ISSN: 2581 – 3633
PubMed - National Library of Medicine - ID: 101745081

*International Journal of Medical Science and Advanced Clinical Research (IJMACR)*

*Available Online at:www.ijmacr.com*

*Volume – 6, Issue – 1, Janaury - 2023, Page No. : 437 - 444*

# Epidural Dexmedetomidine versus Clonidine for post-operative analgesia in patients undergoing Total Abdominal Hysterectomy - A Prospective Double-blind Randomized Trial

[1]Dr. KP. Kameshwaran,MBBS, DLO, Resident 3rd year, Department of AnaesthesiaKarpagaVinayaga Institute of Medical Science and Research Centre Maduranthagam, Chengalpattu Tamil Nadu.

[2]Prof. Dr. P Manohar, MD, Professor,Department of Anaesthesia, KarpagaVinayaga Institute of Medical Science and Research CentreMaduranthagam, ChengalpattuTamil Nadu.

[3]Dr. M Murali Manoj, MD, Associate professor,Department of Anaesthesia,KarpagaVinayaga Institute of Medical Science and Research CentreMaduranthagam, ChengalpattuTamil Nadu.

[4]Dr. Karthikeyan, MD, SPM, KarpagaVinayaga Institute of Medical Science and Research Centre,Maduranthagam, ChengalpattuTamil Nadu.

**Corresponding Author:** Prof. Dr. P Manohar, MD, Professor, Department of Anaesthesia, Karpaga Vinayaga Institute of Medical Science and Research Centre Maduranthagam, Chengalpattu Tamil Nadu.

**How to citation this article:** Dr. K P. Kameshwaran,Prof. Dr. P Manohar,Dr. M Murali Manoj,Dr. Karthikeyan,"Epidural Dexmedetomidine versus Clonidine for post-operative analgesia in patients undergoing Total Abdominal Hysterectomy - A Prospective Double-blind Randomized Trial", IJMACR-January - 2023, Volume – 6, Issue - 1, P. No. 437 – 444.



**Type of Publication:** Original Research Article

**Conflicts of Interest:** Nil

## Abstract

**Background:** The administration of α-2 adrenergic agonist's adjuvant can increase the potential duration of analgesia and reduce the local anesthetic dose needed 30%–40%, hence reduce the occurrence of the side effects of local anesthesia. The present study was conducted with the primary aim of assessing the efficacy of postoperative analgesia between epidural Ropivacaine 0.2% with Clonidine and Ropivacaine 0.2% with dexmedetomidine for total abdominal hysterectomies.

**Methodology**: Patients were randomly selected to 2 groups. GROUP RC: infusion of 0.2 % Ropivacaine 8ml with 2 µg/kg Clonidine in 3ml normal saline. GROUP RD: 0.2% Ropivacaine 8ml with 1 µg/kg of dexmedetomidine in 3ml normal saline. Epidural bolus was given once patient had VAS score of > 4 then Quality and duration of analgesia using Visual Analog Scale. Ramsay Sedation Score (RSS) and hemodynamic parameters like HR, MAP, and $SPO_2$are observed for 24 hours post operatively. Incidence of side effects are also noted.

**Result:** The demographic profile, initial and post-operative block characteristics and cardio-respiratory parameters were comparable and statistically

nonsignificant in both the groups. However, sedation scores with dexmedetomidine were better than Clonidine and turned out to be statistically significant ($P < 0.05$). The earlier onset of analgesia, longer duration of analgesic effects and reduction in Ropivacaine dose were observed in dexmedetomidine group.

**Conclusion:** Dexmedetomidine has shown longer duration of analgesia with better hemodynamic profile and lesser the incidence of adverse effects when comparing to Clonidine. These features make it a valuable tool in achieving the goals of enhanced recovery after surgery.

**Keywords:** Clonidine, dexmedetomidine, epidural anaesthesia, Ropivacaine, abdominal hysterectomy

**Introduction**

Total Abdominal Hysterectomy is the most common major gynecological procedure done hence to give good Intra and Post-operative pain management is the most important goal to achieve earlier recovery and improve patient satisfaction [1]. Use of systemic opioid such as morphine, fentanyl and tramadol has been long recognized as one of the postoperative analgesia but has many unpleasant effects such as nausea, drowsiness, weakness, and longer immobilization and healing time [2]. Epidural analgesia becomes one of the most popular analgesia to control postoperative pain, especially in major abdominal surgery [3]. Epidural analgesia not only provides pain relief but also reduces the postoperative stress response [4]. The administration of α-2 agonists has analgesic and sedative effect when used as adjuvant in regional anesthesia. The administration of α-2 adrenergic agonist's adjuvant can increase the potential duration of analgesia and reduce the local anesthetic dose needed 30%–40% and hence can reduce the occurrence of the side effects [5].

Dexmedetomidine is one of the most potent and high selective alpha-2 adrenergic receptor agonists. Dexmedetomidine can be potential as analgesic and contains sedative properties so it can cause minimal respiratory depression when used as an adjuvant in regional anesthesia [6,7].

Anti-nociceptive mechanism of this drugs when used in epidural anesthesia is mediated in the spinal because it does not have analgesic effect when given systemically [5]. The use of dexmedetomidine during epidural anesthesia has faster onset and longer motor sensory blockade duration with hemodynamic stability that can be accepted [8]. Clonidine is an alpha-2 adrenergic agonist cause the analgesic action of alpha-2 receptor in the dorsal of spinal cord[9,10]. Neuraxial Clonidine has been proven effective as an analgesic for noncancer pain and chronic cancer pain [11]. Clonidine has anti-hypertensive effect and has shown the potential as postoperative analgesia induced by local anesthetic [12].

The present study was conducted with the primary aim of assessing the duration of postoperative analgesia between epidural Ropivacaine 0.2% with Clonidine and Ropivacaine 0.2% with dexmedetomidine for total abdominal hysterectomies. The secondary outcomes measured were the onset of analgesia, hemodynamic variables, and adverse effects in both the groups.

**Materials and methods**

After obtaining the intuitional ethical committee clearance and written informed consent from patients,60 patients belonging to ASA I & II aged 40-60 years undergoing total abdominal hysterectomy surgery under combined spinal epidural (CSE) planned for an epidural analgesia post operatively. Patients who are not willing for CSE, Hema topoi etic disorders, abnormal bleeding or coagulation tests, psychiatric conditions, a history of

substance abuse, and allergies to amide-type local an aesthetics are all excluded. Based on a computer-generated code, patients were assigned at random to one of the two treatment groups listed below: both Ropivacaine and Clonidine (RC) and Ropivacaine and dexmedetomidine (RD).

The preoperative visit included an explanation of the an aesthetic technique and study protocol to the patients. Tablet pantoprozole 40 mg per oral as premedication administered at night prior to surgery. When the patient arrived in the operating room, an 18-gauge cannula was used to secure an IV line, and a ringer lactate drip was started. Non-invasive blood pressure, electrocardiogram, and pulse oximeters were used to monitor the patients, and baseline heart rate (HR), blood pressure, and oxygen saturation were recorded. The drug syringes were prepared by an anesthesiologist who was not involved in data collection or intervention. Patients were administered combined spinal epidural block with 18-gauge Touhy needle and Epidural catheter tip was kept at T11 to T12 level and a test dose of 3 ml of 2% lignocaine hydrochloride solution containing adrenaline 1:200,000 was injected and followed by intrathecal injection using 25 guage Quincke needleusing 3.5 ml of 0.75% Ropivacaine heavy. Patients were randomly selected into 2 groups. GROUP RC: Bolus of 0.2 % Ropivacaine 8ml with 1 µg/kg Clonidine in 3ml normal saline. Group RD: 0.2% Ropivacaine 8ml with 1 µg/kg of dexmedetomidine in 3ml normal saline. Epidural bolus was given once patient had VAS score of > 4 and then Quality and duration of analgesia were assessed by Visual Analog Scale and sedation assessed by Ramsay Sedation Score (RSS). Parameters like HR, MAP, and $SPO_2$were observed for 24 hours post operatively. Incidence of side effects were also noted. Injection paracetamol 1 gm IV infusion is used as rescue analgesia when VAS ≥4. Patients were observed in the operating room for 15 minutes before being transferred to the Post Anaesthesia Care Unit (PACU) for monitoring.

Vital parameters were continuously monitored, and recordings were made every 5 minutes until 30 minutes, then every 15 minutes for the next 120 minutes, and finally every 2 hours for the next 22 hours. Hypotension (systolic arterial pressure less than 90mmHg) was treated with 6mg of Injection Ephedrine, and bradycardia (heart rate less than 50 beats/min) was treated with 0.3mg of Injection Atropine. During the first 24 hours of postoperative period, adverse events like nausea, vomiting, dizziness, pruritus and respiratory depression were noted. Nausea and vomiting were treated with 4mg of intravenous ondansetron.

We included thirty patients in each group for better validation of results. Data were checked, entered, and analysed using SPSS version 22 for Windows (IBM Corp., Armonk, NY, USA). Quantitative data were represented as mean ± standard deviation, and for qualitative data, number and percentages were used. Student's t-test and one-wayannova tests were used as test of significance to find an association for quantitative data. Chi-square test was used as test of significance to find the association for qualitative data. $P < 0.05$ was considered statistically significant.

**Results**

A total of 60 patients included in this study who undergone total abdominal hysterectomy and those who were divided into two groups randomly, Group RC (Ropivacaine with Clonidine and group RD and (Ropivacainewith dexmedetomidine). Demographic variables were comparable between the two groups. Addition of dexmedetomidine to Ropivacaine as an

adjuvant resulted in an onset of analgesic effect (7.67±2.12 mins) was earlier as compared to the addition of Clonidine (9.28±1.98 mins) and the time to peak analgesia (V=0) also was achieved significantly earlier in RD group (11.34±3.12) comparing to the RC group (13.79±4.09). Time to first rescue analgesia also prolonged in Dexmedetomidine group (365.11±19.31) compared to Clonidine group (317.85±17.63). All these analgesic characteristics were statistically significant values on comparison ($P < 0.05$) [Figure 2]. Less number of patients (37%) in Group RD required rescue analgesics top-up when compared to Group RC (93%) and all the variables were statistically significant (<0.05) [Table 2].

Sedation score was stable in RD (2.11±0.98 mins) GROUP RC comparing to the RC (2.98±1.1 mins) group. More number of patients had better sedation score in RD group. For detection of pain, VAS score was used at different time intervals. It was significantly low ($P < 0.05$) at 2, 9 and 16$^{th}$hrs after surgery with a better pain control in Group RD patients than in Group RC patients (Table 3).

Comparing of adverse effects we observed lesser number of side effects such as Nausea, Vomiting, Headache, Dizziness, Dry mouth were noted in RD group than RC group (Table 4). Regarding hemodynamic properties reduced HR were observed in both the groups but statistically not significant. Mean arterial pressure was significantly increased in first 20 mins RD GROUP comparing to the RC group (Figure 1, 2 & 3).

**Discussion**

Epidural administration of α2 agonists in combination with local anesthetics in low doses offers new dimensions in the management of postoperative pain[3]. Studies showed that this goal is partly achieved by improving the performance of epidural administration with adjuvant drugs such as narcotics and alpha-2 adrenoreceptor agonists to induce longer postoperative analgesia and to minimize intraoperative blood loss and postoperative side effects [4,13,14].

Results of this prospective, randomized, double-blinded study demonstrate that addition of 1 µg/kg body weight dexmedetomidine to 0.2% Ropivacaine produces longer duration of analgesia compared to addition of 1 µg/kg body weight of Clonidine to 0.2% Ropivacaine in epidural analgesia following total abdominal hysterectomies. Addition of dexmedetomidine to Ropivacaine also hastens the onset of analgesia and earlier time to achieve the peak analgesic effect. Fewer patients (37%) in Group required rescue analgesic than patients (63%) in Group RC. We also observed time to first rescue analgesia was prolonged in dexmedetomidine group (365.11±19.31) compared to Clonidine group(317.85±17.63).

Administration of alpha-2 agonists adjuvant in epidural is related to the effects of sedation, analgesia, anxiolytic,hypnosis, and sympatholysis[14]. Alpha-2 agonists can provide an interested alternative in the use of anesthetic adjuvant agent because of the efficient anesthesia effect and stable hemodynamic[15,16]. Alpha-2 adrenoceptor agonists produce analgesia by releasing C-fiber transmitters and hyperpolarization of post-synaptic dorsal horn neurons[15].Extension of motor block in local anesthesia results from thealpha-2 adrenoceptor agonists binding to motor neurons in dorsal horn[17].

Sunil Chiru Vella et al (2022) reported GROUP Dexmedetomidine had early onset, early peak effect, prolonged duration, and stable cardiorespiratory parameters when compared with Clonidine group

andless number of patients (42.5%) in GROUP Dexmedetomidine required rescue analgesics when compared to GROUP Clonidine (70%) and was statistically significant [18]. Another author SukhminderJit Singh Bajwa et al concluded from his study that Dexmedetomidine is a better neuraxial adjuvant compared to Clonidine for providing early onset of sensory analgesia, adequate sedation and a prolonged post-operative analgesia[19].

Our study showed better sedation score and lesser adverse effects among RD GROUP comparing to the RC group. The pain score was also better in RD group than RC group. The difference in reversibility of sedation may be due to differences of the elimination half-life of both the drugs [20]. An elimination half-life of 14.6 h of Clonidine indicates a slow on and offset of the drug in comparison to an elimination half-life of 2 h of dexme detomidine [20]. Therefore, dexmedetomidine is more titrable than Clonidine, and recovery is more rapid [21]. However, the incidences of delayed recovery and longer discharge time with dexmedetomidine were also observed by other investigators [22,23]. The variation in different studies may be due to the use of different premedicants, differences in the methodology of study, and type of surgical procedures.

Hemodynamic properties showed reduced HR and $SPO_2$ were observed in both the groups but statistically not significant. Mean arterial pressure was significantly increased in first 20 mins RD GROUP Comparing to the RC group. Dexmedetomidine loses its alpha-2 receptor agonism if infused as bolus via rapid infusion, leading to increase in blood pressure and low heart rate that eventually normalizes in 15 min. This effect is primarily mediated via central alpha2A receptors [24]. Hypertension can also be observed because of activation of alpha-2b receptors [25]. Therefore, extreme care must be taken when using dexmedetomidine in patients who are volume-depleted and have underlying cardiac issues. High doses of dexmedetomidine can result in pulmonary hypertension and can be a limiting factor for its use in patients with underlying cardiac disease.[26]

**Conclusion**

Enhanced recovery after surgery is an approach to patient care that focuses on optimizing the postoperative period. This includes implementing protocols meant to reduce postoperative complications, patient discomfort, and length of hospital stay. Use of dexmedetomidine has been shown to reduce the local anesthetic and analgesic requirements with desired sedation score.

**References**

1. Kamibayashi T, Maze M. Clinical uses of alpha2 - adrenergic agonists.Anesthesiology 2000;93:1345-9.

2. Casati A, Baciarello M. Enantiomeric local an aesthetics: 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; 79:92-105.

4. Pichot C, Longrois D, Ghignone M, Quintin L. Dexmedetomidine and clonidine: A review of their pharmacodynamy to define their role for sedation in intensive care patients. Ann FrAnesthReanim 2012; 31:876-96.

5. Farmery AD, Wilson-MacDonald J. The analgesic effect of epidural clonidine after spinal surgery: A randomized placebo-controlled trial. AnesthAnalg 2009; 108:631-4.

6. Bajwa S, Kul Shrestha A. Dexmedetomidine: An adjuvant making large inroads into clinical practice. Ann Med Health Sci Res 2013; 3:475-83.

7. Ribeiro RN, Nascimento JP. The use of dexmedetomidine in anesthesiology. Rev Bras Anestesiol 2003; 53:97-113.

8. Riessen R, Pech R, Tränkle P, Blume stock G, Haap M. Comparison of the RAMSAY score and the Richmond Agitation Sedation Score for the measurement of sedation depth. Crit Care 2012; 16:3268.

9. Ahmed A, Latif N, Khan R. Post-operative analgesia for major abdominal surgery and its effectiveness in a tertiary care hospital. J AnaesthesiolClinPharmacol 2013; 29:4727.

10. Kehlet H. Acute pain control and accelerated postoperative surgical recovery. SurgClin North Am 1999; 79:431-43.

11. Block BM, Liu SS, Rowling son AJ, Cowan AR, Cowan JA Jr., Wu CL, et al. Efficacy of postoperative epidural analgesia: A meta-analysis. JAMA 2003; 290:2455-63.

12. Moraca RJ, Sheldon DG, Thirlby RC. The role of epidural anesthesia and analgesia in surgical practice. Ann Surg 2003; 238:663-73.

13. Bajwa SJ, Kaur J. Clinical profile of levobupivacaine in regional anesthesia: A systematic review. J AnaesthesiolClinPharmacol 2013; 29:530-9.

14. Saravana Babu M, Verma AK, Agarwal A, Tyagi CM, Upadhyay M, Tripathi S, et al. A comparative study in the post-operative spine surgeries: Epidural Ropivacaine with dexmedetomidine and Ropivacaine with clonidine for post-operative analgesia. Indian J Anaesth 2013; 57:371-6.

15. Kaye AD, Chernobyl sky DJ, Thakur P, Siddaiah H, Kaye RJ, Eng LK, Har bell MW, Lajaunie J, Cornett EM. Dexmedetomidine in enhanced recovery after surgery (ERAS) protocols for postoperative pain. Current pain and headache reports. 2020 May;24(5):1-3.

16. Ribeiro RN, Nascimento JP. The use of dexmedetomidine in anesthesiology. Rev Bras Anestesiol 2003; 53:97-113.

17. LindeHe Mo. The clinical use of dexmedetomidine. Rev Bras Anestesiol 2004; 54:1-4.

18. chiru Vella S, Donthu B, Nall am SR, Salla DB. Postoperative analgesia with epidural dexmedetomidine compared with clonidine following total abdominal hysterectomies: a prospective double-blind randomized trial. Anesthesia: Essays and Researches. 2018 Jan 1;12(1):103.

19. Bajwa SJ, Bajwa SK, Kaur J, Singh G, Arora V, Gupta S, Kul Shrestha A, Singh A, Parmar SS, Singh A, Goraya SP. Dexmedetomidine and clonidine in epidural anaesthesia: A comparative evaluation. Indian journal of anaesthesia. 2011 Mar;55(2):116.

20. Klimscha W, Chiari A, Krafft P. Hemodynamic and analgesic effects of clonidine added repetitively to continuous epidural and spinal blocks. AnesthAnalg 1995; 80:322-7.

21. Fukushima K, Nishimi Y, Mori K. The effect of epidural administered dexmedetomidine on central and peripheral nervous system in man. AnesthAnalg 1997;84: S292.

22. Schein in M, Pihlavisto M. Molecular pharmacology of alpha2- adrenoceptor agonists. Bailliere'sClinAnaesth 2000; 14:247-60.

23. Correa-Sales C. A hypnotic response to dexmedetomidine, an alpha-2 agonist, is mediated in the locus coeruleus in rats. Anesthesiology 1992; 76:948-52.

24. 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.

25. Buerkle H. Peripheral anti-nociceptive action of alpha2- adrenoceptor agonists. Bailliere'sClinAnaesth 2000; 14:411-8.

**Legend Tables and Figures**

Table 1: The demographic profile of patients of both the groups

| Demographic characteristics | RD (n=30) Mean±SD | RC (n=30) Mean±SD | P value |
|---|---|---|---|
| Age (years) | 43.83±4.91 | 44.04±4.24 | 0.321 |
| Weight (kg) | 58.24±6.7 | 59.96±6.1 | 0.431 |
| Body mass index | 29.32±3.08 | 28.04±3.46 | 0.542 |
| ASA I/II | 21/9 | 23/7 | 0.329 |
| Mean duration of surgery | 95.95 | 93.42 | 0.251 |

Table 2: Comparison of bolus dose characteristics in both the groups

| Bolus characteristics | Group RD (n=30) | Group RC (N=30) | P value | T score |
|---|---|---|---|---|
| Onset of analgesia(mins) | 7.67±2.12 | 9.28±1.98 | 0.0017* | 3.03 |
| Time to peak analgesia (mins) | 11.34±3.12 | 13.79±4.09 | 0.005* | 2.60 |
| Time to first rescue top-up | 365.11±19.31 | 317.85±17.63 | <0.0001* | 9.899 |
| Need of Rescue analgesics % | 11(37%) | 19(63%) | 0.192 | 0.867 |
| Total dose of Ropivacaine used | 51.17±14.18 | 68.23±17.33 | <0.0001* | 4.172 |
| Mean Ramsay Sedation score | 2.11±0.98 | 2.98±1.1 | 0.001* | 3.23 |

Table 3: Comparison of post-operative sedation and pain score among study group

| Parameters | Group RD No. of patients % | Group RC No. of patients /% | p |
|---|---|---|---|
| Ramsay Sedation Score | | | |
| Score 1 | 3 (10%) | 7 (23%) | 0.113 |
| Score 2 | 23 (77%) | 15 (50%) | 0.09 |
| Score 3 | 4 (13%) | 8 (27%) | 0.123 |
| Score 4 | 0 | 0 | - |
| Score 5 | 0 | 0 | - |
| Parameters | Group RD (mean) | Group RC (mean) | p |
| VAS score | | | |
| VAS at 0 | 4.12±0.96 | 5.20±1.14 | 0.0001** |
| VAS at 2 hrs | 1.95±0.89 | 2.70±0.99 | 0.001* |
| VAS at 9 hrs | 2.41±1.01 | 3.14±1.02 | 0.003* |
| VAS at 16 hrs | 2.65±0.98 | 3.40±0.96 | 0.002* |
| VAS at 24 hrs | 3.55±1.12 | 4.10±1.10 | 0.02* |

Table 4: Comparison of Adverse effects among study group

| Side effects | Group RD no. of patients % | Group RC No. of patients % |
|---|---|---|
| Nausea | 2 (7%) | 4 (13) |
| Vomiting | 1 (3%) | 1 (3%) |
| Headache | 1 (3%) | 2 (7%) |
| Dizziness | 1 (3%) | 2 (7%) |
| Dry mouth | 1 (3%) | 0 |
| Total | 6 (19%) | 9 (30%) |

Figure 1: Comparison of heart rate changes between two groups

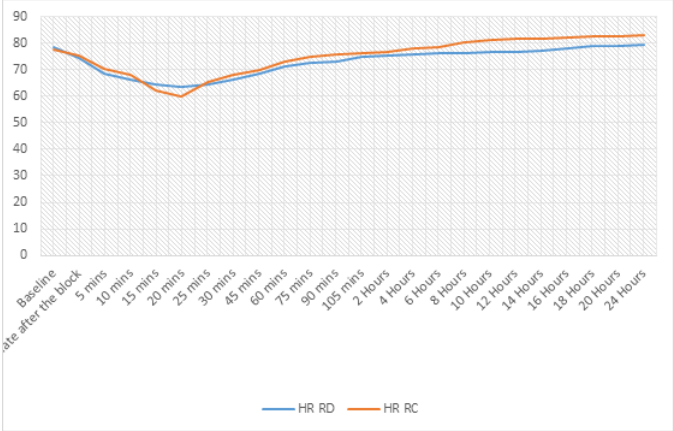


Figure 2: Comparison of MAP changes between two groups

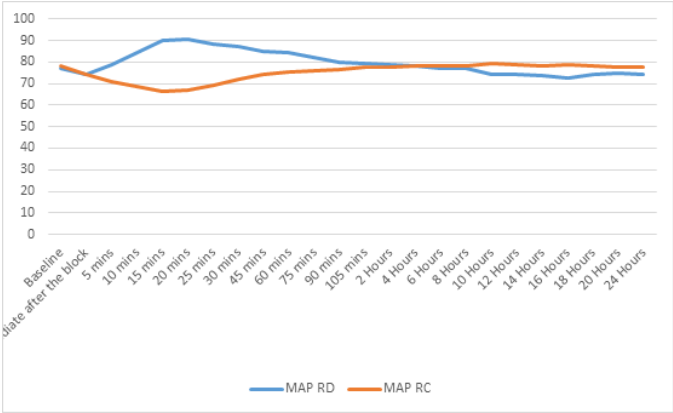


Figure 3: Comparison of $SPO_2$ changes between two groups