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Original Research Article

A Randomized Comparative Evaluation of Dexmedetomidine and Clonidine as an Adjuvant to 0.5% Bupivacaine in Epidural Anaesthesia for Lower Limb Orthopaedic Surgeries

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Abstract

Background and Aims: Alpha-2 adrenergic receptor agonists like dexmedetomidine and clonidine are used as an adjuvant to local anaesthetic agents in epidural anaesthesia. The aim of our study was to compare the effect of adding dexmedetomidine and clonidine as an adjuvant to bupivacaine in epidural anaesthesia on the onset and duration of sensory and motor block and their safety profile in lower limb orthopaedic surgeries.

Methods: This prospective randomized study included 100 patients aged 18-60 years of American Society of Anaesthesiologists physical status I/II scheduled for elective lower limb orthopaedic procedures. Written informed consent was taken from all the patients. Patients were randomly divided into two groups of 50 patients each. Group A patients received 15 ml of 0.5% bupivacaine plus 1 µg/kg of dexmedetomidine while the patients in Group B were given 15 ml of 0.5% bupivacaine plus 2 µg/kg of clonidine through epidural catheter. **Results:** Patients in dexmedetomidine group had significantly earlier onset of sensory block to T10 dermatome, highest level of sensory block and time for complete motor block was also significantly less when compared to the clonidine group. The dexmedetomidine group showed superiority over clonidine group in postoperative block characteristics like the weaning of sensory and motor block, postoperative analgesia. Sedation scores were also better in patients receiving dexmedetomidine as adjuvant. The incidence of side-effects like nausea, vomiting, dry mouth, shivering were comparable in both the groups and statistically non-significant.

Conclusion: Dexmedetomidine is a better adjuvant to local anaesthetic agent than clonidine for epidural anaesthesia and analgesia as it results in early onset and establishment of sensory and motor block, prolonged postoperative analgesia and better sedation.

Keywords: clonidine, dexmedetomidine, adjuvant, bupivacaine, epidural,

Introduction

Epidural anaesthesia is commonly used for lower limb orthopaedic surgeries. It can be extended as per the duration of the surgery and it can also be used to provide postoperative analgesia. By reducing the incidence and severity of perioperative physiologic perturbations and postoperative morbidity it results in improved patient satisfaction and perioperative outcomes. [1,2,3] Many adjuvants to local anaesthetic agents has been used in epidural anaesthesia to improve its efficacy and decrease the incidence of adverse effects. Opioids are commonly used as adjuvants in epidural anaesthesia. However, side effects such as pruritus, nausea, vomiting, urinary retention, and delayed respiratory depression associated with epidural opioids have prompted further research towards non-opioid adjuvants with better safety profile. [4,5,6] Alpha-2 adrenergic receptor agonists don't have the side effects of epidural opioids and have been used as adjuvants in epidural anaesthesia. They have analgesic, sedative, peri-operative sympatholytic and cardiovascular stabilizing effects and exhibit synergism with local anaesthetics. [6,7,8]

Clonidine is a selective partial α2-adrenergic agonist with α2:α1-activity being 220:1. Dexmedetomidine is about 8 times more selective towards the α 2 adrenoreceptor than clonidine with α2:α1-activity being 1620:1, thus reducing the unwanted side effects involving α-1 receptors. [9,10,11,12] The primary mechanism of action of epidural α-2 adrenergic receptor agonists is believed to be at the level of spinal cord. This includes pre- and postsynaptic sites of action. Presynaptically, α2-receptor activation inhibits release of substance P from afferent "C" fibers within dorsal horn. Postsynaptically, it inhibits the development and subsequent transmission of integrated pain signals within second-order neurons of the substantia gelatinosa. [8,9,13,14]

The aim of our study was to compare the effect of adding dexmedetomidine and clonidine as an adjuvant to bupivacaine in epidural anaesthesia on the onset and duration of sensory and motor block and their safety profile in patients undergoing lower limb orthopaedic surgeries.

Methods

This prospective randomized study was conducted at a tertiary healthcare institute from February 2022 to November 2022 after obtaining approval from the institutional ethical committee. 100 patients aged 18-60 years of American Society of Anaesthesiologists physical status I/II scheduled for elective lower limb orthopaedic surgeries were enrolled in this study. Written informed consent was taken from all the patients.

The patients with heart blocks, significant bradyarrthymias, left ventricular failure, bleeding or coagulation disorders, history of drug abuse, allergy to local anaesthetic agents and pregnant and lactating women were excluded from the study. Patients were randomly assigned to one of the two groups of 50 patients each in a double blinded fashion using a computer generated list.

All patients were kept fasting eight hours prior to surgery and tablet alprazolam 0.25 mg was given night before surgery. In the operation theatre, a multiparameter monitor was attached and baseline parameters like heart rate (HR), non-invasive blood pressure (NIBP) and arterial oxygen saturation by pulse oximeter (Sp02) were recorded and electrocardiograph (ECG) monitoring done. An intravenous (IV) access was secured with appropriate size IV cannula. Lumbar epidural space was located using loss of resistance technique to normal saline in lateral decubitus position with 18-gauge Tuohy epidural needle -

Portex Continuous Epidural (Smith Med. Inc.) and epidural catheter was secured 4-5 cm into the epidural space. 3 ml of 2% lignocaine hydrochloride solution with adrenaline 1:200,000 was injected through epidural catheter as test dose to rule out intrathecal or intravascular placement. Group A (n- 50) patients were given 15 ml of 0.5% bupivacaine plus 1 µg/kg of dexmedetomidine while the patients in Group B (n-50) were given 15 ml of 0.5% bupivacaine and 2 µg/kg of clonidine through epidural catheter. This time of epidural drug injection was taken as time zero. Intravenous fluids were administered according to patient's body weight and duration of surgery and blood loss. The anaesthesiologist doing the procedure was unaware of the epidural drug combination being administered. The sensory level achieved was assessed by response to blunt tip pin-prick and the motor blockade was assessed by modified 'Bromage scale' (Grade 0 - No motor block, Grade 1 - Inability to raise extended leg, able to move knees and feet , Grade 2 - Inability to raise extended leg and move knees; able to move feet and Grade 3 - Complete motor block of lower limb). This was assessed at every 5 minutes for 30 minutes. After 25-30 minutes of administration of epidural drugs, effectiveness of sensory and motor block was assessed and the patient was positioned for surgery. The following variables were observed and recorded: time taken for the sensory block to reach T10 dermatome, the highest dermatomal level of sensory block reached, time to reach the highest dermatomal level of sensory block, time taken for establishment of complete motor blockade (Bromage 3), time for two dermatome regression of sensory block, time for regression to Bromage 1, time for regression of sensory block level to S1 dermatome.

Sedation level was assessed by a five-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 and recorded just before the start of surgery and then at 20 minutes interval during the surgery.

Systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), heart rate (HR), oxygen saturation by pulse oximeter (SpO2) and respiratory rate (RR) were monitored continuously and recorded at every 5 minutes for first 30 minutes, at 10 minutes interval till the end of surgery. A 20% fall in systolic blood pressure from baseline or systolic blood pressure less than 90 mm of Hg was considered as hypotension and treated with IV injection of 6 mg mephentermine and repeated if required. Heart rate <50 beats/minute was treated with IV injection of 0.6 mg atropine. Any adverse events like anxiety, nausea, vomiting, pruritis, shivering, dry mouth, respiratory depression during intraoperative and post operative period were recorded. Nausea and vomiting were treated with 0.1 mg/kg of IV ondansetron. Vital parameters were recorded in post-anaesthesia care unit (PACU) at 1, 5, 10, 20 and 30 minutes.

Pain was assessed in PACU by Visual analog scale (VAS), every 30 min postoperatively in which '0' represented no pain and '10' represented worst possible pain. Patients complaining of pain (VAS score >4) in PACU were given epidural top-up for analgesia. Epidural catheter was removed before shifting the patients out of PACU.

Statistical analysis

Sample size was determined taking into consideration that a sample size of 50 patients per group was required to produce a difference of 35% between the two groups for the duration of analgesia and would give a power of 80% and Type I error (α) of 0.05. Unpaired Student's t-test and Chi-square test was used to analyze the compiled data. Statistical Package for Social Science (SPSS) Version 20.0 (IBM SPSS Statistics)

was used to compare the continuous variables between the two groups. Data are expressed as mean ± standard deviation. P value < 0.05 was considered to be statistically significant.

Results

The demographic variables of the patients in both the groups and mean duration of surgery were comparable. The difference was not significant statistically (P>0.05); [Table 1].

Table 1: The Demographic profile of patients and Mean duration of surgery

Demographic variables	Group A	Group B	P value
Sex (Female/Male)	20/30	22/28	0.7576
Age (in years)	35.17	33.87	0.3440
Weight (in kgs)	56.73	58.93	0.2850
Height (in cms)	164.33	165.30	0.2890
BMI	21.02	20.83	0.8426
ASA I/II	44/6	45/5	0.6875
Mean duration of surgery (in minutes)	111.83	112.67	0.8739

The mean time to achieve the T10 dermatomal level of sensory block in group A (Dexmedetomidine) was 8.70 ± 1.12 minutes while in group B (clonidine) was 11.23 ± 1.38 minutes. So adding dexmedetomidine to bupivacaine as adjuvant in epidural anaesthesia led to significantly earlier onset of T10 sensory block when compared to clonidine (P = 0.00001). The highest dermatomal level of sensory block achieved in group A was T 6-7 and in group B was T 7-8. Mean time to attain highest level of sensory block was 12.87 ± 1.04 minutes in group A and 17.13 ± 1.55 minutes in group B, a statistically significant difference (P = 0.00001). Complete motor block was achieved in 19.30 ± 1.62 minutes in group A and in 24.87 ± 1.55 minutes in group B, again a statistically significant difference with P =0.00001. Dexmedetomidine as an adjuvant to bupivacaine in epidural anaesthesia resulted in better initial block characteristics than clonidine [Table -2, Figure-1].

Table 2: Comparison of initial block characteristics

Variables	Group	Mean	SD	P value
Onset time of sensory block at T10 (in minutes)	Group A	8.70	1.12	0.00001
	Group B	11.23	1.38	
Highest dermatomal level of sensory block	Group A	T 6-7		
	Group B	T 7-8		
Time to highest sensory block (in minutes)	Group A	12.87	1.04	0.00001
	Group B	17.13	1.55	
Time for complete motor block (in minutes)	Group A	19.30	1.62	0.00001
	Group B	24.87	1.55	
Mean total dose of Mephentermine required (in mg)	Group A	12		1.0000
	Group B	12		

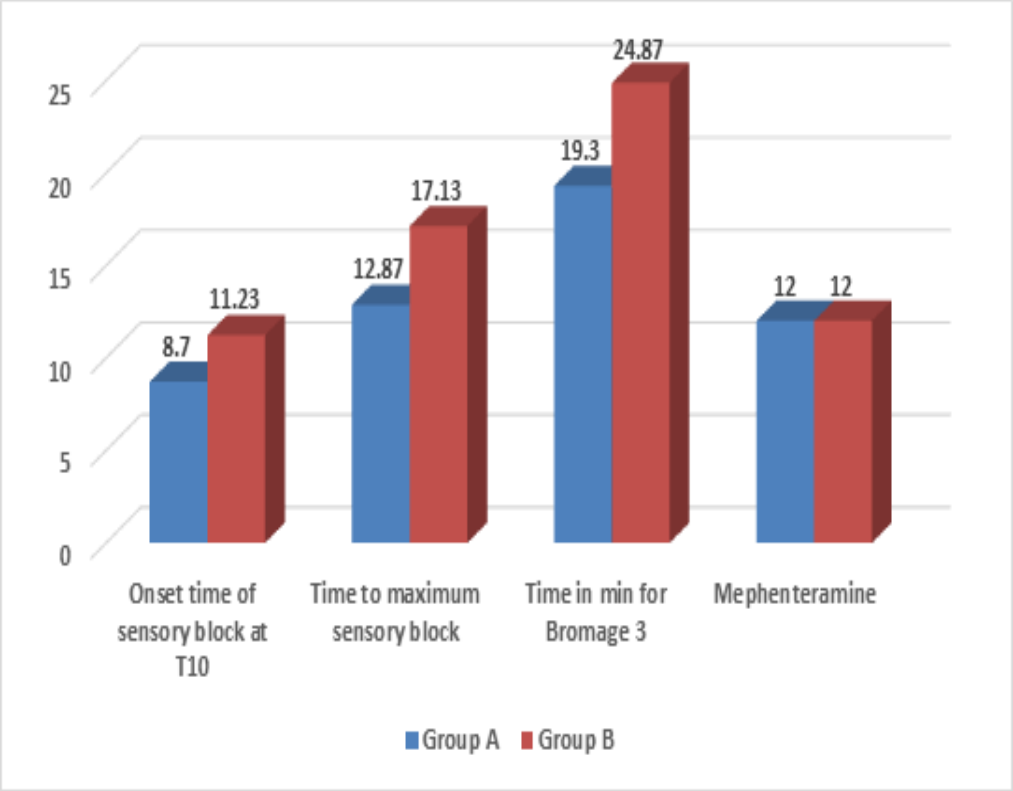

Figure 1: Comparison of initial block characteristics

All postoperative block characteristics like mean time for two dermatomal sensory regression, regression of motor blockade to Bromage 1 and sensory level regression to S1 dermatome, were found to be significantly more in dexmedetomidine group A when compared to clonidine group B (P = 0.00001,0.00001 and 0.0034 respectively). These are desirable properties of an adjuvant to local anaesthetic to be used in epidural anaesthesia and analgesia. Time to demand for rescue analgesia was also significantly more in group A (dexmedetomidine) as compared to group B (clonidine) (P=0.00001). [Table-3, Figure-2].

Table 3: Comparison of postoperative block characteristics

Variable	Group	Mean±SD	P value
Mean time (in minutes) for sensory regression of two dermatome	Group A	136.00 ±6.86	0.00001
	Group B	124.97 ±6.65	
Mean time (in minutes) for regression to Bromage 1	Group A	240.93 ±16.54	0.00001
	Group B	160.17 ±27.58	
Mean time (in minutes) for sensory regression to S1	Group A	314.17 ±18.87	0.0034
	Group B	298.73 ±20.68	
Time to first rescue analgesia	Group A	342.97 ±18.03	0.00001
	Group B	307.97 ±22.54	

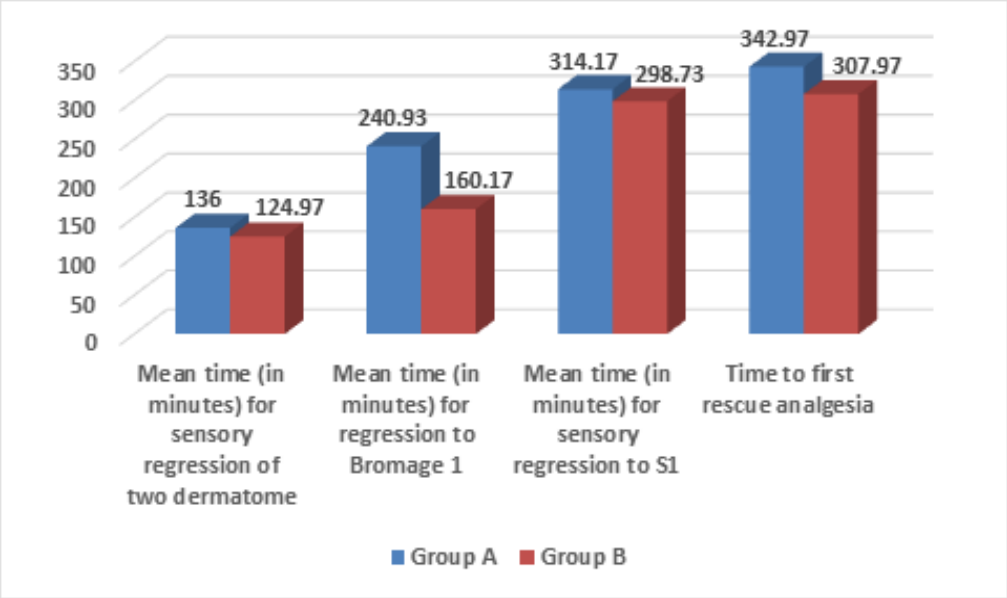

Figure 2: Comparison of postoperative block characteristics

The incidence of side-effects like nausea, vomiting, dry mouth were comparable in both the groups and statistically non-significant (P > 0.05). The difference in incidence of nausea (four patients in Group A and three patients in Group B) and dry mouth (six patients in Group A and seven patients in Group B) were statistically non-significant (P >0.05). Shivering was seen in one patient in group A while two patients in group B had shivering. Significantly higher sedation scores were seen in dexmedetomidine group. Respiratory depression and pruritis were not seen in any patient.

Discussion

Various adjuvants to local anaesthetic agents have been used to add on to the benefits of epidural anaesthesia and make it more beneficial for the patients. Alpha-2 adrenergic receptor agonists like dexmedetomidine and clonidine when used as an adjuvant to local anaesthetic agent enhances the efficacy of epidural anaesthesia and at the same time avoids many unwanted side effects of epidural opioids. [6,7,8] In our study we compared the efficacy of dexmedetomidine and clonidine as an adjuvant to bupivacaine in epidural anaesthesia.

Salgado PF et al [15], demonstrated synergism between epidural dexmedet - omidine and ropivacaine. Patients in dexmedetomidine group in our study had significantly earlier onset of sensory block to T10 dermatome, highest level of sensory block and time for complete motor block was also significantly less when compared to the clonidine group. Similar results were seen by Bajwa et al [16] in their study in patients undergoing vaginal hysterectomy. Arunkumar S et al [17] in their study comparing epidural dexmedetomidine and clonidine as an adjuvant to ropivacaine in lower abdominal and lower limb surgeries also found dexmedetomidine to be better adjuvant in terms of block characteristics. Superiority of dexmedetomidine over clonidine as an adjuvant to local anaesthetic in epidural anaesthesia was also established by Agarwal S et al [18] and Shaikh SI [19] in their studies. Unlike our study Bajwa et al [16] found that dexmedetomidine provided a significantly higher dermatomal spread compared to clonidine when used as an adjuvant to epidural ropivacaine. This was probably due to lower dose of dexmedetomidine (1 µg/kg) used in our study.

The dexmedetomidine group in our study showed superiority over clonidine group in

postoperative block characteristics like the weaning of sensory and motor block, postoperative analgesia. Similar to our findings, Bajwa et al [16] found significant prolongation of time to two segment dermatomal regression and regression to Bromage 1 in dexmedetomidine group when compared to clonidine group. Arunkumar S et al [17], Agarwal S et al [18] and Shaikh SI [19] also found these postoperative block characteristics to be better in dexmedetomidine group when compared to clonidine group. Saravana Babu et al [20] found epidural dexmedetomidine used as adjuvant to ropivacaine provided early onset and prolonged analgesia in spine surgeries when compared to clonidine used as an adjuvant. On the contrary Vieira AM et al [21] concluded that clonidine used as adjuvant to ropivacaine in epidural block provided more prolonged analgesia in post cholecystectomy patients when compared to dexmedetomidine. El-Hennawy AM et al[22] also found that dexmedetomidine did not offer significant advantage over clonidine for analgesia duration when used as an adjuvant to bupivacaine in caudal analgesia

Significantly higher sedation scores were seen in dexmedetomidine group in our study. Similar results were seen in studies done by Bajwa et al [16], Arunkumar S et al [17] and Agarwal S et al [18].

The incidence of side-effects like nausea, vomiting, dry mouth, shivering were comparable in both the groups and statistically non-significant. Similar to this study, Bajwa et al [16] and El-Hennawy et al [22] also found the incidence side-effects to be statistically non-significant on comparison. A comparative study of the adverse events associated with adjuvant use of dexmedetomidine and clonidine in local anesthesia done by Jinjin Jiang et al [23] found no significant effect on adverse events.

Conclusion

Dexmedetomidine used as an adjuvant to epidural bupivacaine leads to early onset and establishment of sensory and motor block, prolonged postoperative analgesia and better sedation when compared to clonidine. Based on these results of our study and corroborative evidence from other studies we conclude that dexmedetomidine is a better adjuvant than clonidine for epidural anaesthesia and analgesia.

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