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A randomized study of epidural clonidine and dexmedetomidine used for post operative analgesia in total knee replacement

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Abstract

Aim: This study of our study was to evaluate the onset and duration of sensory and motor block and side effects of clonidine or dexmedetomidine when used as an adjuvant in epidural anaesthesia in total knee replacement. **Materials and methods**: 60 patients of ASA status I and II, posted for total knee replacement were randomly allocated into two groups of 30 each. Group BC group patients received 18 ml of 0.5% bupivacaine and clonidine 2mcg/kg. Group BD group patients received 18 ml of 0.5% bupivacaine and dexmedetomidine 1.5mcg/kg. Preoperative and postoperative block characteristics as well as hemodynamic parameters were observed and recorded. **Results:** Dexmedetomidine resulted earlier onset and longer duration of sensory and motor block on comparison to clonidine as adjuvant in epidural anesthesia. Sedation scores were statistically significant with dexmedetomidine group in comparison to clonidine group. **Conclusion**: Dexmedetomidine was a better than clonidine as an adjuvant to bupivacaine in epidural anaesthesia in total knee replacement.

Keywords- clonidine **,**dexmedetomidine ,levobupivacaine, total knee replacement

Introduction:

Epidural bupivacaine had been used extensively in the past for providing adequate post-op pain relief in patients undergoing lower abdominal surgeries. [1]. Neuraxial anaesthesia and analgesia provide solid analgesic effect by inhibiting nociceptive transmission from peripheral to central neuronal system, but their analgesic advantages might be limited by the short half life of current local anaesthetics. 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 [3,4,5]. We have chosen bupivacaine as the local anaesthetic because it is longer acting.Literature is available using α-2 agonists like clonidine and dexmedetimidine as adjuvant to local anaesthetics like bupivacaine and ropivacaine in epidural route but very few are there regarding their use with bupivacaine. α-2 adrenergic agonists like clonidine and dexemedetomidine have both analgesic and sedative

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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]. Previous studies have shown that clonidine and dexemedetomidine improved the quality of block when used as adjuvant with ropivacaine or bupivacaine in epidural block but studies are limited where bupivacaine is used as local anaesthetic. This study was designed to compare the analgesic, sedative action and side effects of dexmedetomidine and clonidine when added to bupivacaine for epidural analgesia in patients undergoing total knee replacement.

Material and methods

After obtaining Ethical committee approval and written informed consent. 60 ASA status (I / II) patients of ages 50 -85 years posted for total knee replacement were included in this study.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 BC: bupivacaine and clonidine in which 18 ml of 0.5% bupivacaine and clonidine 2µg/kg was administered in the epidural catheter. Group BD: bupivacaine and dexmedetomidine in which 18 ml of 0.5% bupivacaine 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:

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alert and awake, 2: arousable to verbal command, 3: arousable with gentle tactile stimulation, 4: arousable with vigorous shaking. 5: unarousable).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

A total of 60 patients posted for total knee replacement were enrolled for the study. They were randomly divided into two groups. 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].

Table 1- Demographic profile of patients of both group.

Demographic characteristics	BDgroup (n=30) Mean ±SD	BD 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

Onset of sensory block at T 10 level was earlier in group BD(6.54±2.51 min) compared to the group BC (8.15±2.84 min). Higher dermatomal spread (T6-7) was seen in group BD in comparison to group I(T7-8). Time for maximum sensory level was shorter (12.34±3.75 min) in group BD compared to groupI (15.74±3.96 min). All the above sensory block characteristics were statistically significant in group BD in comparison to group BC. Complete motor block was achieved earlier (15.36±6.81 min) in group BD and 19.14±5.34 min in group BC which was statistically significant. ($p<0.05$). [Table 2].

Table 2 – Comparison of preoperative block characteristics

Block characteristics	BC group (n=30)	BD 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	7.35±2.1	6.55±1.8	0.11

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requirement (mg)			

Many previous studies had shown that dexmedetomidine can be used as intraoperative sedative agent. In our study mean sedation scores were significantly higher in group BD compared to group BC which is statistically significant. [Table 3].

Table -3 Sedation score in both group

Sedation score	BC group(n=30)	BD 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	

Mean time to 2 segmental dermatomal regression was 140.64±10.15 min and 130.45±9.76 min in group BD and BC respectively. Return of motor power to bromage 1 was 250.22±38.26 min in BC group and 280.52 ± 25.44 min in group BD. Both the block characteristics were statistically significant. The time for rescue analgesia was comparatively shorter (315.18±24.81 min) in the group BC and 350.66±25.8 min in group BD 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 -4 Comparisons of post op block characteristics

Post op block characteristics	BC group (n=30)	BD 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.

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Side effect	BC group(n=30)	BD 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

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.

Discussion

In our study bupivacaine – dexmedetomidine combine produced earlier onset of epidural block, prolonged duration of sensory block and more sedation in comparison to bupivacaine-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 bupivacaine 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 bupivacaine 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 levobupivacaineManal 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

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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 bupivacaine.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 [20] All the above studies showed that dexmedetomidine was a better adjuvant to bupivacaine in epidural anaesthesia. It provided earlier onset and prolonged sensory block. Patient comfort, satisfaction and anxiolysis was better when dexmedetomidine was used as adjuvant to bupivacaine in epidural route.

Conclusion

Dexmedetomidine had an edge over clonidine as adjuvant when used with bupivacaine in epidural anaesthesia total knee replacement.

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