A COMPARATIVE STUDY OF EPIDURAL ROPIVACAINE (0.75%) PLUS CLONIDINE WITH ROPIVACAINE (0.75%) PLUS DEXMEDETOMIDINE FOR LOWER ABDOMINAL AND LOWER LIMB SURGERIES

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ABSTRACT

BACKGROUND

Epidural anaesthesia is one of the most common regional anaesthetic techniques used for lower abdominal and lower limb surgeries. Epidural anaesthesia provides effective surgical anaesthesia and can also achieve the extended duration of surgical needs, provides prolonged postoperative analgesia, lowers the incidence of haemodynamic changes. The quality and duration of analgesia is improved when a local anaesthetic is combined with alpha-2 adrenergic agonist as neuraxial adjuvants.

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

A prospective randomised double blinded study was conducted in 60 patients of either sex between the ages of 20 and 60 years of (American Society of Anaesthesiologists) ASA I/II grade who underwent lower abdominal and lower limb surgeries. The patients were randomly allocated into two groups; Ropivacaine + Clonidine (RC) and Ropivacaine + Dexmedetomidine (RD) comprising of 30 patients each. Group RC received 15 mL of Ropivacaine (0.75%) with 75 µg Clonidine and group RD received 15 mL of Ropivacaine (0.75%) with Dexmedetomidine 50 µg epidurally. Onset of sensory analgesia using bilateral pin-prick method, onset of motor blockade using Bromage scale, time to two dermatome regression of sensory level, time to first demand for analgesia, intraoperative haemodynamic parameters and complications were observed. Statistical analysis was done by chi-square test for qualitative data and unpaired student t-test for quantitative data using statistical package for social science (SPSS) version 19 for windows and value of $p<0.05$ was considered significant and $p<0.001$ as highly significant.

RESULTS

The demographic profile and cardiorespiratory parameters were comparable and statistically non-significant in both the groups. The side effect profile was also comparable with a little higher incidence of nausea and dry mouth in both the groups which was again a non-significant entity ($P>0.05$). Dexmedetomidine group (RD) had rapid onset of sensory and motor blockade ($p<0.05$), prolonged duration of sensory and motor block ($p<0.05$) and postoperative analgesia ($p<0.05$).

CONCLUSION

Dexmedetomidine is a better neuraxial adjuvant to epidural Ropivacaine compared to clonidine for providing early onset and long duration of sensory analgesia and motor blockade, longer post-operative analgesia.

KEYWORDS

Clonidine, Dexmedetomidine, Ropivacaine, Epidural Block.

HOW TO CITE THIS ARTICLE: Shailesh K, Raval DL, Kumari A, et al. A comparative study of epidural ropivacaine (0.75%) plus clonidine with ropivacaine (0.75%) plus dexmedetomidine for lower abdominal and lower limb surgeries. J. Evolution Med. Dent. Sci. 2017;6(54):4076-4081, DOI: 10.14260/Jemds/2017/881

BACKGROUND

The surgical and anaesthetic techniques have evolved and improved drastically over the last two decades. Intrathecal anaesthesia and epidural anaesthesia are the most popular regional anaesthesia techniques used for lower limb, lower abdominal surgeries. The advantage of epidural anaesthesia being, it[1,2] provides prolonged postoperative analgesia; reduces the incidence of haemodynamic changes.

Different local anaesthetics[3] are used for epidural anaesthesia, most popular being Lignocaine and Bupivacaine. The drawback of Lignocaine is its intermediate duration of action; and the drawback of Bupivacaine is although long acting, is narrow margin of cardiovascular or central nervous system toxicity.[4]

Recently Ropivacaine has been introduced as a new amide which has all advantages of Bupivacaine with less cardiac toxicity,[5] it appears that it may be an ideal local anaesthetic for epidural anaesthesia.[6]

Intraoperative haemodynamic stability, sedation, and an ability to provide smooth and prolonged postoperative analgesia are the main desirable qualities of an adjuvant in neuraxial anaesthesia.[7]

Financial or Other, Competing Interest: None.
Submission 24-05-2017, Peer Review 22-06-2017,
Acceptance 29-06-2017, Published 06-07-2017.
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The quality and duration of analgesia is improved when a local anaesthetic is combined with alpha2 agonist. Both Clonidine and Dexmedetomidine are alpha2 adrenergic agonists which have analgesic properties and potentiate local anaesthetic effect.[8-10]

Dexmedetomidine is a highly selective alpha-2 adrenergic agonist with an affinity of eight times greater than Clonidine. It allows haemodynamic stability, sedative, anxiolytic, analgesic, neuroprotective effect. It causes more intense motor blockade and co-operative sedation without increasing the incidence of side-effects.[11,12]

Neuraxial Clonidine enhances the action of local anaesthetic, increases the intensity and duration of analgesia. It has sedative properties while side-effects are hypotension, bradycardia.[13-15]

The purpose of this study was to compare sensory and motor characteristics, haemodynamic and analgesia potentiating effect of epidurally administered Dexmedetomidine and Clonidine when combined with Ropivacaine (0.75%).

MATERIALS AND METHODS

After approval from institutional ethical committee and informed written consent of patients, present study was conducted in 60 patients of either sex belonging to ASA grade I or II between age group of 20 to 60 years undergoing lower abdominal and lower limb surgeries satisfying inclusion criteria: Patient age 20 – 60 yrs., ASA Grade I or II, Patient wt. 40-80 kg.

In this prospective randomised controlled study, patients were divided into two different groups (Each group with 30 patients). Exclusion criteria were Patient's refusal, Hypersensitivity to drugs used in our study, local Infection, coagulation abnormalities, significant neurological disease with sensory or motor deficit, history of psychiatric disease which is excluded by pre-operative history and basic investigation.

All basic laboratory investigations include complete haemogram, bleeding time, clotting time, blood sugar, renal function test, urine routine and micro, serology, etc. ECG and chest radiogram were asked for and reviewed in indicated patients.

All patients were kept nil by mouth for 6 hrs. prior to anaesthesia. On the morning of day of surgery, baseline vital parameters were noted. Intravenous line was secured with all aseptic and antiseptic precautions and monitoring devices were attached which included heart rate, electrocardiograph (ECG), pulse oximetry (SpO2), non-invasive blood pressure (NIBP), respiratory rate and the baseline parameters were recorded. Inj. Ringer's lactate (RL) 500 mL started. Inj. Glycopyrrolate 0.2 mg intramuscular was given as premedication half an hour before surgery in pre-anaesthetic room.

In the operation theatre, Inj. Ondansetron 4 mg given intravenously and baseline parameters were recorded and second pint of RL was started. In sitting position, epidural catheter was inserted through 18 gauge Tuohy needle into the epidural space at L_{2-3} intervertebral space using loss of resistance to air technique, epidural catheter was secured 3–4 cm into epidural space with all aseptic and antiseptic precautions. Test dose was given with 3 mL of Inj. 2% Lignocaine with Inj. Adrenaline (5 mcg/mL) to exclude accidental intravascular or subarachnoid catheter position.

60 patients were allocated by computer generated randomisation in 2 equal groups in double blinded manner by an investigator with no clinical involvement in the trial. Even numbered patients received 15 mL Ropivacaine (0.75%) plus 75 µg Clonidine- group RC. Odd numbered patients received 15 mL Ropivacaine (0.75%) plus 50 µg Dexmedetomidine– group RD. Drug solutions were prepared by an anaesthesiologist who was blinded to the nature of the study in 20 mL syringe. The patients were unaware about their study groups. The anaesthesiologist giving the epidural block as well as the observer who monitored the parameters were both blinded to the study drug. Both groups had received drugs epidurally, after 4 – 6 minutes of test dose according to their groups. The bilateral pin-prick method was used to evaluate and check the sensory level while a 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) was used to measure the motor blockade effect after the epidural administration of the drugs. Surgical position was made approximately 25–30 minutes after administration of drugs in every patient with complete establishment of sensory and motor block. The following block characteristics were observed and recorded: initial period of onset of analgesia and motor blockade (modified Bromage scale 1), the complete establishment of motor blockade (modified Bromage scale 3), the time to two segment regression of analgesic level, total duration of analgesia (time to first feeling of pain). Onset of sensory analgesia was defined as the time taken to achieve loss of pin-prick 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 analogue scale score of >3. 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 hours 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 3 min. after administration of study drug till a block of Bromage grade 3 motor blockade was achieved.

When the anaesthetic effects of epidural blockade is inadequate to perform surgery satisfactorily, spinal anaesthesia was given with Inj. Bupivacaine Heavy (0.5%) according to weight and height, and all these patients were excluded from our study.

After giving epidural anaesthesia, pulse rate, blood pressure, respiratory rate, SpO_2 were noted continuously and recordings were made every 5 min. until 30 min., and at 10 min. interval thereafter up to 60 min. and then at 15 min. interval for next hour and finally at 30 min. in the third hour. If hypotension occurs [BP < 90 mmHg systolic] then injection Mephentermine 9 mg IV was given. If bradycardia occurs [pulse < 60 beats/min.] then injection Atropine 0.6 mg IV was given.

Patients were also monitored for complications like nausea, vomiting, bradycardia, hypotension, dry mouth,

shivering, respiratory depression, headache, dizziness, urinary retention, etc. during intraoperative period. All patients were shifted to recovery room at the end of surgery and monitored. When there was a reversal of epidural block observed patients were shifted to ward. When VAS ≥ 5, first dose of post-operative analgesia was given in the form of Inj. Tramadol 1 mg/kg + Inj. Bupivacaine 0.0625% (8 mL) through epidural catheter. Then subsequent doses of post-operative analgesia were given with same drugs when VAS ≥ 5 through epidural catheter and it was removed after 24 hours of insertion.

Sample size was determined with the help of Open-Epi software version 3. Total sample size of 50 (25 in each group) was derived from findings of duration of sensory analgesia in group RD (mean 316 min. and SD 31.15 min.) and group RC (mean 281 min. and SD 37 min.) in a reference study done by Sruthi Arunkumar, V.R Hemanth Kumar et al. Mean difference was 35. Two-sided confidence level (1-alfa) was 95% that means <5% chance of drawing a false-positive conclusion.

Power (1-beta % chance of detecting) was considered 95% that means <5% chance of a false-negative conclusion. The ratio of sample size (Group 2/Group 1) was considered 1**.** By putting the mean and standard deviation value in Open-Epi software version 3, sample size was calculated which was 50 (25 in each group). I had taken total sample size 60 (30 in each group) which was more than 50 calculated from reference study, which was essential for more significance of data. Assumptions were that both the combinations of drugs in both groups (RD and RC) were equivalent in the duration of sensory analgesia.

The statistical analysis was done by unpaired student t-test for quantitative data and chi-square test for qualitative data. In the present study, the data collected were entered into a master chart and statistical tables were prepared. In order to compare the quantitative data, mean and standard deviation were computed. The equality of the mean value of the two groups were tested by applying unpaired student's 't' test. All statistical calculations P value<0.05 were considered statistically 'significant.'

P value>0.05 statistically considered 'not significant.'

The all data were analysed using SPSS version 19 and Microsoft Excel 2013 (IBM). P value was calculated and interpreted as-

Value of P < 0.05 as statistically significant and P < 0.0001 as highly significant.

RESULTS

The present study was conducted in 60 patients of either sex belonging to ASA Grade I or II in age group of 20 to 60 years. Patients undergoing lower abdominal and lower limb surgeries under epidural anaesthesia were selected for this study. Patients were randomly divided into two groups: RC and RD receiving Clonidine and Dexmedetomidine as adjuvants respectively (30 patients in each group). The statistical analysis was done by Unpaired student's 't' test for quantitative data and chi-square test for qualitative data.

Both groups were comparable for demographic profile as there was no significant difference between the two groups in respect to age and sex distribution [Figure 1], and weight characteristics. Mean duration of surgery was comparable in both the groups and statistically non-significant (P >0.05) [Table 1].

Particulars	Group RD Mean ± SD	Group RC Mean ± SD	P Value	Significant
Age (years)	46.30 ± 12.1	47.86 ± 9.30	0.5777	Not Significant
Weight (kg)	55.33 ± 5.61	55.53 ± 6.34	0.8975	Not Significant
Duration of surgery (minutes)	112 ± 30.91	102 ± 21.35	0.1502	Not Significant

Table 1. The Demographic Profile of Patients of both Study Groups

In Group RD 20% of the patients were male and 80% of the patients were female. In Group RC 23.33% of the patients were male and 76.67% of the patients were female [Figure 1].

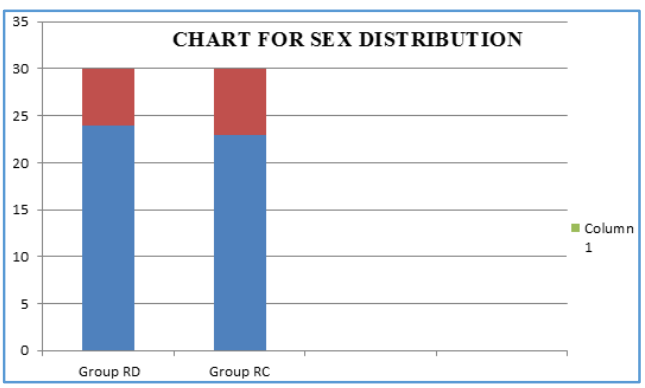

Figure 1. Chart for Sex Distribution of both Study Groups

There is a significant difference in the block characteristics between the two groups.

The onset and duration of sensory blockade was found to be earlier and prolonged respectively in Group RD than in Group RC, which was statistically significant. Thus, Dexmedetomidine provided early onset and prolonged duration of sensory blockade which was statistically significant [Table 2].

Particulars	Group RD (Mean ± SD)	Group RC (Mean ± SD)	P value	Significant
Time of onset of sensory blockade at shin of tibia (second)	240.66 ± 97.90	400.33 ± 64.88	0.0001	Highly Significant
Sensory block at T_{10} level (second)	525.66 ± 90.57	615 ± 97.21	0.0005	Highly Significant
Time to two segment dermatomal regression (minutes)	137.16 ± 12.88	126.76 ± 12.44	0.0022	Significant

Table 2. Comparison of Sensory Blockade of both Study Groups

We found significant difference between the two groups in terms of onset of motor blockade [Table 3].

Particulars (min)	Group RD (Mean± SD)	Group RC (Mean± SD)	P value	Significant
Time of onset of motor blockade (modified Bromage 1 in seconds)	522 ± 156.38	603.33 ± 125.14	0.0300	Significant
Time to complete motor blockade (modified Bromage 3 in minutes)	23.76 ± 4.56	26.70 ± 5.81	0.0333	Significant

Table 3. Comparison of Motor Blockade of both Study Groups

Though there was significant decrease in Heart rate [Figure 2] by approximately 20% between 30 and 45 minutes of epidural injection in both groups, there was no significant difference in the fall in Heart rate between two groups (P>0.05).

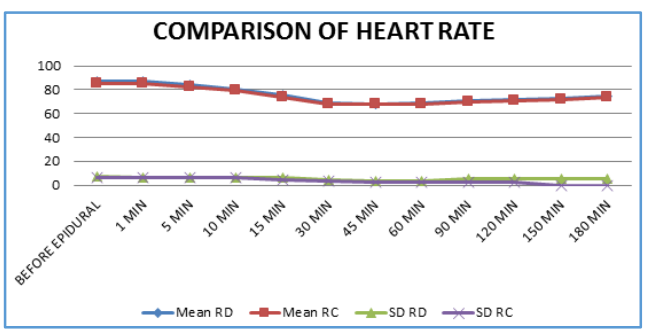

Figure 2. Comparison of Heart Rate in both Study Groups over Time

We also found significant fall in mean arterial pressure [Figure 3] by approximately 15% between 30 and 45 min. in both groups, however, there was no significant difference in the occurrence of hypotension between the two groups (P > 0.05).

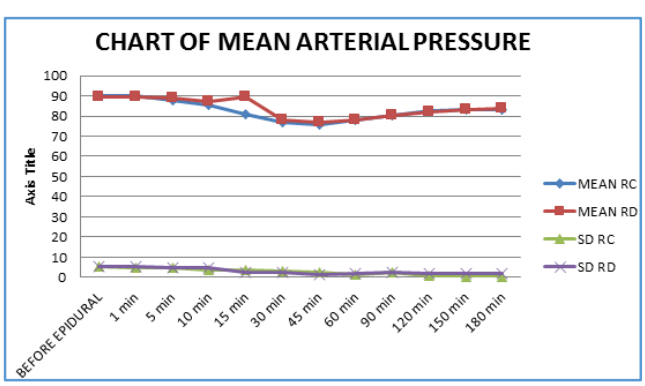

Figure 3. Comparison of Mean Arterial Pressure of both Study Groups over Time

Dexmedetomidine provided a smooth and prolonged post-operative analgesia as compared to clonidine [Table 4].

Particulars	Group RD Mean ± SD	Group RC Mean ± SD	P value	Significant
First feeling of pain (min.)	344 ± 24.94	311 ± 28.20	0.0001	Highly Significant

Table 4. Comparison of Total Duration of Analgesia of both Study Groups

The comparative incidence of various side effects in both the groups were observed in the intra-op and post-op period. There was slight higher incidence of nausea in both groups, but statistically non-significant. The incidence of other side effects like dry mouth, 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.

DISCUSSION

Epidural anaesthesia is considered as a gold standard technique as it provides complete and dynamic anaesthesia. The benefits include suppression of stress response by sympatholysis, stable haemodynamics with reduction in cardiac morbidity, reduction in pulmonary complications due to active physiotherapy and early mobilisation, reduced blood loss and decrease in thromboembolic complications following surgery.[16]

The addition of adjuvants like α_2-agonists provide[17] the rapid establishment of both sensory and motor blockade, prolonged duration of analgesia into the post-operative period, dose-sparing action of local anaesthetics and stable cardiovascular parameters make these agents a very effective adjuvant in regional anaesthesia.[18-22]

Motor blockade tends to be denser with α2-agonists. It is also devoid of respiratory depression, pruritus, nausea and vomiting.[23]

The present study was undertaken to evaluate the effect of Dexmedetomidine and Clonidine as an adjuvant to epidural Ropivacaine in patients undergoing lower abdominal and lower limb surgeries.

Patients were randomly divided in two groups according to inclusion criteria and they received drugs epidurally according to their groups.

In our study, mean age, weight, sex distribution and duration of surgery, haemodynamic parameters were comparable among both the groups (P>0.05).

In the present study, sensory block was assessed by pin-prick method. The onset of sensory blockade at shin of tibia was found to be earlier in Group RD (240.66 ± 97.90 seconds) than in Group RC (400 ± 64.88 seconds) which was statistically highly significant (P<0.001).

The onset of sensory blockade at T_{10} was found to be earlier in Group RD (525.66 ± 90.5 seconds) than in Group RC (615 ± 97.21 seconds) which was statistically highly significant (P<0.001). This finding was consistent with the previous observations made by Bajwa et al, who found that the onset of sensory analgesia at T10 was faster in the group receiving Dexmedetomidine (8.52 ± 2.36 min.) when compared with patients receiving Clonidine (9.72 ± 3.44 min.) and this was also associated with a faster and higher level of sensory blockade.

In study done by Sruthi Arunkumar, VR Hemanth Kumar et al[24] also showed significantly earlier onset of sensory

blockade in patients receiving Dexmedetomidine (8.53 ± 1.81 min.) when compared to the patients receiving Clonidine (11.93 ± 1.96 min.), which supported our findings.

The mean time for two segment regression was significantly prolonged (P<0.05) in Group RD (137.16 ± 12.88 min.) as compared to Group RC (126.76 ± 12.44 min.). Thus, time for two segment regression was markedly prolonged when Dexmedetomidine was used as an adjuvant. This finding was consistent with the previous observations made by Bajwa et al, who found that time for two segment regression was more in the groups receiving Dexmedetomidine (136.46 ± 8.12 min.) when compared with groups receiving Clonidine (128.08 ± 7.54 min.).

Motor block was assessed by modified Bromage scale. In our study, time of onset of motor blockade (Modified Bromage Scale 1) was 522 ± 156.38 seconds in Group RD while 603.33 ± 125.14 seconds in Group RC. Time of complete motor blockade (Modified Bromage Scale 3) was earlier in Group RD which was 23.76 ± 4.56 minutes as compared to 26.70 ± 5.81 minutes in Group RC. So, the differences in onset of complete motor blockade between the groups were statistically significant (P<0.05). Our finding is consistent with previous observations done by Bajwa et al, who 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 min.) as an adjuvant.

A study done by Sruthi Arunkumar, V. R Hemanth Kumar et al[24] 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. This may be attributed to the lower doses of Clonidine (1 µg/kg) used in their study.

We observed decrease in heart rate from baseline to end of surgery in both the groups but there was significant fall approximately by 20% in 30 - 45 minutes after epidural injection in both the groups. However, there was no significant difference in fall in heart rate between two groups (p>0.05). There was significant fall in mean arterial pressure approximately by 15% in 30-45 min. after epidural injection. However this change was not statistically significant between two groups (P> 0.05).

Sruthi Arunkumar, V.R Hemanth Kumar et al [24] in their study, found that the heart rate 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) between both groups receiving Dexmedetomidine and Clonidine respectively, which correlates with our finding.

Similar observations were observed by Bajwa et al, where there was a 15% fall of heart rate and blood pressure from the baseline, which was statistically not significant between both groups receiving Dexmedetomidine and Clonidine.

The difference in total duration of analgesia was highly significant between the two groups (P<0.001). Thus postoperative analgesia (Time for first feeling of pain) was significantly prolonged in Group RD (344 ± 24.94 min.) when Dexmedetomidine was used as an additive with Ropivacaine as compared to Group RC (311 ± 28.20 min.) where Clonidine was used. This was found to be consistent with the study done by Bajwa et al 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.).

Sruthi Arunkumar, V. R. Hemanth Kumar et al[24] in their study they found that the duration of sensory analgesia was more in group RD (316 ± 31.15 min.) than group RC (281 ± 37 min.). This may be because of lower doses of Clonidine (1 µg/kg) may be considered to explain the shorter duration in comparison to our study.

There was higher incidence of nausea in both groups but not statistically significant. No complications like dry mouth, vomiting, bradycardia, hypotension, shivering, respiratory depression, headache, dizziness, urinary retention found during intraoperative or postoperative period among both groups.

Sruthi Arunkumar, V.R Hemanth Kumar et al[24] in their study, had two patients in group RC and one patient in group RD who had dry mouth.

The study conducted by Bajwa et al showed a higher incidence of nausea and dry mouth during the postoperative period.

CONCLUSION

From this study, we concluded that Dexmedetomidine may be a useful alternative to Clonidine as an adjuvant to epidural Ropivacaine because of its early onset and long duration of sensory and motor blockage, longer post-op analgesic effects.

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