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Epidural 0.125% levobupivacaine with dexmedetomidine Versus Clonidine for Total Abdominal Hysterectomies: A Prospective Double Blind Randomized Trial

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Abstract

Context: Role of anesthesia for total abdominal hysterectomies is concerned with relieving pain during both intraoperative and the postoperative period. Several adjuvants are used to enhance the quality and duration of epidural anesthesia. *Aims:* We compared clonidine and dexmedetomidine as additives to levobupivacaine for epidural analgesia with emphasis on onset and duration of sensory block, duration of analgesia, and adverse effects. *Settings and design:* It is a randomized, double blind and prospective study conducted in tertiary care center. *Subject and Methods:* Sixty patients of American Society of Anesthesiologists (ASA) physical status Classes I and II who underwent total abdominal hysterectomies were randomly allocated into two equal groups. Group LC received 10 ml of 0.125% levobupivacaine + 1 $\mu g.kg^{-1}$ of clonidine and Group LD received 10 ml of 0.125% levobupivacaine + 1 $\mu g.kg^{-1}$ of dexmedetomidine through the epidural catheter. We evaluated onset of analgesia, time of peak effect, duration of analgesia, cardiorespiratory vitals, adverse effects, and need of rescue analgesics. *Statistical analysis:* Student's t-test and chi-square test. *Results:* Group LD demonstrated early onset, fast peak effect, prolonged postoperative analgesia, and stable cardiorespiratory vitals when compared with Group LC. There was a statistically significant reduction in analgesic requirement in group LD as compared to group LC. There were no major adverse effects in either group. *Conclusion:* As compared to clonidine, dexmedetomidine is a better neuraxial adjuvant to levobupivacaine, since it provides early onset, prolonged postoperative analgesia and stable cardiorespiratory vital parameters, without increasing adverse effects.

Keywords: Clonidine; Dexmedetomidine; Epidural analgesia; Levobupivacaine; Total abdominal hysterectomy.

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Introduction

Administration of α_2 agonists in epidural blocks, as adjuvants with local anesthetics in low doses offers new arena in the management of postoperative pain [1]. Levobupivacaine, S(−) enantiomer of bupivacaine, is known to have much safer pharmacological profile with reduced cardiac and neurological adverse effects because to its rapid protein binding rate [2,3]. Clonidine is a specific α_2 adrenergic agonist having 200 fold selectivity for α_2

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over α_1 receptor. Dexmedetomidine, an imidazole compound has 8 times more specificity for α_2 adrenergic receptors as compared to clonidine [4]. Dexmedetomidine is conferred with sedative, analgesic, and sympatholytic properties that blunt many of the cardiovascular stress responses that occurr during the perioperative period [5]. We conducted this study with the primary aim of comparing the duration of postoperative analgesia between epidural levobupivacaine 0.125% with clonidine and levobupivacaine 0.125% with dexmedetomidine for total abdominal hysterectomies. The secondary outcomes, such as onset of analgesia, hemodynamic variables, and adverse effects were evaluated in both the groups.

Materials and Methods

After obtaining hospital ethics committee approval and written informed consent was taken from each patient. Sixty adult female patients of American Society of Anesthesiologists (ASA) physical status Class I and II, between the age of 40 and 60 years undergoing total abdominal hysterectomy were enrolled for this study. The patients with coagulopathies, infection at injection site, mental retardation, second or thirddegree heart block, renal and hepatic insufficiency, uncontrolled hypertension and diabetes, and allergy to study drugs were excluded from the study. During preanesthetic visit, patients were meticulously examined clinically and routine investigations such as complete blood count, coagulation profile, serum creatinine, and electrocardiogram (ECG) were done. Entire procedure and 10 cm visual analog scale (VAS) (0, no pain and 10, worst pain imaginable) were explained during the preoperative visit. Patients were kept nil oral for 6 hours. Sixty patients were randomized using a computer generated randomization list [Fig. 1]. Patients were randomly allocated in to one of the two equal groups (30 patients in each group): group LD (dexmedetomidine group) and Group LC (clonidine group). After the patient entered the operation theater, an 18gauge intravenous (IV) cannula was secured, and intravenous fluid was started. And all standard monitors, namely blood pressure (BP), peripheral oxygen saturation by pulse oximetry (SpO_2), and ECG, were attached, and baseline vital parameters were recorded. With all aseptic precautions, back was painted and draped. At L_3-L_4 intervertebral space, local infiltration with 2% lidocaine was done and the epidural space was identified with an 18 gauge Tuohy needle (B. Braun, Melsungen, Germany) using the loss of resistance technique. None of our patients experienced accidental dural puncture. We placeda 20 gauge epidural catheter 4 cm into the epidural space and it was secured in place for postoperative analgesia. Intra vascular and intrathecal placement of epidural catheter was ruled out with a test dose of 3 ml epidural lignocaine 1.5% with adrenaline (1: 200,000). Subsequently, subarachnoid injection was given using a 25 gaugequincke spinal needle at L4–L5 intervertebral level and 15 mg 0.5% heavy bupivacaine was injected. The patient was laid back to the supine position. BP, Heart rateand SpO_2 were recorded every 3 minute for 15 min and every 5 min thereafter. The onset and level of sensory block was assessed using pin prick method and was recorded each minute until the start of surgery. Surgery was commenced only after the adequate level of sensory block was achieved. Once the surgery was completed, the patient was shifted to recovery room. The first dose of epidural injection was given when patient reported his VAS score is ≥3. Sixty patients were randomized into two equal groups: Group LD were injected with a 10 ml of levobupivacaine 0.125% with dexmedetomidine 1 $\mu g.kg^{-1}$, whereas Group LC were injected with a 10 ml of levobupivacaine 0.125% with clonidine 1 $\mu g.kg^{-1}$, through epidural catheter when the patient complains of pain (VAS ≥3). The epidural injection were given after negative aspiration test and post injection vitals were recorded. Pain was assessed using VAS scale of pain and sedation by Ramsay sedation score. BP, respiratory rate (RR), heart rate and SpO_2 were measured every 10 min until 30 min and thereafter every hour for 10 h.[8] We gave IVdiclofenac sodium 75 mg as rescue analgesic. After the epidural injection was given, the onset of analgesia (time from injection of the study medication to the first reduction in pain intensity to almost complete relief) and duration of analgesia (time from epidural injection to the time of the first request for rescue analgesic) were recorded in both groups. Any adverse effects such as nausea, vomiting, bradycardia,hypotension were looked for, recorded, and treated accordingly. Decrease in BP and HR by > 20% from the preoperative value was considered as hypotension or bradycardia, respectively, and was treated by intravenous fluid bolus, ephedrine, or atropine, as required. Nausea and vomiting were treated with IV ondansetron.

The data obtained from our study was tabulated and analyzed using the computer software (SPSS for Windows, Version 16.0. Chicago, SPSS Inc.). We used Student's t-test for numerical values and chi-square test for categorical values. The P value < 0.05 was considered as statistically significant.

Results

The demographic profile of the patients and duration of the surgery in both groups were comparable.(Table 1) Group LD demonstrated an earlier onset (6.41 ± 0.85 min) of analgesia as compared to the addition of clonidine (7.67 ± 1 min). In addition to earlier onset, dexmedetomidine also helped in achieving the peak analgesic level in a shorter time (10.20 ± 7.85 min) compared with clonidine (12.23 ± 5.76 min). The duration of analgesia was significantly prolonged in dexmedetomidine group (445.33 ± 9.75 min) in comparision to clonidine group (324.17 ± 10.75 min). (Fig. 2) These analgesic characteristics were statistically highly significant ($p < 0.0001$) (Table 2). In comparison to Group LC (66.67%), less number of patients (46.67%) in Group LD required IV rescue analgesics.

In our study, we obsereved that during initial 240 min (baseline to 240 min), p value of VAS score being >0.05, it was statistically insignificant.(Fig. 3) VAS scores of two Groups LC and LD becomes statistically significant at 320–460 min time intervals ($p < 0.05$). Clonidine group demonstrated higher VAS score requiring rescue analgesia at 320

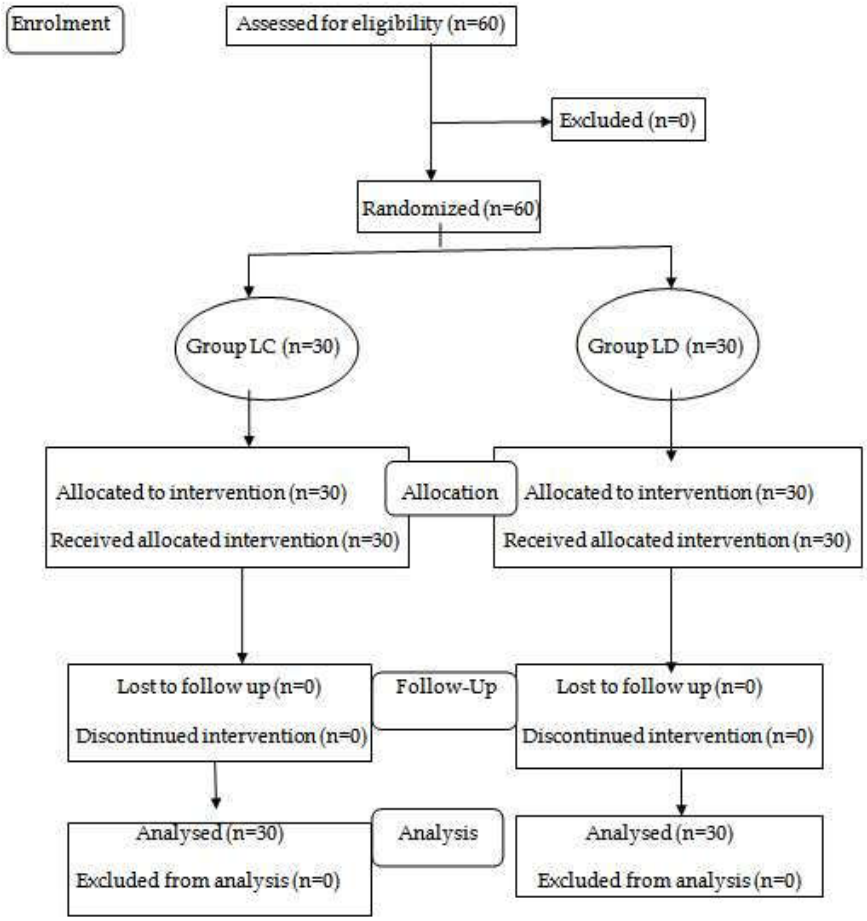

Fig. 1: Consort flow diagram

Table 1: Demographic profile of patients

Character	Group LC (n=30)	Group LD (n=30)	p-value
Age (years)	50.17 ± 7.90	49.83 ± 7.50	0.433
Weight (kg)	59 ± 6.94	58.83 ± 6.68	0.462
Duration of surgery (min)	106.83 ± 13.07	107.50 ± 12.52	0.420

Group LC – Levobupivacaine + Clonidine ; Group LD – Levobupivacaine + Dexmedetomidine, p value> 0.05; not significant.

Table 2: Comparison of analgesic characteristics between two groups

Analgesic characteristics	Group LC (n=30)	Group LD (n=30)	p -value
Duration of analgesia (min)	324.17 ± 10.75	445.33 ± 9.75	<0.00001
Time of onset of analgesia (min)	7.67 ± 1	6.41 ± 0.85	<0.00001
Time of peak onset of analgesia	12.23 ± 5.76	10.20 ± 7.85	<0.00001
Need of rescue analgesics n (%)	20 (66.67)	14 (46.67)	

Group LC – Levobupivacaine + Clonidine; Group LD – Levobupivacaine + Dexmedetomidine, P value <0.001; higly significant.

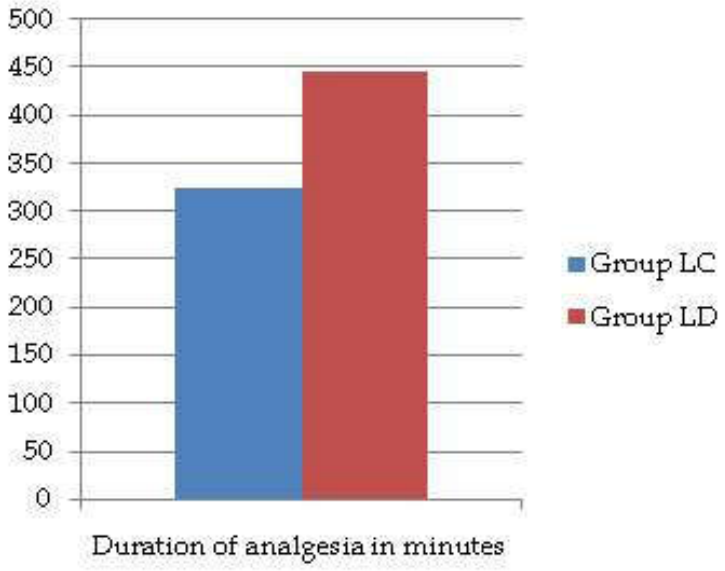

Fig. 2: Duration of Analgesia between two groups

Group LC – Levobupivacaine + Clonidine; Group LD – Levobupivacaine + Dexmedetomidine.

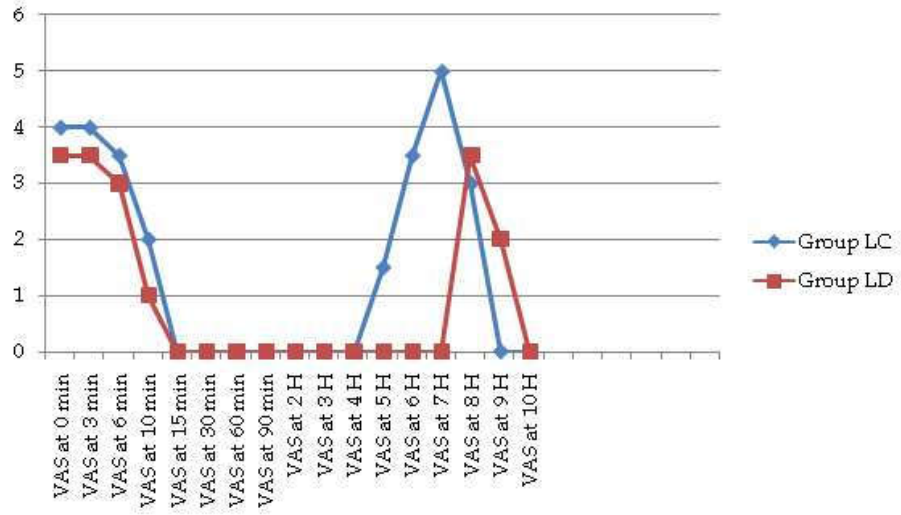

Fig. 3: Comparison of visual analog scale scores between groups

Group LC – Levobupivacaine + Clonidine; Group LD – Levobupivacaine + Dexmedetomidine.

min and peak VAS scores at 340–380 min, whereas in dexmedetomidine group VAS score begin to increase only after 390 min and reached maximum VAS scores at 460–490 min.The incidence of sedation, nausea, vomiting, and shivering were not statistically significant in either group. There were no episodes of hypotension, bradycardia, dizziness, and respiratory depression in either group.

Discussion

The CSE technique is an effective modality for patients undergoing infra-umbilical surgeries who need effective and prolonged postoperative analgesia. CSE technique is a combination of the density, rapidity, and reliability of a subarachnoid block with the flexibility of epidural anesthesia to prolong the duration of analgesia [6]. Levobupivacaine, a long acting Senantiomer of bupivacaine is conferred with less cardiac and neural toxicity than bupivacaine. Levobupivacaine is found to be safe and effective for epidural and spinal anesthesia [7,9]. α_2 agonists with anxiolysis, sedation, analgesic, and hypnotic properties are increasingly used as neuraxial adjuvants. α_2 agonists are devoid of side effects such as nausea, vomiting, pruritus, and urinary retention as compared to opioids [10].

Dexmedetomidine is a highly specific α_2 adrenergic agonist with 8 times greater affinity than clonidine and hence higher doses of it can be used with less α1 effect. When used neuraxially, clonidine enhances the action of local anesthetics, increases the intensity and duration of analgesia. It is conferred with sedative properties, and the adverse effects are hypotension and bradycardia [11].

In our study, we observed that addition of 1 $\mu g.kg^{-1}$ of dexmedetomidine to 0.125% levobupivacaine prolongs the duration of analgesia compared to addition of 1 $\mu g.kg^{-1}$ body weight of clonidine to 0.125% levobupivacaine in epidural block following total abdominal hysterectomies. In addition, dexmedetomidine achieved the faster onset of analgesia. Lesser patients (46.67%) in Group LD required diclofenac sodium injection as rescue analgesic than patients (66.67%) in Group LC.

There were no clinically significant variations in cardio-respiratory parameters throughout the study period, which proves the said effects of α_2 agonists in maintaining a haemodynamically stable peri-operative, and post-operative period [12,13].

The safety profile of both these drugs was good as none of the patient in either group demonstrated deep sedation or respiratory depression which is in concordance with several other studies [14,15,16,17].

Conclusion

Our results allow us to conclude that dexmedetomidine 1 $\mu g.kg^{-1}$ is a better neuraxial adjuvant to levobupivacaine 0.125% in comparison to clonidine 1 µg.kg-1 for providing early sensory onset and longer postoperative epidural analgesia without any major adverse effects in total abdominal hysterectomies.

Key messages:

In comparison to clonidine, dexmedetomidineis a safe and reliable neuraxial adjuvant to levobupivaine, as it provides early onset and prolonged postoperative anlagesia, without any side effects.

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Conflicts of interest: There are no conflicts of interest.

References

1. Kamibayashi T, Maze M. Clinical uses of alpha$_2$ adrenergic agonists. Anesthesiology. 2000;93:134-59.
2. Casati A, Baciarello M. Enantiomeric local anaesthetics: Can ropivacaine and levobupivacaine improve our practice? Curr Drug Ther. 2006;1:85-9.
3. Leone S, Di Cianni S, Casati A, Fanelli G. Pharmacology, toxicology, and clinical use of new long acting local anesthetics, ropivacaine and levobupivacaine. Acta Biomed. 2008 Aug;79(2):92-105.
4. Bajwa S, Kulshrestha A. Dexmedetomidine: An adjuvant making large in roads into clinical practice. Ann Med Health Sci Res. 2013;3:475-83.
5. Ribeiro RN, Nascimento JP. The use of dexmedetomidine in anesthesiology. Rev Bras Anestesiol. 2003;53:97-113.
6. Rawal N, Schollin J, Wesström G. Epidural versus combined spinal epidural block for cesarean section. Acta Anaesthesiol Scand. 1988;32:61-6.
7. Bajwa SJ, Kaur J. Clinical profile of levobupivacaine in regional anesthesia: A systematic review. J Anaesthesiol Clin Pharmacol. 2013;29:530-9.
8. Leone S, Di Cianni S, Casati A, Fanelli G. Pharmacology, toxicology, and clinical use of

new long acting local anesthetics, ropivacaine and levobupivacaine. Acta Biomed. 2008;79:92-105.

9. Burlacu CL, Buggy DJ. Update on local anesthetics: Focus on levobupivacaine. Ther Clin Risk Manag. 2008;4:381-92.
10. Afonso J, Reis F. Dexmedetomidine: Current role in anesthesia and intensive care. Rev Bras Anestesiol. 2012;62:118-33.
11. Arunkumar S, Hemanth Kumar VR, Krishnaveni N, Ravishankar M, Jaya V, Aruloli M. Comparison of dexmedetomidine and clonidine as an adjuvant to ropivacaine for epidural anesthesia in lower abdominal and lower limb surgeries. Saudi J Anaesth. 2015;9:404-8.
12. Taittonen MT, Kirvelä OA, Aantaa R, Kanto JH. Effect of clonidine and dexmedetomidine premedication on perioperative oxygen consumption and haemodynamic state. Br J Anaesth. 1997;78:400–6.
13. Cortinez LI, Hsu YW, Sum-Ping ST, Young C, Keifer JC, Macleod D, et al. Dexmedetomidine pharmacodynamics: Part II: Crossover comparison of the analgesic effect of dexmedetomidine and remifentanil in healthy volunteers. Anesthesiology. 2004;101:1077–83.
14. Saravana Babu M, Verma AK, Agarwal A, Tyagi CM, Upadhyay M, Tripathi S, et al. A comparative study in the postoperative spine surgeries: Epidural ropivacaine with dexmedetomidine and ropivacaine with clonidine for postoperative analgesia. Indian J Anaesth. 2013;57(4):371-76.
15. Bajwa SJ, Bajwa SK, Kaur J, Singh G, Arora V, Gupta S, et al. Dexmedetomidine and clonidine in epidural anaesthesia: A comparative evaluation. Indian J Anaesth. 2011;55:116-21.
16. Chiruvella S, Donthu B, Nallam SR, Salla DB. Postoperative analgesia with epidural dexmedetomidine compared with clonidine following total abdominal hysterectomies: A prospective doubleblind randomized trial. Anesth Essays Res. 2018;12:103-8.
17. Shaikh SI, Revur LR, Mallappa M. Comparison of epidural clonidine and dexmedetomidine for perioperative analgesia in combined spinal epidural anesthesia with intrathecal levobupivacaine: A randomized controlled double-blind study. Anesth Essays Res. 2017;11:503-7.