Original Research Article

A Comparative Study of α2- Agonists as an Adjuvant to Ropivacaine in Epidural Anesthesia for Infraumblical Surgeries

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Abstract

Background: Alpha-2 agonist are being extensively evaluated as an alternative to neuraxial opoids, as an adjuvants in regional anaesthesia The faster onset of action of local anaesthetics, rapid establishment of both sensory and motor blockade, prolonged duration of analgesia into postoperative period, dose sparing action of local anaesthetics and stable cardiovascular parameters make these agents a very effective adjuvant in regional anaesthesia. The aim of our study is to compare the efficacy of two α2- adrenergic agonists, dexmedetomidine and clonidine when used as an adjuvant to ropivacaine in epidural anesthesia for infraumblical surgeries. **Materials & Methods:** In our study we included 50 patients, of ASA Grade-I or II, between 20- 65 years of age requiring neuraxial blockade for infraumblical surgeries. All the patients were randomly allocated into two groups of 25 each. Group-C: received 15 ml of 0.75% epidural ropivacaine with clonidine 1µg/kg Group-D: received 15 ml of 0.75% epidural ropivacaine with dexmedetomidine 1µg/kg. Patients were monitored for onset of sensory and motor blockade, time to 2 dermatome regression of sensory level, time to first demand for rescue analgesia, sedation, hemodynamic parameters and adverse effects in perioperative period. **Results:** The onset of sensory block (Group D-8.55 ± 2.81 min, Group C- 12.99 ± 2.96 min), duration of sensory blockade (Group D- 326 ± 35.15 and Group C- 261 ± 36.15) and sedation were found to be significantly better in the dexmedetomidine group. No significant difference was found in terms of onset of motor blockade and hemodynamic changes. **Conclusion:** Dexmedetomidine is a better neuraxial adjuvant compared to clonidine for providing early onset of sensory analgesia, adequate sedation and a prolonged post-operative analgesia.

Key words: Clonidine, dexmedetomidine, epidural, ropivacaine

Introduction

Acute postoperative pain management is a key aspect of postoperative care as it affects the perioperative morbidity and mortality. Effective control of per operative pain blunt autonomic, somatic and endocrine stress responses to surgery with resultant potential for decrease in per operative morbidity and mortality.[1]

Epidural anesthesia is one of the most useful and versatile procedures in modern anesthesiology, used both for providing anesthesia and postoperative analgesia. It contributes to intra operative hemodynamic stability and has shown to reduce perioperative stress response thereby causing a decrease in perioperative complications and improving patient outcome. It helps in early mobilization by relieving postoperative pain, which decreases the incidence of thromboembolic events.[2-4]

Epidural bupivacaine has been used since long but it is highly cardio toxic. Recently ropivacaine became better alternative in choice of LA, due to long duration of action and less cardiovascular effects. However, the negative inotropic potency of ropivacaine on isolated cardiac tissue appears to be considerably less cardio toxic than that of bupivacaine.[5- 7]

Addition of adjuvants to LA faster onset of motor and sensory block, prolong duration of action and postoperative analgesia with lower consumption of local anaesthetic. In recent years, as an adjuvants in regional anaesthesia α-2 agonists are being extensively evaluated as an alternative to neuraxial opioids, which are associated with certain side effects like pruritus, urinary retention, nausea and vomiting.[8]

Epidural administration of α-2 agonists is associated with anxiolysis, sedation, hypnosis, analgesia and sympatholysis. α-2 agonists directly stimulates pre- and postsynaptic α -2 adrenoceptors in the dorsal horn grey matter of the spinal cord and provide pain relief by an opioid independent mechanism by inhibiting the release of nociceptive neurotransmitters. The faster onset of action of local anesthetics, rapid establishment of both sensory and motor blockade, prolonged duration of analgesia into postoperative period, dose sparing action of local anesthetics and stable cardiovascular parameters make these agents a very effective adjuvant in regional anaesthesia.[9- 14]

Clonidine is an alpha-2 adrenergic agonist that has ability to potentiate the effects of local anaesthetics and has been used as an adjuvant to epidural local anaesthetics to improve the quality of postoperative analgesia after major abdominal surgeries.[15]

Compared to clonidine, dexmedetomidine is highly selective alpha-2 agonist with an affinity of eight times greater than clonidine, has shorter duration and has a reversal drug for its sedative effect, atipamezole. These properties render dexmedetomidine suitable for sedation and analgesia, as premedication, as an anaesthetic adjunct for general and regional anaesthesia, and as postoperative sedative and analgesic.[16- 19]

The anaesthetic and analgesic requirement gets reduced to a huge extent by use of these drugs because of their analgesic property and augmentation of local anaesthetic effects.[20- 21] The aim of our study was to compare effect of dexmedetomidine and clonidine as an adjuvant to ropivacaine for infraumblical surgeries in epidural anesthesia.

Materials & Methods

After approval from institutional ethical committee and informed written consent from patients and their legal guardians, this prospective randomized double blind study was conducted on 50 patients belonging to ASA grade I and II, aged between 20- 65 years scheduled for elective infraumbilical surgeries and randomly divided into two groups comprising 25 patients in each group by using envelope method.

Group C- received 15 ml of 0.75% epidural ropivacaine + clonidine 1µg/kg

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Group D- received 15 ml of 0.75% epidural ropivacaine + dexmedetomidine 1µg/kg. Blinding was achieved by making total volume to 16 ml in both groups.

Patients with bleeding or coagulation abnormalities, psychiatric diseases, history of drug abuse and allergy to local anaesthetics, any local sepsis or deformity of spinal lumber region and patient's refusal were excluded from study.

After arrival in operating room, routine monitoring including continuous ECG, NIBP and SpO2 were attached and baseline vital parameters were recorded prior to epidural block. Intravenous (IV) access was secured with 18G cannula and Ringer lactate solution was started at a maintenance rate of 5ml/kg/hour. Routine general anaesthesia equipments and anaesthesia work station, breathing circuits, laryngoscope, endotracheal tubes, oxygen mask, drugs required for general anaesthesia and emergency drugs were kept ready as per protocol.

Under all aseptic precautions, epidural block performed at T12- L1 space with 18G Touhy's epidural needle (Epi kit system 1) in sitting position. The epidural space identified by loss of resistance technique with LOR syringe and catheter secured into epidural space. Epidural test dose given with 3ml of 2% lignocaine containing adrenaline 1:2,00,000 to rule out Intrathecal or intravascular access. 5minutes after test dose 16 ml of the study drug was administered epidurally as per randomization.

After drug administration following parameters were accessed:

Onset of sensory block: was assessed by pinprick test using 22G hypodermic needle after completion of injection till complete loss to pinprick sensation at T10 dermatome, and it was assessed every 15 min after 2 h of epidural bolus injection till 2 dermatome regression of sensory level was observed. The grading of pin-prick test was done as score 0=normal sensation, 1= Blunted sensation and 2= absence of sensation.

Motor blockade: assessed by using modified Bromage scale every 5mins after completion of epidural injection till a block of grade 3 motor blockade was achieved, then every 1hr interval up to 6-8 hrs post-operatively.[Table 1]

Table 1 Modified Bromage scale

Modified Bromage scale	
0	No block
1	Inability to raise extended legs
2	Inability to flex legs
3	Inability to flex ankle and foot

Onset of sensory analgesia was defined as the time taken to achieve loss of pinprick sensation at T10 dermatome level from the end of epidural injection of the study drug.

Duration of analgesia was defined as the time taken from the onset of sensory block at T10 to administration of first rescue analgesic dose to the patient. Duration of analgesia was recorded using VAS (visual analogue score) estimated on 0-10 cm scale after completion of surgery at time interval of 15mins,30mins,60mins and then every 1hrs interval up to 6-8 hrs postoperatively. Rescue analgesia with injection tramadol 100mg IV was administered by nursing staff whenever VAS score of ≥ 3 was recorded any time during the observation period of 6-8 hrs postoperatively.

The level of sedation was assessed 10 min after grade 3 motor blockade and at the end of surgery based on the Ramsay sedation scale.

Hemodynamic parameters were monitored every 5 min for the first 30 min, every 10 min thereafter till the end of surgery. Hypotension defined as fall in systolic BP by >20% of baseline and treated with injection mephentermine in titrated boluses. Bradycardia defined as HR<55bpm or fall below 20% of baseline and treated with injection atropine 0.6 mg. IV fluid was given as per body weight and operative loss requirement. Any side-effects seen after administration of study drug was noted and treated appropriately.

The data were analyzed using SPSS version 19 and Microsoft Excel 2011 (IBM). The following statistical tests were used for analysis. Demographic data: ANOVAs test, onset of sensory block and motor block: Unpaired Student's t-test, sedation: Chi-square test, hemodynamic variation: Unpaired Student's t-test, complications: Chi-square test.

Results

The two groups were comparable with respect to demographic characteristics (age, gender distribution, height and weight), type and the duration of surgery with no significant difference between the two groups. [Table 2]. Both groups had patients undergoing abdominal and vaginal hysterectomies, hernioplasty, and lower limb surgeries.

Table 2 Demographic parameters and duration of surgery

Parameters	**Group- C** (Mean ± SD)	**Group- D** (Mean ± SD)	P- value
Age (years)	38.60±9.5	40.10±8.0	>0.05
Gender (male:female)	15:10	18:17	>0.05
Height (in cm)	155.30±6.55	155.63±5.53	>0.05
Weight (in kg)	55±8.10	57.50±6.96	>0.05
Mean duration of surgery (mins)	98.33±35.64	95.33±38.99	>0.05

We found significant difference in onset of sensory block at T10, with earlier onset of sensory block in the patients receiving dexmedetomidine (8.55 ± 2.81 min) compared to the patients receiving clonidine (12.99 ± 2.96 min). [Table 3]

Table 3 Block parameters and sedation score

Parameters	**Group- C** (Mean ± SD)	**Group- D** (Mean ± SD)	P- value
onset of sensory block (min)	12.99 ± 2.96	8.55 ± 2.81	<0.05
onset of motor blockade (min)	22.27 ± 4.63	22.30 ± 4.37	<0.05
duration of sensory analgesia (min)	261 ± 36.15	326 ± 35.15	<0.05
Sedation Score grade-3(%)	13.3	46.6	<0.05

We found no statistically significant difference between the two groups in terms of onset of motor blockade (grade-3). Time to complete motor blockade in Group D was 22.30 ± 4.37 min and Group C was 22.27 ± 4.63 min. [Table 3]

In this study, we found that the duration of sensory analgesia was more in group D (326 ± 35.15 min) than group C (261 ± 36.15 min). [Table 3]

We found significantly better sedation in the patients who received dexmedetomidine than those who received clonidine, with profound sedation in 46.6% patients who were arousable by gentle tactile stimulation (grade-3) compared to 13.3% in clonidine group and statistically this difference was found to be significant (p<0.05). [Table 3]

After 30 and 50 min of epidural injection there was a significant fall in HR and mean arterial pressure by 20- 25% in both groups; however there was no significant difference in the fall of HR and mean arterial pressure between the two groups (P = 0.592). We found no significant difference in the atropine and mephentermine requirement in both the groups.

Discussion

Epidural anesthesia is a gold standard technique as it provides complete and dynamic anesthesia. The benefits of epidural anesthesia include suppression of stress response by sympatholysis, stable hemodynamics with reduction in cardiac morbidity, reduction in pulmonary complications due to active physiotherapy and early mobilization, reduced blood loss and decrease in thromboembolic complications following surgery.[22- 24]

With emphasis on opioid-related side effects such as respiratory depression, nausea, urinary retention and pruritis, α-2 agonists are being extensively evaluated as an alternative to epidural local anesthetics.[8, 25-26] α-2 agonists have been extensively studied and employed clinically to achieve the desired effects in regional anaesthesia.[9, 10,18,27] Clonidine has been used successfully over the last decade for the said purpose and the introduction of dexmedetomidine has further widened the scope of α-2 agonists in regional anaesthesia.[16,28]

The present study was undertaken to compare the analgesic efficacy, peri-operative and post-operative, as well as sedation effects of α-2 agonists. The demographic profile was comparable with respect to mean age, body weight, height, gender distribution, type and duration of surgery.

Our study showed significantly earlier onset of sensory blockade in the patients receiving dexmedetomidine (8.55 ± 2.81 min) when compared to the patients receiving clonidine (12.99 ± 2.96 min). Our this finding was consistent with 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 to the patients receiving clonidine (9.72 ± 3.44 min).[17]

We found no statistically significant time to complete motor blockade between the two groups, Group D in 22.30 ± 4.37 min and Group C in 22.27 ± 4.63 min. Bajwa et al. 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) as an adjuvant. This may be attributed to the larger doses of dexmedetomidine (1.5 µg/kg) and clonidine (2 µg/kg) used in their study.[17]

In our study, we found that the duration of sensory analgesia was more in Group D (326 ± 35.15 min) than Group C (261 ± 36.15 min). 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).[17]

We found significantly better sedation in the patients who received dexmedetomidine than those who received clonidine. Our study results are consistent with Bajwa et al and Oriol-Lopez et al. They showed a significantly higher level of sedation in the patients who received dexmedetomidine in comparison to clonidine.[17, 19]

We found that the HR 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). Similar observations were observed by Bajwa et al. and Schnaider et al. where a 15% fall of HR and blood pressure from the baseline which was not statistically significant. We observed similar hemodynamic changes in both the study groups.[17,29]

Conclusion

Based on the results and methodology employed, our study concluded that dexmedetomidine is an effective adjuvant to ropivacaine for epidural anesthesia compared to clonidine in a dose of 1 µg/kg, as dexmedetomidine provides faster onset, prolonged duration of action with better sedation.

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