaine is a longer acting amide local anaesthetic with good anaesthetic and analgesic effects when administered epidurally.[8] It is less cardiotoxic and less neurotoxic when compared to bupivacaine.[3,4] Hence it has been increasingly used in the past decade. We chose ropivacaine over bupivacaine for its lesser incidence of cardiotoxicity and neurotoxicity.

Addition of adjuvants to the local anaesthetics would result in more effective analgesia and motor blockade.[9] A wide variety of adjuvant medications have been epidurally along with local anaesthetics and α_2-agonists are one class of medications. Clonidine and dexmedetomidine belong are α_2-agonists drugs.[5] They are used perioperatively for sedation, anxiolysis and to decrease the pressor response to laryngoscopy and endotracheal intubation.[5] They have been used neuraxially and shown to result in better quality as well as longer duration of analgesia.

Dexmedetomidine is more α_2 receptor specific (α_2:α_1 = 1620:1) when compared to clonidine (α_2:α_1 = 220:1).[6] Hence we wished to compare clonidine and dexmedetomidine administered epidurally as adjuvants to ropivacaine and noted for changes in heart rate and blood pressure, sedation score and motor blockade as assessed by modified Bromage scale.

A study has been done comparing epidural clonidine (2 µg/kg) and dexmedetomidine (1.5 µg/kg) in addition to Inj. Ropivacaine (17 ml) and have been shown to result is comparable and stable haemodynamic profile without statistical significance. They also noted that dexmedetomidine resulted in higher sedation scores than clonidine which was statistically significant ($p < 0.05$). They concluded dexmedetomidine as a better drug when compared to clonidine with respect to onset of analgesia, postoperative pain relief and sedation score.[10] In our study we used 1 µg/kg of dexmedetomidine or clonidine. Our study correlates with the above mentioned with respect to haemodynamic parameters, however we noted statistically significant sedation and motor blockade only for brief period of time and later it was statistically insignificant.

In another study where dexmedetomidine (1 µg/kg) and clonidine (2 µg/kg) were used with epidural bupivacaine (15 ml) showed statistically significant motor blockade and sedation scores using dexmedetomidine when compared to clonidine. Although clonidine dose (2 µg/kg) used was higher than dexmedetomidine (1 µg/kg) it resulted in lesser motor blockade and sedation scores.[11] However, the haemodynamic parameters compared between the two groups were similar and statistically insignificant.[11]

A study was conducted using 1 µg/kg of dexmedetomidine or clonidine in addition to epidural ropivacaine (15 ml) and they observed to have statistically insignificant difference with respect to haemodynamic parameters and motor blockade. However, dexmedetomidine resulted in statistically significant sedation scores when compared to clonidine.[12] Our study correlates with this study that dose of dexmedetomidine and clonidine used were same. However, we noted statistically significant motor blockade and sedation scores for brief period of time in Group-RD when compared to Group-RC. We did not come across any major adverse effects in either of the groups.

CONCLUSION

Clonidine and Dexmedetomidine when used as adjuvants along with ropivacaine in epidural anaesthesia result in stable haemodynamic parameters as assessed by heart rate, systolic and diastolic blood pressure changes, and the difference is statistically insignificant. They have comparable modified Bromage scores and sedation scores across most intervals of time. They are safe when administered epidurally without significant adverse effects.

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