Original Article

Comparative study of clonidine and dexmedetomidine used as adjuvant to epidural ropivacaine in orthopaedic lower limb surgery

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Abstract

Background: A lot of researches have been done to find an ideal adjuvant to ropivacaine in regional anaesthesia that inhibits intra and post operative pain and prolong the duration of anaesthesia without any side effects. **Aim**: This study was conducted to evaluate the onset, extent and duration of sensory and motor block and side effects of clonidine or dexmedetomidine when used as an adjuvant to ropivacaine in epidural anaesthesia in lower limb orthopaedic surgery. **Materials and Methods**: A prospective randomized study was conducted on 60 patients of American society of anaesthesiologists' status I and II, posted for lower limb orthopaedic surgery. All patients were randomly allocated into two groups of 30 each; group I was ropivacaine - clonidine group (RC) and group II was ropivacaine - dexmedetomidine group (RD). Group I (RC) patients received 16 ml of 0.75% ropivacaine and clonidine 2mcg/kg. Group II (RD) patients received 16 ml of 0.75% ropivacaine and dexmedetomidine 1.5mcg/kg. The onset, extent, duration of sensory and motor blocks, and side effects were recorded. **Results:** Dexmedetomidine had a visible edge over clonidine as it enabled an earlier onset and longer duration of sensory and motor block. Sedation scores were statistically significant with RD group in comparison to RC group. RD group showed visible superiority over RC group in various post-operative block characteristics like the weaning of sensory and motor block, prolonged post-operative analgesia. **Conclusion**: Dexmedetomidine was a better alternative to clonidine as an adjuvant to ropivacaine in epidural anaesthesia in orthopaedic lower limb surgeries.

Keywords: Clonidine**,** dexmedetomidine , ropivacaine, orthopaedic**.**

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INTRODUCTION

Nowadays, regional anaesthesia is the preferable mode of anaesthesia for orthopaedic lower limb surgeries. Epidural anaesthesia reduced the periopeative stress responses to surgery and improves surgical outcome[1]. Local anaesthetics and opioids are the drugs most widely used in epidural anaesthesia which is either by single injection or by infusion. The analgesic duration can be prolonged by increasing dose of local anaesthetics; however the risk of accompanied systemic neurotoxicity can be increased[2]. Therefore, adjuvant can be added to local anaesthetics to prolong the analgesic duration and to limit the dose requirement of local anaesthetics. Recently, several neuraxial adjuvants, including clonidine, opioids, dexamethasone, ketamine, magnesium sulphate and midazolam have demonstrated the synergistic analgesic effect with local anaesthetics with varying degrees of success. But the search for ideal adjuvant for a particular local anaesthetic goes on[3]. Recemic bupivacaine is most frequently used long acting local anaesthetic agent in regional anaesthesia. But the low dose bupivacaine is often used in order to reduce cardiovascular side effects which may not provide an adequate anaesthesia level for surgery[4]. Nowadays ropivacaine has replaced bupivacaine

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in regional anaesthesia for the same reason[5]. So we have chosen ropivacaine as the local anaesthetic because it is longer acting and devoid of cardiac side effects. α-2 adrenergic agonists like clonidine and dexemedetomidine have both analgesic and sedative properties when used as an adjuvant in regional anaesthesia[6]. Dexmedetomidine has an eight-fold greater affinity for α_2 adrenergic receptors than clonidine and much less α1 activity. Its higher selectivity α_{2A} receptors are responsible for the hypnotic and analgesic effects[7]. This study was designed to compare the analgesic, sedative action and side effects of dexmedetomidine and clonidine when added to for epidural ropivacaine analgesia in patients undergoing lower limb orthopaedic surgeries.

MATERIAL AND METHODS

Ethical committee approval and written informed consent were obtained from 60 ASA status (I / II) patients of ages 25-45 years posted for lower limb orthopaedic surgeries. Patients with history of uncontrolled hypertension, cardiac, respiratory, hepatic, neurological, neuromuscular disease; with allergy to the used drugs, contraindication or failure of epidural anaesthesia were excluded from the study. ECG, pulse oximetry (SPO_2) and non-invasive blood pressure (NIBP) were monitored. After infusion of 500ml of lactated Ringer's solution, patients were put in the sitting position. 3 ml of lidocaine 2% was used to infiltrate the skin and subcutaneous tissues. A 17 gauge tuohy epidural needle was used at L3-L4 space. After loss of resistance, the epidural catheter was advanced 3-4 cm into the epidural space. Patients with any evidence of needle or catheter entry into an epidural vein or into the CSF were excluded from this study. A test dose of 3 ml or 2% lignocaine solution containing adrenaline 1: 200,000 was injected. After 4-6 min of injecting the test dose and excluding intravascular or subarachnoid injection, patiens were allocated to one of two groups in double blinded fashion based on computer generated code. Group I: ropivacaine and clonidine (RC) in which 16 ml of 0.75% ropivacaine and clonidine 2µg/kg was administered in the epidural catheter. Group II: ropivacaine and dexmedetomidine (RD) in which 16 ml of 0.75% ropivacaine and 1.5µg/kg dexmedetomidine was administered in the epidural catheter. The drug syringes were prepared by an anaesthetist who was blind about the study. Sensory block was assessed using the blunt end of a 27-gauge needle. Motor blockade was assessed by using the modified bromage scale (bromage 0: The patient is able to move the hip, knee and ankle; bromage 1: the patient is unable raise extended leg; bromage 2: The patient is unable to move the hip and knee but able to move the ankle; bromage 3: The patient is unable to move the hip, knee and ankle). The time to reach the peak sensory level and bromage 3 motor blocks were recorded before surgery. The regression time for sensory and motor block were recorded in post anaesthesia care unit. All durations were calculated from the time of epidural injection. The two groups were monitored pre and intraoperatively for heart rate, non-invasive blood pressure and O_2 saturation (SpO_2). Hypotension was defined as systolic blood pressure <90 mmHg or >30% decrease in baseline values and was treated by fluids and vasopressors. Tachycardia was defined as heart rate >100/min. Bradycardia was defined as heart rate >55/min and was treated by inj 0.5 mg atropine. Intraoperative nausea, vomiting, pruritus, sedation or any other side effects were recorded. Sedation was assessed by sedation score (1: alert and awake, 2: arousable to verbal command, 3: arousable with gentle tactile stimulation, 4: arousable with vigorous shaking. 5: unarousable).

Statistical Methods

Data were presented as mean ± SD. *t*-test was used to compare the two groups for quantitative data and chi-square test was used for qualitative data by SPSS V18. Value of $p<0.05$ was considered statistically significant.

RESULTS

The demographic profiles of the patients in both the groups were comparable with regards to age, sex, height, weight and body mass index. The ASA status of patients was similar in both the groups and mean duration of surgery was comparable in both the groups. ($p>0.05$) [Table 1]. Onset of sensory block at T 10 level was earlier in RD group (6.54±2.51 min) compared to the RC group (8.15±2.84 min). Higher dermatomal spread (T6-7) was seen in RD group in comparison to RC group (T7-8). Time for maximum sensory level was shorter (12.34±3.75 min) in RD group compared to RC group (15.74±3.96 min). All the above sensory block characteristics were statistically significant in RD group in comparison to RC group. Complete motor block was achieved earlier (15.36±6.81 min) in RD group and 19.14±5.34 min in RC group which was statistically significant. ($p<0.05$) [Table 2]. In our study mean sedation scores were significantly higher in RD group compared to RC group which is statistically significant. [Table 3]. Mean time to 2 segmental dermatomal regressions was 140.64±10.15 min and 130.45±9.76 min in RD and RC group respectively. Return of motor power to bromage 1 was 250.22±38.26 min in RC group and 280.52 ± 25.44 min in RD group. Both the block characteristics were statistically significant. The time for rescue analgesia was comparatively shorter (315.18±24.81 min) in the RC group and 350.66±25.8 min in RD group which was statistically significant. ($P<0.05$). [Table 4]. The Cardio-respiratory parameters like heart rate, mean arterial

pressure, spo2 and respiratory rate were stable and more or less similar in both the groups throughout the study period. Table 5 showed the comparative incidence of various side effects in both the groups which were statistically not significant. We did not observe respiratory depression in any patient in both the group.

Table 1: Demographic profile of patients of both group

Demographic characteristics	RC group (n=30) Mean ±SD	RD group(n=30) Mean ±SD	P value
Age (yrs)	45.5±10.6	47.9±9.4	0.36
Sex (m:f)	20:10	18:12	0.79
Weight (kg)	60.82±10.45	62.42±8.94	0.53
Height (cm)	150.4±8.25	152.65±8.4	0.30
BMI(Kg/m^2)	27.6±2.95	28.46±3.22	0.28
ASA (I/II)	25/5	26/4	1.0
Mean duration of surgery (min)	90.45±15.1	94.21±14.35	0.33

Table 2: Comparison of preoperative block characteristics

Block characteristics	RC group (n=30)	RD group(n=30)	P Value
Onset time of sensory block at T 10(mins)	8.15±2.84	6.54±2.51	0.0235
Max sensory block level	T7-T8	T6-T7	
Time to max sensory block(mins)	15.74±3.96	12.34±3.75	0.001
Time for complete motor block(mins)	19.14±5.34	15.36±6.81	0.02
Total ephedrine requirement (mg)	**7.35±2.1**	**6.55±1.8**	**0.11**

Table 3: Sedation score in both group

Sedation score	RC group(n=30)	RD group(n=30)	P Value
1	18	9	0.037
2	9	15	0.187
3	3	6	0.471
4	0	0	
5	0	0	

Table 4: Comparisons of post op block characteristics

Post op block characteristics	RC group (n=30)	RD group(n=30)	P Value
Mean time to two segment regression (mins)	130.45±9.76	140.64±10.15	0.0002
Mean time to sensory regression at S 1(mins)	290.18±34.65	340.54±35.84	0.0001
Mean time to regression to bromage 1(mins)	250.22±28.26	280.52±25.44	0.0001
Time to first rescue top up(mins)	315.18±24.81	350.66±25.8	0.0001

Table 5: Comparison of side effects in intra and post operative period

Side effect	RC group(n=30)	RD group(n=30)
Nausea	5	4
Vomiting	1	2
Shivering	3	3
Headache	0	1
Dizziness	0	0
Dry mouth	1	1
Respiratory depression	0	0

DISCUSSION

The pharmacologic properties of α-2 agonists like clonidine and dexmedetomidine have been used extensively in various routes. Epidural administration of these drugs is associated with sedation, analgesia, anxiolysis, hypnosis and sympatholysis[8]. Clonidine has been used as adjuvant to local anaesthetics successfully over the last few decade. In this study, clonidine was compared with dexmedetomidine as adjuvants to ropivacaine in epidural anaesthesia. In our study ropivacaine – dexmedetomidine combine produced earlier onset of epidural block, prolonged duration of sensory block and more sedation in comparison to ropivacaine - clonidine combine which was statistically significant. There was no statistical difference in haemodynamic parameters in both groups. Disma *et al* in their study found that clonidine produced a local anaesthetic sparing effect with a dose dependent decrease in ED50 of ropipivacaine for caudal anaesthesia. In addition, there was a dose dependent prolongation of postoperative analgesia following lower abdominal surgery in children. A dose of 2 µg kg of clonidine provides the optimum balance between improved analgesia and minimal side effects[10]. Wallet *et al* in their study found that the addition of clonidine to epidural ropipivacaine and sufentanil for patient controlled epidural analgesia in labour improved analgesia, reduced the supplementation rate and reduced pruritus. Blood pressure was significantly lower in the clonidine group over time but without clinical consequence.[11] Milligan *et al* opined that, in patients undergoing total hip replacement, the addition of the alpha (2)-adrenergic agonist clonidine to epidural infusions of levobupivacaine significantly improved postoperative analgesia[12]. Akin *et al* in their study found that caudal clonidine prolonged the duration of analgesia produced by caudal levobupivacaine without causing significant side effects and this was because of a spinal mode of action[13]. Mahran *et al* opined that both clonidine and fentanyl can be used as effective additive to epidural levobupivacaine for postoperative analgesia after radical cystectomy with no significant difference between them in vital signs, analgesic, sedative effects and safety profile[14]. Our study also found similar findings using

clonidine as adjuvant to epidural ropivacaine. Manal *et al* in a comparative study of epidural morphine and epidural dexmedetomidine used as adjuvant to levobupivacaine in major abdominal surgery, found that dexmedetomidine was a good alternative to morphine as an adjuvant to levobupivacaine in epidural anaesthesia in major abdominal surgeries[15]. Zeng XZ *et al* in their study found that low-dose epidural dexmedetomidine improved thoracic epidural anaesthesia for nephrectomy. Sensory and motor blockade duration was longer in the dexemedetomidine group than in the control group. The muscle relaxation score were significantly higher in the dexemedetomidine group compared with the control group. Pain score and analgesic requirement was lower in dexemedetomidine group[16]. Ahmed Sobhy Basuni *et al* used dexmedetomidine as supplement to low-dose levobupivacaine in spinal anaesthesia for knee arthroscopy. They opined that dexmedetomidine was a good alternative to fentanyl for supplementation of low-dose levobupivacaine in spinal anaesthesia for knee arthroscopy[17]. Aliye Esmaoglu *et al* concluded that intrathecal dexmedetomidine addition to levobupivacaine for spinal anaesthesia shortens sensory and motor block onset time and prolongs block duration without any significant adverse effects[18]. Our study found similar findings using dexmedetomidine as adjuvant to epidural ropivacaine. A.M. El-Hennawy *et al* studied the effect of adding clonidine or dexmedetomidine to bupivacaine in caudal block in children. They found that addition of dexmedetomidine or clonidine to caudal bupivacaine significantly plolonged analgesia in children undergoing lower abdominal surgeries with no significant advantage of dexmedetomidine over clonidine and without an increase in incidence of side-effects[19]. Al-Mustafa *et al*. used dexmedetomidine as an intrathecal adjuvant to bupivcaine and found that its effect was dose-dependent and that its use accelerated the onset of sensory block to reach T10 dermatome. Bajwa *et al* showed in their study that dexmedetomidine was a better adjuvant than clonidine in epidural ropivacaine anesthesia for patient comfort, superior sedative and anxiolytic properties, intra-operative and postoperative analgesia.[21] Wu H-H *et al* in a retrospective study opined that neuraxial dexmedetomidine was a favorable adjuvant to local anaesthetics which provides better and longer analgesia. Neuraxial dexmedetomidine was associated with good sedation scores and lower analgesic requirements and stable into-operative hemodynamics.[22] Crews *et al*. found in their study that the use of continuous levobupoivacaine in addition to morphine via a thoracic epidural catheter produced a excellent segmental sensory block and analgesia.[23]

CONCLUSION

Use of dexmedetomidine as an adjuvant to ropivacaine was a good alternative to other adjuvants like clonidine, morphine and other opioids in epidural anaesthesia. Both clonidine and dexmedetomidine provided adequate sensory, motor block and their side effects were well tolerated by the patients but dexmedetomidine had an edge over clonidine as adjuvant when used with ropivacaine in epidural anaesthesia.

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