Scholars Journal of Applied Medical Sciences (SJAMS) **ISSN 2320-6691 (Online)**
Sch. J. App. Med. Sci., 2015; 3(6D):2416-2421 **ISSN 2347-954X (Print)**

(An International Publisher for Academic and Scientific Resources)
www.saspublishers.com DOI: 10.36347/sjams.2015.v03i06.055

Research Article

Comparative Evaluation of Clonidine and Dexmedetomidine Used For Epidural Analgesia in Lower Abdominal and Lower Limb Surgery

Dr Sidharth Sraban Routray[1], Dr Khagaswar Raut[2], Dr Debadas Biswal[3], Dr Kamalakanta Pradhan[4], Dr Debasis Mishra[5]
[1, 2, 3, 4]Asst Prof, [5]Senior resident
Department of anaesthesiology and critical care, SCB Medical College, Hospital, Cuttack, Odisha, India

***Corresponding author**
Dr Sidharth Sraban Routray
Email: drkitusraban@gmail.com

Abstract: Epidural anaesthesia with adjuvants is the preferred method for intra and postoperative pain relief in lower abdominal and lower limb surgeries but search for ideal adjuvant without any side effect goes on. 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 in epidural anaesthesia in lower abdominal and lower limb surgery. 60 patients of ASA status I and II, posted for lower abdominal and lower limb orthopaedic surgery were randomly allocated into two groups of 30 each. Group I(LC group) patients received 18 ml of 0.5% levo bupivacaine and clonidine 2mcg/kg. Group II(LD group) patients received 18 ml of 0.5% levo bupivacaine and dexmedetomidine 1.5mcg/kg. Preoperative and postoperative block characteristics as well as hemodynamic parameters were observed and recorded. The results were Dexmedetomidine had an earlier onset and longer duration of sensory and motor block on comparison to clonidine. Sedation scores were statistically significant with dexmedetomidine group in comparison to clonidine group. In conclusion Dexmedetomidine was a better than clonidine as an adjuvant to levo bupivacaine in epidural anaesthesia in lower abdominal and lower limb surgery.
Keywords: clonidine**,** dexmedetomidine, levo bupivacaine.

INTRODUCTION

Epidural anaesthesia and analgesia provides both intra and post operative pain relief in various lower abdominal and lower limb surgeries. 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]. 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 in regional anaesthesia for the same reason but it is shorter acting than levo bupivacaine. Levobupivacaine is the isolated S (-) isomer of bupivacaine. Due to lower affinity of S(-) isomer to cardiac sodium channel compared to R isomer, it is less cardio toxic [5]. So we have chosen levo bupivacaine as the local anaesthetic because it is longer acting and devoid of cardiac side effects.

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 levo bupivacaine. 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]. 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 levo 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 levo bupivacaine for epidural 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 25-65 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: levo bupivacaine and clonidine in which 18 ml of 0.5% levo bupivacaine and clonidine 2µg/kg was administered in the epidural catheter. Group II: levo bupivacaine and dexmedetomidine in which 18 ml of 0.5% levo 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 intra operatively 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. Intra operative 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

A total of 60 patients posted for lower abdominal and lower limb surgeries 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, and 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 group II (6.54±2.51 min) compared to the group I (8.15±2.84 min). Higher dermatomal spread (T6-7) was seen in group II in comparison to group I(T7-8). Time for maximum sensory level was shorter (12.34±3.75 min) in group II compared to group I (15.74±3.96 min). All the above sensory block characteristics were statistically significant in group II in comparison to group I. Complete motor block was achieved earlier (15.36±6.81 min) in group II and 19.14±5.34 min in group I which was statistically significant. ($p<0.05$). [Table 2].

Many previous studies had shown that dexmedetomidine can be used as intra operative sedative agent. In our study mean sedation scores were significantly higher in group II compared to group I 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 group II and I respectively. Return of motor power to bromage 1 was 250.22±38.26 min in I group and 280.52 ± 25.44 min in group II. Both the block characteristics were statistically significant. The time for rescue analgesia was comparatively shorter

(315.18±24.81 min) in the group I and 350.66±25.8 min in group II 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	LCgroup (n=30) Mean ±SD	LD 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	LC group (n=30)	LD 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 groups

Sedation score	LC group(n=30)	LD 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	LC group (n=30)	LD 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	LC group(n=30)	LD 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

Nowadays, a lot of adjuvants are used with local anaesthetics in the epidural anesthesia. Primary aim of these adjuvants is to fasten and prolong the sensory and motor block and produce more sedation, analgesia and patient satisfaction without any side effect. 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 decades. Introduction of dexmedetomidine has raised question about use of clonidine. The faster onset of action, and prolonged duration of analgesia in the post-operative period, makes these agents a very effective adjuvant to local anaesthetics in regional anaesthesia. In this study, clonidine was compared with dexmedetomidine as adjuvants to levo bupivacaine in epidural anaesthesia. This study was the first study to compare the analgesic and sedative efficacy when clonidine and dexmedetomidine were used as adjuvants to levo bupivacaine in epidural anesthesia. The demographic profile of our patients was comparable with respect to mean age, sex, height, body weight, body mass index, ASA status and duration of Surgery.

In our study levo bupivacaine – dexmedetomidine combine produced earlier onset of epidural block, prolonged duration of sensory block and more sedation in comparison to levo bupivacaine-clonidine combine which was statistically significant. There was no statistical difference in haemodynamic parameters in both groups. Studies were there in which either clonidine or dexmedetomidine were used as adjuvant to epidural levo bupivacaine. No study had compared clonidine and dexmedetomidine using as adjuvant to epidural levo bupivacaine.

Disma *et al.;* in their study found that clonidine produced a local anaesthetic sparing effect with a dose dependent decrease in ED50 of levo 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 levo 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 levo bupivacaine significantly improved postoperative analgesia[12].

Akin *et al.;* in their study found that caudal clonidine prolonged the duration of analgesia produced by caudal levo bupivacaine 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 levo bupivacaine 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 levo bupivacaine.

Manal *et al.;* in a comparative study of epidural morphine and epidural dexmedetomidine used as adjuvant to levo bupivacaine in major abdominal surgery, found that dexmedetomidine was a good alternative to morphine as an adjuvant to levo bupivacaine 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 levo bupivacaine in spinal anaesthesia for knee arthroscopy. They opined that dexmedetomidine was a good alternative to fentanyl for supplementation of low-dose levo bupivacaine in spinal anaesthesia for knee arthroscopy [17]. Aliye Esmaoglu *et al.;* concluded that intrathecal dexmedetomidine addition to levo bupivacaine 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 levo 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 prolonged 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 bupivacaine 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 favourable 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]. All the above studies showed that dexmedetomidine was a better adjuvant to levo bupivacaine in epidural anaesthesia. It provided earlier onset and prolonged sensory block. Patient comfort, satisfaction and anxiolysis were better when dexmedetomidine was used as adjuvant to levo bupivacaine in epidural route.

CONCLUSION

Use of dexmedetomidine as an adjuvant to levo bupivacaine 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 levo bupivacaine in epidural anaesthesia.

REFERENCES

1. Tziavrangos E, Schug SA; Regional anaesthesia and peri operative outcome. Current opinion in anaesthesiology 2006; 19(5): 521-525.
2. Becker DE, Reed KL; Local anaesthetics: review of pharmacological considerations. Anesthesia progress, 2012; 59(2): 90-102.
3. Ulke ZS, Senturk M; Non-analgesic effects of thoracic epidural anesthesia. Agriculture, 2007; 19(2): 6-12.
4. Huang Y, Pryor M. Mather L, Veering B. Cardiovascular and central nervous system effects of intravenous levo bupivacaine and bupivacaine in sheep. Anesth Analg, 1998; 86: 797-804.
5. Bardsley H, Gristwood R, Baker H, Watson N, Nimmo W; A comparison of the cardiovascular effects of levo bupivacaine and rac-bupivacaine following intravenous administration to healthy volunteers. Brint J. Clin Pharmacol, 1998; 46(3): 245-9.
6. Kamibayashi T, Maze M; Clinical uses of alpha-2 adrenergic agonists. Anaesthesiology 2000; 93:1345-9.
7. Scafati A; Analgesia and alpha agonists 2 Medens Rev, 2004; 4: 7.
8. Mauro VA, Brandao ST; Clonidine and dexmedetomidine through epidural route for postoperative analgesia and sedation in a cholecystectomy. Rev bras Anaesthesiol, 2004; 4: 1-10.
9. Kanazi GE, Aouad MT, Jabbour Khoury SI, Al Jazzar MD, Alameddine MM, Al-Yaman R *et al.;* Effect of low dose dexmedetomidine or clonidine on the characteristics of bupivacaine spinal block. Acta Anaesthesiol scand, 2006; 50(2): 222-7.
10. Disma N, Frawley G, Mameli L; Effect of epidural clonidine on minimum local anaesthetic concentration (ED50) of levo bupivacaine for caudal block in children. Paediatr Anaesth. 2011; 21 (2): 128-35.
11. Wallet F, Clement JH, Bouret C; Effectts of a continuous low-dose clonidine epidural regimen on pain, satisfaction and adverse events during labour: a randomized, double-blind, placebo-controlled trial. Eur J Anaesthesiol. 2010; 27(5): 441-7.
12. Milligan KR, Convery PN, Weir P; The efficacy and safety of epidural infusions of levo bupivacaine with and without clonidine for postoperative pain relief in patients undergoing total hip replacement. Anesth Analg. 2000 Aug; 91(2): 393-7.
13. Akin A, Ocalan S, Esmaglu A; The effects of caudal or intravenous clonidine on postoperative analgesia produced by caudal levo bupivacaine in children. Pediatric anesthesia 2010; 20: 350-355.
14. Mahran E. Ibrahim W; Is the combination of epidural clonidine- levo bupivacaine has same analgesic efficacy and safety as the combination Fentanyl – levo bupivacaine after radical cystectomy. Egyptian journal of anaesthesia 2014; 30(2): 143-147.
15. Manal M. Kamal, Sahar M; Talaat Comparative study of epidural morphine and epidural dexmedetomidine used as adjuvant to levo bupivacaine in major abdominal surgery Egyptian Journal of Anaesthesia. 2014; 30(2): 137-141.
16. Zeng XZ; Xu YM, CuiXG; Low-dose epidural dexmedetomidine improves thoracic epidural anaesthesia for nephrectomy Anaesthesia and Intensive Care 2014; 42(2): 185-90.
17. Ahmed Sobhy Basuni, Hoda Alsaid Ahmed Ezz; Dexmedetomidine as supplement to low-dose levo bupivacaine in spinal anaesthesia for knee arthroscopy Egyptian Journal of Anaesthesia 2014; 30(2): 149-153.
18. Aliye Esmaoglul, Sumeyra Turk, Adnan Bayram, Aynur Akin; The effects of Dexmedetomidine Added to Spinal Levobupivacaine for Transurethral Endoscopic Surgery, Balkan Med J 2013; 30: 186-90.

19. E-Hennawy M, Abd-Elwahab AM, Abd-Elmaksoud AM; Addition of clonidine or dexmedetomidine to bupivacaine prolongs caudal analgesia in children. Br. J. Anaesth. 2009; 103 (2): 268-274.
20. Al-Mustafa MM, Abu-Halaweh SA, Aloweida AS, Murshidi MM, Ammari BA, Awwad ZM, *et al.;* Effect of dexmedetomidine added to spinal bupivacaine for urological procedures. Saudi Med J. 2009; 30(3): 365-70.
21. Bajwa SJS, Bajwa SK, Kaur J, Singh G, Arora V, Gupta S, *et al.;* Dexmedetomidine and clonidine in epidural anaesthesia: a comparative evaluation. Indian J Anaesthe 2011: 55 (2): 116.
22. Wu H-H, Wang HT, Jin JJ, Cui GB, Zhou KC, Chen Y, *et al.;* Does Dexmedetomidine as a Neuraxial Adjuvant Facilitate Better Anesthesia and Analgesia? A Systematic Review and Meta-Analysis. PLoS ONE 2014; 9(3): e93114.
23. Crews JC, Hord AH, Denson DD, Schatzman C; Comparison of the analgesic efficacy of 0.25% levo bupivacaine combined with 0.005% morphine, 0.25% levo bupivacaine alone, or 0.005% morphine, alone for the management of postoperative pain in patients undergoing major abdominal surgery. Anesth Analg 1999; 89(6): 1504.