

Comparison of the Effect of Dexmedetomidine and Clonidine as an Adjuvant to Epidural Levobupivacaine on Duration of Post-Operative Analgesia in Total Abdominal Hysterectomy-A Randomized Controlled Trial

Mahesh Kumar Murugan^{1*}, Karthik K², Vishak Manoj Baskar³, Jayaprithika⁴

¹SRM Medical College Hospital And Research Centre, Address: Mahesh Kumar M, No 28, Narayanaswamy main road, West Saidapet, Chennai 600015. E mail ID: muruganmahesh97@gmail.com, ORCID: 0009-0000-5428-8634, Contribution: study design and sample collection, statistics, manuscript writing

²Professor, Contributing author, Address: B block, 2nd floor, Department of anesthesiology, SRM MCH and RC, kattankulathur 603203, Affiliation: Professor, SRM Medical College Hospital and Research Centre, Email ID: karthikkishnamoorthy1981@gmail.com, ORCID: 0000-0002-8537-3716, Contribution: statistics, manuscript review and alignment, discussion,

³Address: pattathuvila, TC30/1664, Pettah, Trivandrum 695024, Affiliation: Assistant professor, SRM Medical College Hospital and Research Centre, ORCID: 0000-0001-9997-4435, Email ID: manojvishak@gmail.com, Contribution: statistics, discussion and limitations

⁴1/24, vellikkidangu, Vandhuvancherry (PO), Vedharamyam (TK), Nagapattinam 614714, Affiliation: senior resident, SRM Medical College Hospital and Research Centre, ORCID: 0009-0001-8757-4714, E mail ID: preethimaniarumugam96@gmail.com, Contribution: discussion and limitations

Abstract

Background: The combination of local anesthetics with α_2 -adrenergic agonists enhances both quality and duration of analgesia. clonidine has been extensively studied, but dexmedetomidine remain limited. This study aims to compare clonidine and dexmedetomidine as adjuvants to epidural levobupivacaine in patients undergoing total abdominal hysterectomy. The primary objective was to compare the effects of dexmedetomidine and clonidine as adjuvants to epidural levobupivacaine on the duration of postoperative analgesia.

Materials and methods: Patients were randomized into two groups -Group C received 15 ml of 0.5% levobupivacaine with 1 mcg/kg clonidine epidurally. Group D received 15 ml of 0.5% levobupivacaine with 1 mcg/kg dexmedetomidine epidurally. Postoperative pain was evaluated using the Visual Analog Scale (VAS). Onset of sensory blockade, motor blockade and the total number of 0.125% levobupivacaine boluses administered on postoperative day 0 (POD 0) were also recorded.

Result: Group C (clonidine) had a significantly longer duration of analgesia than Group D (dexmedetomidine) (452.5 vs 371.2 minutes, $p < 0.001$). Group D showed a faster onset and wider spread of sensory block, as well as more intense motor blockade (T6– T12, $p < 0.001$). Analgesic requirements on POD 0 were comparable between groups. Hemodynamic stability was significantly better in Group D from 5 to 120 minutes intraoperatively ($p < 0.001$). Heart rate was stable in Group D across all time intervals ($p < 0.01$).

Conclusion: Dexmedetomidine at a dose of 1 mcg/kg is an effective adjuvant to levobupivacaine for epidural anesthesia, which is comparable to clonidine.

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Key words: local anesthetics, dexmedetomidine, clonidine, analgesia, Postoperative pain, epidural anesthesia.

Introduction

The modern anesthetic practice has made regional anaesthesia an essential part due to the effectiveness, safety, and cost-efficiency of the method in a broad spectrum of surgery. The regional methods reduce the use of systemic analgesic agents, allow maintenance of airway reflexes, and promote faster recovery, therefore, improving overall patient outcomes [1]. Epidural anaesthesia is especially effective in situations involving long surgeries as well as offering effective postoperative analgesia [2]. Its application has been linked with early mobilisation, decreased opioid dose, and decreased rates of postoperative pulmonary and thromboembolic complications particularly in infra-umbilical surgeries such as total abdominal hysterectomies [2,3]. Effective postoperative pain management is an important concern, as inadequately controlled pain may restrict ambulation, elevate morbidity, extend hospital stays, and diminish patient satisfaction. However, this method is limited by the potential for systemic toxicity, especially concerning cardiovascular and central nervous systems [4]. Levobupivacaine, pure S (–) enantiomer of bupivacaine, produces effective sensory blockade with relatively less motor blockade, making it well suited for postoperative analgesia while allowing early mobilization [6]. Clonidine, α_2 -agonists used in clinical practice, has been shown to prolong motor and sensory blockade along with improve postoperative analgesia after administered

epidurally. Dexmedetomidine, newer or more selective α_2 -agonist, provides stronger analgesic and sedative effects with a characteristic arousable sedation and has been shown to further prolong the period of neuraxial blockade [8].

Aims and Objective:

To compare the effect of dexmedetomidine and clonidine as adjuvants to epidural levobupivacaine on the duration and quality of postoperative analgesia in patients undergoing total abdominal hysterectomy.

The Primary Objective is to compare duration of postoperative analgesia among dexmedetomidine and clonidine when used as adjuvants to epidural levobupivacaine and the Secondary objective is to compare the onset time of sensory blockade among 2 study groups, to compare the onset time of motor blockade among 2 study Groups, total no. of 0.125% levobupivacaine 6 ml stat dose on POD #0 and to evaluate and compare hemodynamic changes associated with two adjuvants.

Materials and methods:

This study has been designed as randomized (simple randomization), prospective, controlled clinical trial in contrast having effect of dexmedetomidine as well as clonidine as adjuvants to epidural levobupivacaine on duration as well as quality of postoperative analgesia in patients going through lower abdominal surgeries. The study has been held in SRM Medical College Hospital and Research Centre, Kattankulathur.

Ethical considerations, study has been held in accordance with Biomedical as well as Health Research Guidelines of Indian Council of Medical Research (ICMR) and in compliance with principles of Declaration of Helsinki (2013). Informed consent forms, participant information sheet and the study protocol were reviewed and accepted by Institutional Ethics Committee, SRM Medical College Hospital and Research Centre, Kattankulathur. Ethical Clearance Number: SRMIEC-ST0724-1753, dated 15 October 2024, following review and approval during the IEC meeting. Subject selection, Each participant was well informed of the study by written consent before they have been enrolled in study. Inclusion criteria includes, Patients aged 18 to 65yrs of both sexes, ASA physical status I, II, III, Patients scheduled for elective lower abdominal surgeries. Exclusion criteria includes Sepsis or coagulopathy, Uncorrected hypovolemia, local infection at epidural insertion site, Pre-existing neurological disorders Significant cardiac, hepatic, or renal disease, BMI 30 kg/m², Surgeries expected to last more than two hours, Patient not giving consent or refusal to participate. After obtaining ethical committee approval, CTRI approval (CTRI was done) and informed written consent, Patients were enrolled using simple random sampling and randomized into two groups using a coding system in computer-generated randomization table. Group D (n = 32), Epidural levobupivacaine with Dexmedetomidine, Group C (n = 32): Epidural levobupivacaine with Clonidine, this study adheres to consort guidelines shown, concert flow chart (figure 1). The person who enrolled and assigned participants to the interventions had no access to the random allocation sequence and the participants were blinded. All patients underwent a thorough pre-anesthetic evaluation, including detailed history, clinical examination, and routine laboratory investigations. Baseline vital parameters such as heart rate, blood pressure, respiratory rate, and oxygen saturation were recorded. In the operating theatre, standard monitors were attached. Under strict aseptic precautions, patients were placed in the sitting position. The L3–L4 intervertebral space was identified, and the epidural space was located using an 18G Tuohy needle by the loss-of-resistance to air technique. An epidural catheter was threaded 5 cm into the epidural space, with the tip positioned around the T12 level. A test dose of 3 mL of 2% lignocaine with 1:200,000 adrenaline was administered to rule out intrathecal or intravascular placement. Group D: Received 15 mL of 0.5% levobupivacaine with dexmedetomidine 1 µg/kg epidurally, Group C: Received 15 mL of 0.5% levobupivacaine with clonidine 1 µg/kg epidurally. The study drug was administered slowly through the epidural catheter as per randomization. The drugs used in the study were commercially available preparations of levobupivacaine, clonidine, and dexmedetomidine. Sensory blockade was assessed using a cold swab test until onset of sensory block at T8 dermatome. Time to onset of sensory block and Maximum sensory level achieved was noted. Assessment of motor blockade was done using Modified Bromage scale. Patients were monitored for Heart rate, Mean arterial pressure, Oxygen saturation, Respiratory rate. Measurements were recorded at 5-minute intervals initially, followed by 10-minute intervals (figure 2). Patients were monitored for complications such as: Hypotension and bradycardia, Appropriate treatment was provided as per institutional protocol. Patients were monitored for complications such as Hypotension and bradycardia; Appropriate treatment was provided as per institutional protocol. Duration of postoperative analgesia was assessed by recording the time to first request for rescue analgesia (Break out interval). Patients were followed until complete regression of sensory and motor blockade.

Data entry and analysis: Microsoft Excel 2013 has been utilised to enter patient data as well as create a master chart, which will be made available as an accessory file. We double-checked the entered data for errors. Statistical Package for Software Solutions (SPSS) version 21 has been utilised to analyze the data that was exported from the master chart.

SAMPLE SIZE CALCULATION

Sample size was calculated from the study by Sheikh SI et al (2017) [50]., based on comparison of duration of sensory regression between the two groups, using the following parameters:

- $\alpha = 0.05$ ($Z_{\alpha/2} = 1.96$)
- Power = 80% ($Z_{\beta} = 0.84$)
- Mean duration in dexmedetomidine group (M_1) = 314.17
- Mean duration in clonidine group (M_2) = 298.73
- Standard deviations: $S_1 = 18.8$, $S_2 = 20.6$

Using the formula:

$$n = \frac{(Z_{\alpha/2} + Z_{\beta})^2 \times (S_1^2 + S_2^2)}{(M_1 - M_2)^2}$$

The calculated sample size was 26 patients per group.

Accounting for possible dropouts (6 patients per group), the final sample size was 32 patients in each group, making a total of 64 patients.

n=6, not meeting inclusion criteria, n=4 refused to participate, other reasons n=4.

Descriptive statistics (standard deviation and mean) have been utilized to display continuous variables, whereas frequency distribution as well as percentage have been utilised to display categorical variables. Chi-square tests have been utilised to observe for associations between categorical variables, and p-value of 0.05 has been estimated statistically significant.

RESULTS:

The mean breaks out interval (mean duration of analgesia) in Group D was 371.2 ± 29.69 minutes and in Group C was 452.5 ± 28.95 minutes (Table 1 & Figure 2). The difference between the groups was indicating a statistically significant difference with a P value of <0.001 . Group C showed a significantly longer breakout interval compared to Group D. Figure 2 shows the Comparison of mean duration of postoperative analgesia (breakout interval) between groups

Sensory blockade levels at T6, T8, T10, and T12 (Table 2 & Figure 3). The mean sensory levels in Group D were T6: 9.1 ± 0.31 , T8: 8.2 ± 0.28 , T10: 7.3 ± 0.20 , and T12: 6.4 ± 0.22 , while in Group C, the corresponding means were T6: 12.1 ± 0.48 , T8: 11.1 ± 0.45 , T10: 10.1 ± 0.39 , and T12: 9.0 ± 0.49 . The differences between groups at all levels were statistically significant, with a P value of <0.001 . Earlier onset and broader spread of sensory blockade were observed

in Group D across all dermatomes ($p < 0.001$).

Motor blockade scores at all tested dermatomal levels (T6, T8, T10, and T12) (Table 3 & Figure 4). The mean motor blockade scores in Group A were 18.3 ± 1.21 at T6, 17.3 ± 1.22 at T8, 16.4 ± 1.26 at T10, and 15.5 ± 1.26 at T12. In comparison, Group C showed lower mean scores of 14.7 ± 1.17 , 13.7 ± 1.17 , 12.7 ± 1.12 , and 11.7 ± 1.10 at the same levels, respectively. Independent samples t-tests revealed highly significant differences across all levels, with P values < 0.001 . Motor blockade was more intense in Group D with significantly higher scores at T6 to T12 ($p < 0.001$).

As illustrated in Table 4 and graphical representation in Figure 5, the mean number of doses of 0.125% levobupivacaine 6 ml administered on postoperative day 0 (POD 0) was significantly higher in Group D (5.34 ± 0.902) compared to Group C (3.3 ± 0.693). Postoperative analgesic requirement was significantly higher in Group D than Group C on POD 0 ($p < 0.001$). Figure 7 shows Comparison of rescue analgesic requirement (number of 0.125% levobupivacaine doses on POD 0) between Groups.

Discussion:

This study compared dexmedetomidine and clonidine as adjuvants to epidural levobupivacaine in total abdominal hysterectomy, focusing on postoperative analgesia, block characteristics, analgesic requirements, and hemodynamic stability. Clonidine significantly prolonged postoperative analgesia compared with dexmedetomidine (452.5 vs. 371.2 min, $p < 0.001$) and reduced rescue analgesic requirements (3.3 vs. 5.34 doses, $p < 0.001$). Conversely, dexmedetomidine produced a faster onset and denser sensory and motor blockade and provided more stable perioperative hemodynamics, including superior control of blood pressure and heart rate ($p < 0.001$). In this study of total abdominal hysterectomy, clonidine provided a significantly longer duration of postoperative analgesia than dexmedetomidine when used as an adjuvant to epidural levobupivacaine ($p < 0.001$). This finding contrasts with most previous studies reporting superior analgesic duration with dexmedetomidine. Studies by Saravana Babu M et al. in spine surgery and Swami SS et al. in brachial plexus blocks, demonstrated longer analgesia with dexmedetomidine [1–4]. Differences in drug dosing and pain assessment methods may account for this discrepancy.

Previous studies have largely demonstrated superior analgesic duration with dexmedetomidine. Swami SS et al. reported significantly longer analgesia with dexmedetomidine than clonidine in supraclavicular brachial plexus blocks for upper limb surgeries (456 ± 97 vs. 289 ± 62 min) [4]. In contrast, Neogi M et al. reported comparable analgesic durations with both agents in pediatric caudal blocks [6]. The present finding of longer analgesia with clonidine highlights that the relative efficacy of these α_2 -agonists may vary with surgical context, local anesthetic choice, dosing, and pain assessment methods.

Onset and spread of sensory blockade, In the present study, patients receiving dexmedetomidine with levobupivacaine achieved faster onset and broader spread of sensory blockade compared with clonidine. Sensory block to T6 and T8 levels was established earlier in the dexmedetomidine group, indicating a more rapid and extensive distribution. These findings are in line with several other studies. Arun Kumar A et al. demonstrated that dexmedetomidine produced a significantly earlier onset of sensory blockade (8.53 ± 1.81 min) compared with clonidine (11.93 ± 1.96 min), along with greater dermatomal spread [1]. Similarly, Bajwa SJ et al. reported a faster attainment of sensory level at T10 with dexmedetomidine (8.52 ± 2.36 min) than clonidine (9.72 ± 3.44 min) [2]. Salgado RF et al. further supported these observations, showing that dexmedetomidine in combination with ropivacaine enhanced the quality of sensory blockade [7]. Further studies support these findings. Agarwal S et al. reported a faster onset and earlier attainment of maximum sensory block with dexmedetomidine than clonidine when added to epidural bupivacaine [9]. Similarly, Shaikh SI demonstrated a shorter onset time and faster achievement of maximum sensory block with dexmedetomidine, with comparable dermatomal spread between groups [11]. Dexmedetomidine's higher α_2/α_1 selectivity and greater lipid solubility enhance spinal α_2 -receptor binding, resulting in faster onset, denser blockade, and greater sympatholysis, which likely explains the earlier onset and wider sensory spread observed across studies [1,12,13].

Motor blockade in the present study, dexmedetomidine was associated with a denser motor block compared to clonidine, as evidenced by higher Bromage scores at both T6 and T8 dermatomal levels ($p < 0.001$). These findings indicate that dexmedetomidine, when used as an adjuvant to epidural levobupivacaine, produces an earlier and profound motor blockade. Literature shows variable results regarding motor block onset. Bajwa SJ et al. reported a faster onset with dexmedetomidine than clonidine, possibly due to higher adjuvant doses [2]. Agarwal et al. noted delayed onset with clonidine but earlier motor recovery, suggesting a trade-off between onset and duration [9]. In contrast, Arun Kumar A et al. reported no significant difference in the time to complete motor blockade between

the two groups Sheikh SI also supported these findings, showing delayed regression of motor block with dexmedetomidine relative to clonidine [11]. Thus, these studies suggest that while dexmedetomidine may not consistently shorten the onset of motor block, it generally provides a denser and more sustained blockade than clonidine. Dexmedetomidine's higher $\alpha_2:\alpha_1$ selectivity (1600:1 vs. 220:1 for clonidine) suppressing excitatory neurotransmitter release and potentiating local anesthetic effects on motor and sensory fibers. Its greater lipophilicity also facilitates neural penetration, collectively accounting for the denser and more prolonged motor blockade [1,12,14].

Postoperative Analgesic Requirement On postoperative day 0, patients in the dexmedetomidine group required more epidural top-up doses of 0.125% levobupivacaine (5.34 ± 0.90) than those in the clonidine group (3.30 ± 0.69 ; $p < 0.001$), indicating that clonidine provided more effective early postoperative analgesia. Several studies report reduced rescue analgesic requirements with dexmedetomidine. Arun Kumar A et al. found fewer rescue doses compared to clonidine, consistent with longer sensory blockade [1], while Jain D, Salgado RF, and Sheikh SI observed prolonged sensory and motor blocks and delayed need for analgesia with dexmedetomidine [7,8,11]. In contrast, some studies show variable results. Bajwa SJ et al. reported only moderate prolongation of time to rescue analgesia with dexmedetomidine [2]. Overall, epidural α_2 -agonists, whether clonidine or dexmedetomidine, enhance postoperative pain control and often eliminate the need for systemic rescue agents [16– 18].

Perioperative Hemodynamic Stability. In this study, dexmedetomidine provided more stable intraoperative heart rate and blood pressure than clonidine, likely due to its stronger sympatholytic effect, which attenuates catecholamine-mediated stress responses and blunts perioperative hemodynamic fluctuations (e.g., SBP 62.3 ± 5.0 vs. 89.4 ± 7.6 ; DBP 81.4 ± 6.6 vs. 47.4 ± 4.4 ; HR 69.5 ± 4.3 vs. 75.8 ± 4.4 ; all $p < 0.001$) [12]. Enhanced hemodynamic stability with dexmedetomidine is especially beneficial in high-risk patients with cardiovascular comorbidities. Although α_2 -agonists may cause mild, predictable hypotension or bradycardia, these events were easily managed and required no intervention in our study [19]. Arun Kumar A et al. reported $\approx 20\%$ reductions in heart rate and $\approx 25\%$ in blood pressure 30–50 minutes post-epidural, with no significant difference between dexmedetomidine and clonidine [1]. Similarly, Bajwa SJ and Schnaider TB et al. observed modest ($\sim 15\%$) declines without increased need for rescue interventions. Epidural dexmedetomidine has been associated with more pronounced hemodynamic effects. Jain D et al. reported significant pulse rate reductions versus saline [8], and Fukushima K et al. observed decreased heart rate and blood pressure within 10 minutes of $2 \mu\text{g/kg}$ dexmedetomidine [21], consistent with our findings. Saravana Babu M et al. noted greater blood pressure declines with clonidine than dexmedetomidine, without clinically significant bradycardia, hypotension, or respiratory compromise [3]. These results underscore dexmedetomidine's utility as an epidural adjuvant, offering effective analgesia with stable cardiovascular profiles.

Adverse effects and Complications in this study, no major adverse events occurred, and hemodynamics remained stable without significant respiratory depression, sedation, or motor complications. Agarwal S et al. and Shaikh SI et al. reported hypotension as the most common effect, consistent with α_2 -agonist pharmacodynamics, with sedation generally more pronounced for dexmedetomidine [9,11]. Krishnamurthy BK et al. reported no clinically significant complications with either adjuvant during ultrasound-guided adductor canal blocks for total knee replacement, indicating that both agents have a favorable safety profile with only mild, manageable adverse effects [5]. Clonidine is preferable for prolonged postoperative analgesia and reduced rescue analgesic needs, while dexmedetomidine provides faster onset, denser sensory and motor blockade, and superior intraoperative hemodynamic stability—beneficial for high-risk cardiovascular patients. The choice of epidural adjuvant should be individualized based on perioperative risk, surgical conditions, and the desired balance between analgesic duration, block characteristics, and hemodynamic control.

LIMITATIONS

The relatively small sample size ($n = 64$) may limit the statistical power of the study and restrict generalizability of the findings. Regression times of sensory and motor blockade were not recorded, limiting comprehensive assessment of block duration. The study evaluated only short-term outcomes; long-term safety and potential neurological sequelae were not assessed. The study population was restricted to patients undergoing infra-umbilical surgeries, which may limit applicability to other surgical procedures or anatomical regions.

CONCLUSION

Both dexmedetomidine and clonidine are effective epidural adjuvants to levobupivacaine for total abdominal hysterectomy surgeries. Dexmedetomidine offers faster onset and denser sensory and motor blockade, while

clonidine provides longer postoperative analgesia with fewer rescue doses. Choice of adjuvant should be based on the clinical need for rapid block onset or prolonged pain relief.

DECLARATIONS

1. Abrivations:

SA	Spinal anaesthesia
PDPH	Post-dural puncture headache
USG	Ultrasonography
RA	Regional anaesthesia
IVS	Intervertebral space
PUS	Pre-procedural ultrasound
RUS	Real-time ultrasound
LA	Local anaesthesia
CSF	Cerebrospinal fluid
IV	Intravenous
PNS	Peripheral nervous system
µm	Micrometre
CNB	Central neuraxial block
MHz	Mega Hertz
cm	Centimetre
PS	Paramedian sagittal
PSO	Parasagittal oblique view
TI	Transverse interspinous view
GA	General anaesthesia
MAC	Minimal Alveolar Concentration
ASRA	American Society of Regional Anaesthesia
MI	Myocardial ischaemia
DVT	Deep vein thrombosis
POD	Postoperative delirium
POCD	Post-operative cognitive dysfunction
ASA PS	American Society of Anaesthesiologists Physical Status
BMI	Body mass index
CSE	Combined spinal epidural
RCT	Randomized control trial
Tab	Tablet
HR	Heart rate
RR	Respiratory rate
SpO2	Oxygen saturation
NIBP	Non-invasive blood pressure
ECG	Electrocardiogram
ml	Millilitre
µg	Microgram
mg	Milligram
Inj	Injection
Group R	Group real-time ultrasound
Group P	Group pre-procedural ultrasound
IQR	Inter-quartile range
%	Percentage
mmHg	Millimetres of Mercury
min	Minutes

sec	Seconds
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Ethics Approval: This research was conducted in accordance with the declaration of Helsinki and the appropriate ethical approval for this study was obtained from the institutional ethics Committee of SRM Medical College Hospital and Research Centre.

Approval no.: SRMIEC-ST0724-1753

Consent to Participate: Written and Informed Consent was obtained from all participants prior to inclusion in the study.

Consent for publication: Not Applicable available data and material :All data supporting the findings of this study are available within the paper and its Supplementary Information.

Competing interests: The authors declare that they have no competing interests.

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Authors' Contributions: M.M. contributed in study design and sample collection, statistics, manuscript writing. K.K. helped with conceptualization and study design. V.M helped with review of the final draft. J.A helped with manuscript writing.

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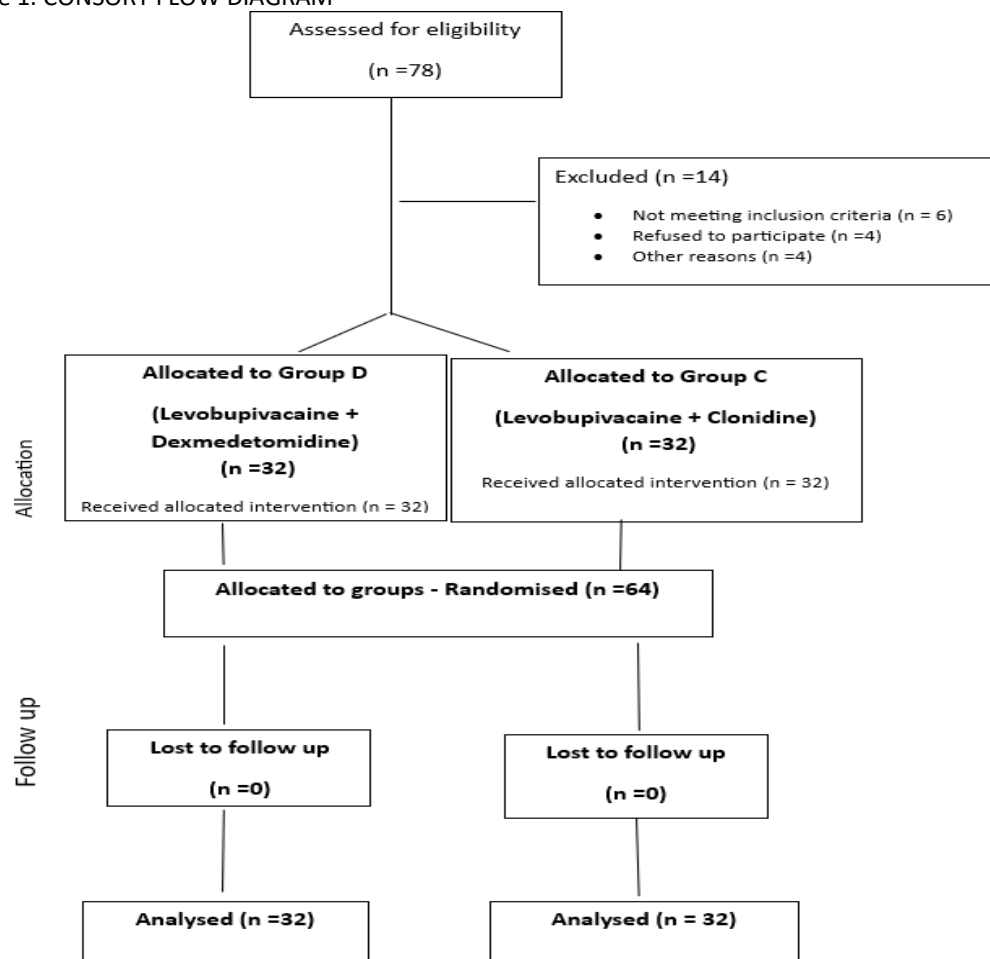
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Figure 1. CONSORT FLOW DIAGRAM



Tables:

Table 1: Comparison of mean duration of postoperative analgesia (breakout interval) between groups

Break out interval (in mins)	Mean	Std. Deviation	T value	P value
Group D	371.2	29.69	-11.089	<0.001*
Group C	452.5	28.95		

Table 2: Comparison of sensory blockade onset and spread (T6–T12 levels) between groups

Sensory Blockade (in mins)		Mean	Std. Deviation	T value	P value
T6	Group D	9.1	0.31	-29.305	<0.001*
	Group C	12.1	0.48		
T8	Group D	8.2	0.28	-30.837	<0.001*
	Group C	11.1	0.45		
T10	Group D	7.3	0.2	-36.314	<0.001*
	Group C	10.1	0.39		
T12	Group D	6.4	0.22	-27.07	<0.001*
	Group C	9	0.49		

Table 3: Comparison of motor blockade intensity (T6–T12 levels) between groups

Motor blockade (in mins)		Mean	Std. Deviation	T value	P value
T6	Group D	18.3	1.21	12.321	<0.001*
	Group C	14.7	1.17		
T8	Group D	17.3	1.22	12.244	<0.001*
	Group C	13.7	1.17		
T10	Group D	16.4	1.26	12.512	<0.001*
	Group C	12.7	1.12		
T12	Group D	15.5	1.26	12.592	<0.001*
	Group C	11.7	1.1		

Table 4: Comparison of rescue analgesic requirement (number of 0.125% levobupivacaine doses on POD 0) between Groups

0.125% levobupivacaine 6 ml stat dose on POD 0	Mean	Std. Deviation	T value	P value
Group D	5.34	0.90	10.104	<0.001*

Group C	3.3	0.69		
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FIGURES:

Figure 1. CONSORT FLOW DIAGRAM

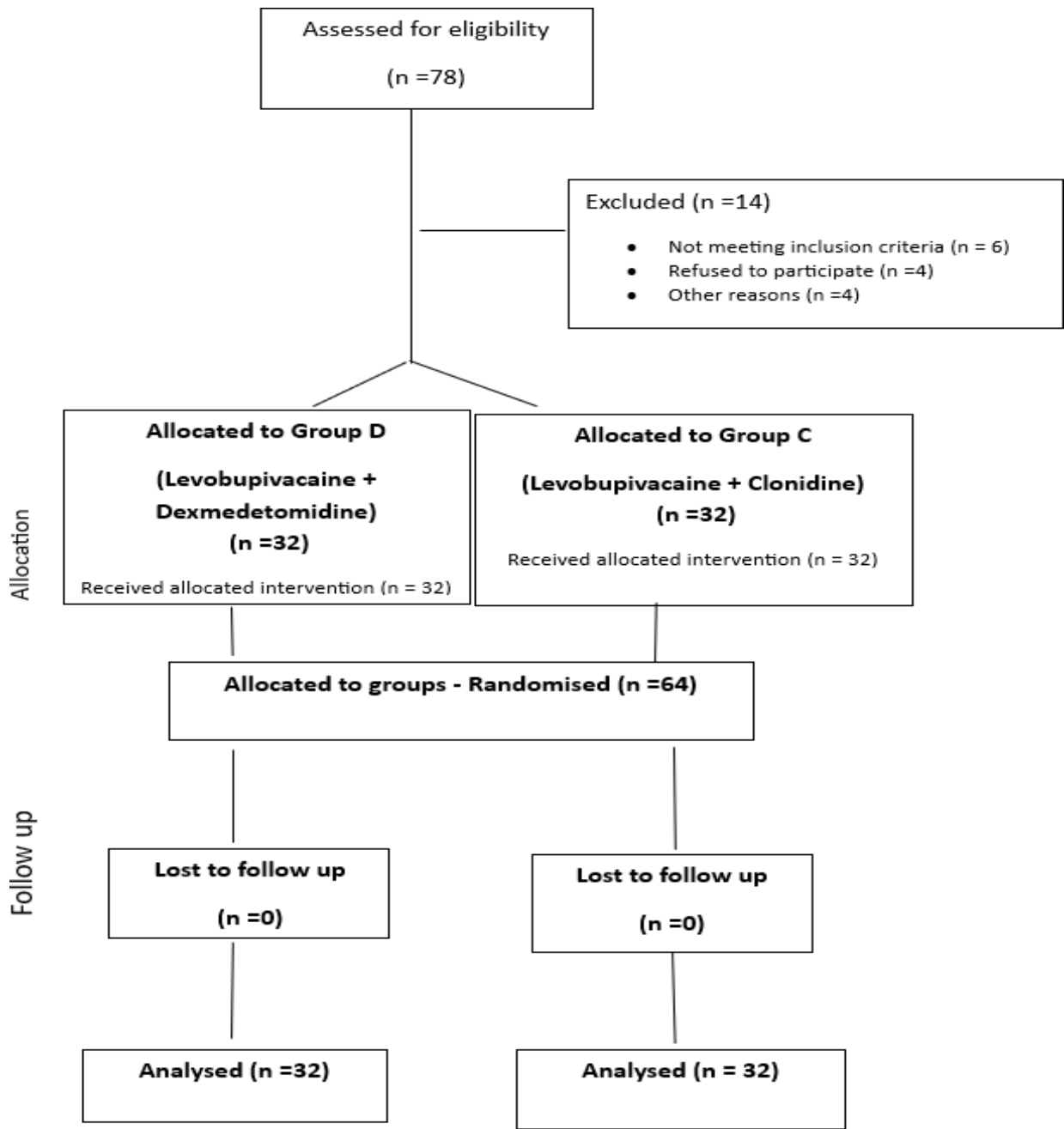


Figure 2: Comparison of mean duration of postoperative analgesia (breakout interval) between groups (in mins)

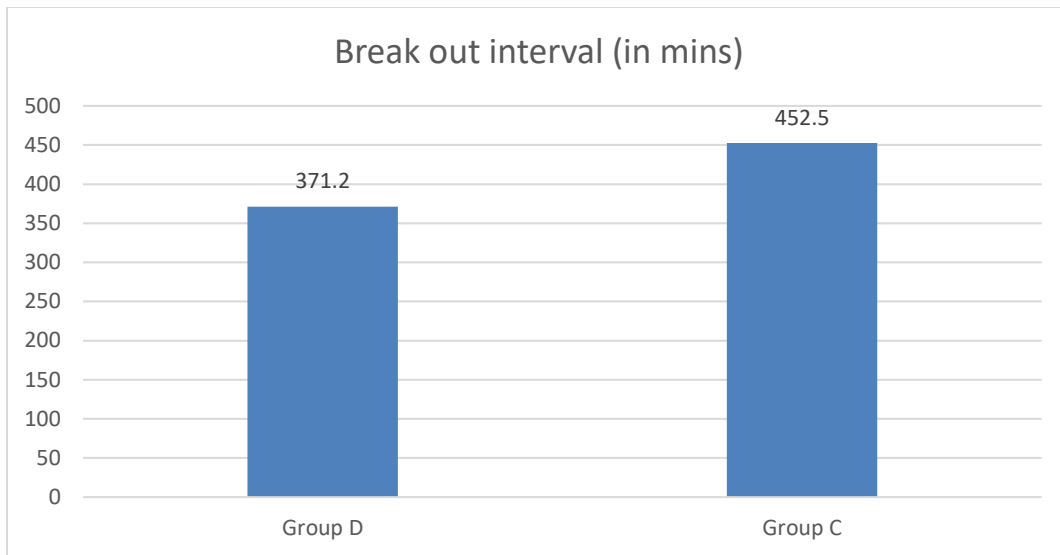


Figure 3: Comparison of sensory blockade onset and spread (T6–T12 levels) between groups

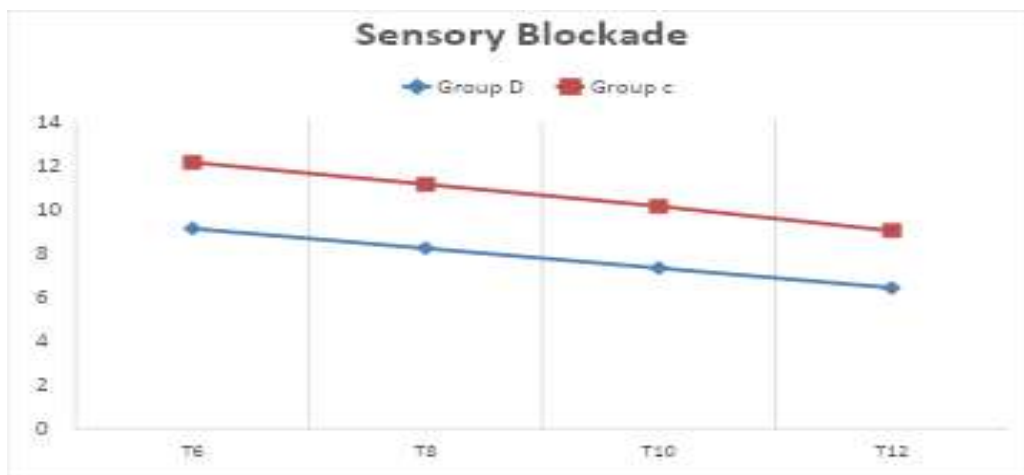


Figure 4: Comparison of motor blockade intensity (T6–T12 levels) between groups

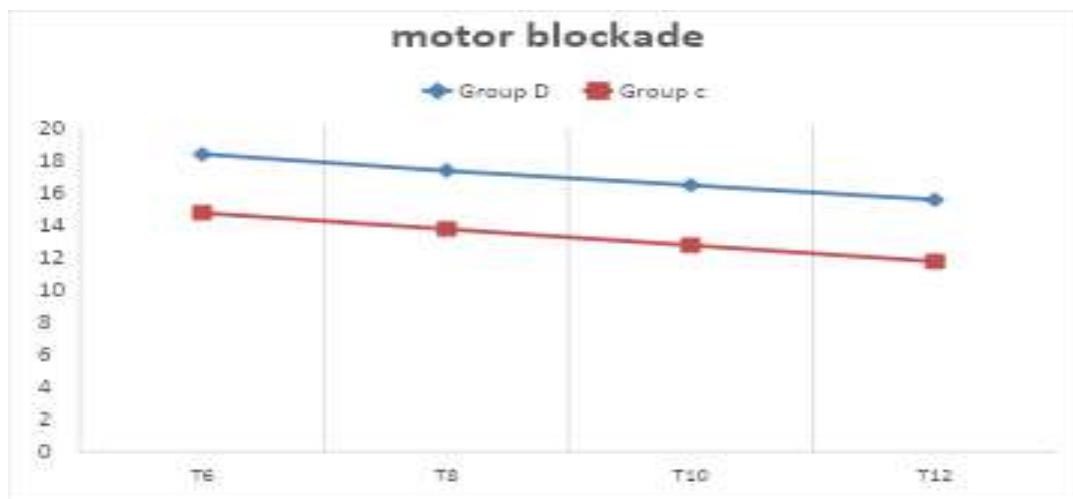


Figure 5: Comparison of rescue analgesic requirement (number of 0.125% levobupivacaine doses on POD 0)

between Groups

