

## ORIGINAL RESEARCH

## REGIONAL ANESTHESIA

# Dexmedetomidine vs dexamethasone as adjuvants to levobupivacaine in ultrasound-guided erector spinae plane block for patients undergoing modified radical mastectomy: a randomized double-blind study

Heba Ismail Ahmed<sup>1</sup>, Ashgan Raouf Ali<sup>2</sup>, Norhan Hisham El Emam<sup>3</sup>, Mohamed Magdy<sup>4</sup>,  
Reham Mohamed Gamal<sup>5</sup>

**Author affiliation:**

1. Heba Ismail Ahmed, Kasr Alainy, Faculty of Medicine, Cairo University, Cairo- Egypt-11562; E-mail: [drheba@hotmail.com](mailto:drheba@hotmail.com)
2. Ashgan Raouf Ali, Kasr Alainy, Faculty of Medicine, Cairo University, Cairo- Egypt-11562; E-mail: [ashganraouf@yahoo.com](mailto:ashganraouf@yahoo.com)
3. Norhan Hisham El Emam, National Cancer Institute, Cairo University, Cairo- Egypt-11562; E-mail: [norhan24593@icloud.com](mailto:norhan24593@icloud.com)
4. Mohamed Magdy, National Cancer Institute, Cairo University, Cairo- Egypt-11562; E-mail: [mohammed.magdy@nci.cu.edu.eg](mailto:mohammed.magdy@nci.cu.edu.eg)
5. Reham mohamed Gamal, National Cancer Institute, Cairo University, Cairo- Egypt-11562; E-mail: [rehamgamal\\_nci@hotmail.com](mailto:rehamgamal_nci@hotmail.com)

**Correspondence:** Reham Mohamed Gamal; E-mail: [rehamgamal\\_nci@hotmail.com](mailto:rehamgamal_nci@hotmail.com)

## Abstract

**Background & Objective:** Erector Spinae Plane block (ESPB) is used in patients subjected to modified radical mastectomy (MRM) as a part of balanced anesthesia technique, and to offer prolonged postoperative analgesia. Local anesthetic agents are usually combined with various adjuvants to augment the effect. We compared dexmedetomidine (Dex) versus dexamethasone as adjuvants to ESPB in patients undergoing MRM.

**Methodology:** This randomized controlled study involved 90 patients subjected to MRM under general anesthesia with preoperative ESPB using 30 ml levobupivacaine 0.25%. They were randomly assigned into three equal groups according to the adjuvants used. Dex Group (n = 30) received 1 µg/kg dexmedetomidine, Dexa Group (n = 30) received 10 mg dexamethasone, and ESPB Group (n = 30) received no adjuvants. Patients were monitored for pain using VAS scores and vital signs. The primary outcome measure was total morphine consumption. The secondary outcomes were intraoperative fentanyl consumption, pain intensity, and analgesia duration.

**Results:** The postoperative analgesia duration was significantly longer in the Dex group compared with the ESPB group (P = 0.029) but not in the dexamethasone group. Intraoperative fentanyl and postoperative morphine consumption were significantly lower in the Dex group than in the ESPB group. VAS scores were significantly lower in the Dex group than in the ESPB group at rest and movement. VAS scores of the Dexamethasone group were similar to that of the ESPB group at rest and movement.

**Conclusion:** As an adjuvant to levobupivacaine in erector spinae plane block, dexmedetomidine reduces pain at rest and with movement, reduces intraoperative fentanyl and postoperative morphine consumption, and prolongs the analgesia duration. It is superior to dexamethasone in pain reduction and duration of analgesia.

**Key words:** Analgesia; Dexamethasone; Dexmedetomidine; Erector Spinae Plane Block; Radical Mastectomy; Postoperative Pain

**Citation:** Ahmed HI, Ali AR, El Emam NH, Magdy M, Gamal RM. Dexmedetomidine vs dexamethasone as adjuvants to levobupivacaine in ultrasound-guided erector spinae plane block for patients undergoing modified radical mastectomy: a randomized double-blind study. *Anaesth. pain intensive care* 2022;27(1):65–72.

DOI: [10.35975/apic.v27i1.2127](https://doi.org/10.35975/apic.v27i1.2127)

Received: Oct 08, 2022; Reviewed: Nov 10, 2022; Accepted: Nov 22, 2022

## 1. Introduction

Breast cancer is the most common women malignancy worldwide.<sup>1</sup> In Egypt, it accounts for approximately 39% of females suffering from cancer.<sup>2</sup> Surgery is the mainstay treatment of breast cancer, where modified radical mastectomy (MRM) is preferred when conservative surgery is impossible. However, severe acute postoperative pain commonly follows this major procedure.<sup>3</sup> Moreover, persistent postmastectomy pain may affect 20% to 50% of the patients.<sup>4</sup> Acute postoperative pain is a strong risk factor associated with the development of postmastectomy pain.<sup>5</sup>

Therefore, adequate management of acute postoperative pain after MRM is crucial to improve the quality of recovery and prevention of persistent pain. Opioids are considered the core postoperative analgesic choice, but several undesirable adverse effects discourage their use.<sup>6</sup> Various regional techniques have been tried for MRM, including epidurals, paravertebral block, and intercostal nerve block.<sup>7</sup> More recently, ultrasound-guided fascial plane blocks have been used to manage acute postmastectomy pain and help prevent chronic post-surgical pain.<sup>8</sup> These blocks do not interfere with the epidural space and can be used in patients with coagulation disorders.<sup>9</sup>

The erector spinae plane block (ESPB) is one of these fascial plane blocks, where the local anesthetic (LA) is injected deeper to the erector spinae muscle to block somatic and sympathetic fibers.<sup>10</sup> Various adjuvants to LA have been used to improve the quality and duration of nerve block effects, such as nalbuphine,<sup>11</sup> clonidine,<sup>12</sup> dexamethasone,<sup>13</sup> and dexmedetomidine.<sup>14</sup> Evidence suggests that dexamethasone as an adjuvant to peripheral nerve block may prolong the duration of sensory block and reduce pain intensity and opioid consumption.<sup>15</sup> Dexmedetomidine is a highly selective  $\alpha_2$ -adrenergic receptor with sedative, anxiolytic, and analgesic sparing effects.<sup>16</sup>

We compared the effect of adding dexmedetomidine or dexamethasone as adjuvants to ESPB in patients undergoing modified radical mastectomy.

## 2. Methodology

This randomized, controlled double-blind study was conducted at the National Cancer Institute, Cairo University, after approval by the institutional review board and the scientific committees of the National Cancer Institute and Faculty of Medicine, Cairo University. The study included 90 female patients ASA II and III,

aged 18-65 y and body mass index (BMI) 20-35 kg/m<sup>2</sup> scheduled for modified radical mastectomy (MRM)

under general anesthesia.

Exclusion criteria were known sensitivity or contraindication to the drugs used in the study, history of psychological disorders, contraindications to regional anesthesia (local sepsis, pre-existing peripheral neuropathies, and coagulopathy), severe respiratory or cardiac conditions, advanced liver or kidney disease, and pregnancy. All patients provided written informed consent before inclusion in the study.

Complete history taking, physical examination, and laboratory and radiological investigations were done. The patients were instructed on how to report pain using the Visual Analogue Scale, where 0 = "no pain" and 10 = "worst possible pain."

The patients were randomly assigned into three equal groups using computer-generated random numbers in opaque sealed envelopes. A clinical pharmacist prepared syringes containing the injectates according to the randomization table.

The patients were fasted for a minimum of 6 h for food and 2 h for water and clear fluids. All patients were premedicated with midazolam 0.01-0.02 mg/kg IV.

The patients were subjected preoperatively to ESPB according to the randomization by a staff member blinded to the drugs used.

Dex Group (n = 30) received ESPB with addition of 1  $\mu$ g/kg dexmedetomidine to 30 ml levobupivacaine 0.25%. Dexamethasone Group (n = 30) received ESPB with the addition of 10 mg dexamethasone to 30 ml levobupivacaine 0.25%. ESPB Group (n = 30) received ESPB with 30 ml levobupivacaine 0.25%. Both the investigator assessing the postoperative pain and the patient were blinded to the drugs used.

The block was done at the level of T5 with the patient sitting. The ultrasound machine used was Fujifilm Sonosite M-Turbo® with a 6–13-MHz linear transducer set for small parts and a depth of 4-6 cm. The ultrasound probe was placed on the back in a transverse orientation to identify the tip of the T5 transverse process. It was recognized as flat, squared-off acoustic shadows with a faint image of the pleura. The probe was rotated to a longitudinal orientation to visualize the following layers superficial to the acoustic shadows of the transverse processes: skin, subcutaneous tissue, trapezius, erector spinae muscle, and T5 transverse process.

A skin wheal using 3 ml of lidocaine 1% was made 2-3 cm above the upper aspect of the transducer. An echogenic block needle was inserted in-plane to the ultrasound beam in a cranial-to-caudal direction until contact with the T5 transverse process. The correct location of the needle tip in the fascial plane deep to the erector spinae muscle was confirmed by injecting 0.5-1

ml glucose 5% and seeing the fluid lifting the erector spinae muscle off the transverse process without distending the muscle. After aspiration to avoid intravascular injection, the local anesthetic was injected according to group allocation.

All patients were monitored continuously using ECG, NIBP, SpO<sub>2</sub>, and EtCO<sub>2</sub> throughout the surgical procedure. Induction of general anesthesia was performed with fentanyl 2 µg/kg IV and propofol 2 mg/kg IV. Tracheal intubation was facilitated by atracurium 0.5 mg/kg IV. Anesthesia was maintained with inhaled sevoflurane 2-2.5% in oxygen-air (FiO<sub>2</sub> = 0.5). Maintenance doses of atracurium (0.1 mg/kg) were provided every 30 min. After induction of anesthesia, paracetamol 500 mg and ketorolac 30 mg IV were injected as a part of multimodal analgesia. Rescue analgesia with fentanyl 1 µg/kg was used when the mean arterial blood pressure (MAP) or heart rate (HR) rose above 20% of the baseline levels. Ringer acetate solution was infused to replace the fluid deficit, and the patients were mechanically ventilated at an appropriate setting to keep the EtCO<sub>2</sub> at 30-35 mmHg. MAP and HR before induction of general anesthesia was defined as a baseline reading. Another reading was taken immediately before surgical incision and at 30-min intervals intraoperatively. The residual neuromuscular block was reversed and extubation was performed after complete recovery of the airway reflexes.

Patients were transferred to the post-anesthesia care unit (PACU), where the VAS score, MAP, and HR were recorded immediately and every 2 h. Inj. paracetamol 500 mg/6 h and ketorolac 30 mg/8 h were administered as a part of multimodal analgesia. Rescue analgesia with morphine 3 mg boluses was provided when the VAS score ≥ 4. The total amount of morphine used in 24 h was recorded. The maximum allowed dose of morphine was 0.5 mg/kg/24 h. Side effects such as nausea, vomiting, sedation, and respiratory depression (respiratory rate <10/min) were recorded. Postoperative nausea / vomiting (PONV) were rated on a four-point verbal scale; (none = no nausea, mild = nausea but no vomiting,

moderate = vomiting one attack, severe = vomiting > one episode). Ondansetron 0.1 mg/kg IV was given to patients with moderate or severe PONV. Sedation was assessed in the PACU with Ramsay Sedation Scale (RSS). An RSS score of 5 or 6 equals excessively high sedation levels; a score of 2 equals adequate sedation levels needing observation; and a score of 1 equates to inadequate or insufficient sedation levels.<sup>17</sup>

The primary outcome measure was the total amount of morphine consumed for 24 h postoperatively. The secondary outcome measures were total intraoperative fentanyl consumption, pain intensity on VAS, time to first rescue analgesia, hemodynamic changes, RSS, adverse events, block-related complications, and the patient satisfaction.

As no study addresses the same research question in these cases, the sample size was calculated according to a preliminary analysis of the first 30 patients (10 in each group) as a pilot study. For a pooled standard deviation of 2.37 units, a sample size of 30 patients per group was required to achieve a 90% confidence level (90 patients divided into three equal groups).

### Statistical analysis

SPSS version 27.0 was used for the data analysis. Quantitative variables were tested for normality using the Kolmogorov-Smirnov test. The quantitative data were described as means and standard deviations or medians and ranges. Comparison of means (or medians) of two independent groups was made using t-test. To show the effect of time on vital signs, parametric repeated measures ANOVA was used to show changes over time, both intra- and postoperative. Post-hoc test was used for pairwise comparisons and was Tukey adjusted. Chi-square and Fisher Exact were used for testing proportion independence. P-value was always two-tailed and set significant at a 0.05 level

## 3. Results

The three groups had no significant differences in the baseline characteristics (Table 1).

**Table 1: Baseline characteristics of the three studied groups**

Variable	Dexa Group (n = 30)	Dex Group (n = 30)	ESPB Group (n = 30)	p-value
Age (years)	48.9 ± 8.8	46.8 ± 9.3	48.1 ± 8.3	0.658
Weight (kg)	79.3 ± 13.2	80.9 ± 10.5	79.8 ± 10.2	0.845
BMI (kg/m <sup>2</sup> )	28.9 ± 4.6	27.2 ± 6.4	29.7 ± 4.7	0.167
ASA Class (II/III)	24/6	27/3	26/4	0.654
Side of Surgery (Rt/Lt)	15/15	14/16	15/15	1.000

*Data are presented as mean ± SD*

**Table 2: Intraoperative Fentanyl and postoperative morphine consumption in the three studied groups**

Parameter	Dexa Group (n = 30)	Dex Group (n = 30)	ESPB Group (n = 30)	p-value
Time to first analgesia requirement (h)*	4 (2-24)	14 (4-24)	4 (2-20)	0.031
Patients requiring postoperative analgesia	23 (77.7%)	18 (60.0%)	24 (80.0%)	0.180
Fentanyl (µg)	150 (100-200)	100 (100-200)	150 (100-300)	0.009
Morphine (mg)	3 (3-12)	3 (3-9)	6 (3-9)	0.006

\* Calculated for patients requesting rescue analgesia only

Data are presented as median (range), or number (%)

**Table 3: VAS score at rest and on movement in the three studied groups during the 24 postoperative h**

Parameter	Dexa Group (n = 30)	Dex Group (n = 30)	ESPB Group (n = 30)	p-value <sup>1</sup>	p-value <sup>2</sup>	p-value <sup>3</sup>
<b>VAS score at rest</b>						
Immediate	2 (0-4)	0 (0-4)	2 (0-6)	1.000	<b>0.010</b>	0.072
After 2 h	2 (0-5)	0 (0-5)	2 (0-5)	1.000	<b>0.033</b>	0.051
After 4 h	2 (0-6)	1 (0-5)	2 (0-5)	1.000	<b>0.008</b>	<b>0.013</b>
After 8 h	2 (0-7)	1 (0-5)	2 (0-5)	1.000	<b>0.003</b>	<b>0.024</b>
After 12 h	2 (0-4)	1 (0-2)	2 (0-6)	1.000	<b>0.015</b>	0.148
After 24 h	2 (1-5)	2 (0-4)	2 (1-5)	1.000	<b>0.030</b>	<b>0.034</b>
<b>VAS score on movement</b>						
Immediate	1 (0-3)	1 (0-5)	2 (0-7)	0.052	<b>0.011</b>	1.000
After 2 h	2 (0-5)	1 (0-6)	2 (0-6)	0.203	<b>0.042</b>	1.000
After 4 h	2 (0-6)	2 (0-5)	3 (0-6)	0.134	<b>0.003</b>	0.549
After 8 h	2 (0-7)	2 (0-6)	3 (0-6)	0.372	<b>0.002</b>	0.200
After 12 h	2 (1-6)	2 (0-3)	3 (1-7)	0.266	<b>0.021</b>	0.954
After 24 h	3 (1-7)	2 (1-5)	3 (2-6)	0.638	<b>0.002</b>	0.078

Data are presented as median (range)

p-value1: Dexamethasone vs. ESPB, p-value2: Dex vs. ESPB, p-value3: Dexamethasone vs. Dex

There were no significant differences between the three groups in the number of patients requiring rescue analgesia. The postoperative analgesia duration was significantly longer in the Dex group compared to the ESPB group ( $P = 0.029$ ). The Dexa group was not significantly different from the Dex and ESPB groups ( $P = 0.181$  and  $P = 1.000$ , respectively). Intraoperative fentanyl consumption was significantly lower in the Dex group compared to the ESPB group ( $P = 0.006$ ), while the difference between Dexa and ESPB groups was insignificant ( $P = 0.387$ ). Postoperative morphine consumption was significantly lower in the Dex group ( $P = 0.012$ ) and Dexa group ( $P = 0.032$ ) compared to the ESPB group (Table 2).

VAS scores of patients in the Dex group were

significantly lower than that of the ESPB group at rest and movement in all times measured. Dex group had significantly lower VAS scores than the Dexa group after 4, 8, and 24 h at rest, while the two groups had comparable VAS scores with movement. VAS scores of the Dexa group were similar to that of the ESPB group at rest and movement at all times (Table 3). All patients of the three groups had adequate sedation levels (Ramsey score 2) during the postoperative period from 2 h up to 24 h.

Postoperative nausea and vomiting were less frequent in the Dexa Group than in the Dex and ESPB Groups, but the difference was insignificant (Table 4).

Heart rate remained comparable among the three groups

**Table 4: Frequency of postoperative nausea and vomiting in the three studied groups**

PONV	Dexa Group (n = 30)	Dex Group (n = 30)	ESPB Group (n = 30)	p-value
No	23 (76.7%)	16 (53.3%)	18 (60%)	0.407
Mild	5 (16.7%)	9 (30%)	7 (23.3%)	
Moderate	2 (6.7%)	5 (16.7%)	5 (16.7%)	

*Data are presented as n (%)*

preoperatively as well as during surgery. Intraoperative MAP dropped immediately after induction, then trivial changes were observed in the three groups. During the postoperative period, HR and MAP showed minor changes in all patients with no significant differences between the three groups. In general, the values of HR and MAP were within the clinically accepted ranges during the intra- and postoperative periods (Figures 1 & 2).

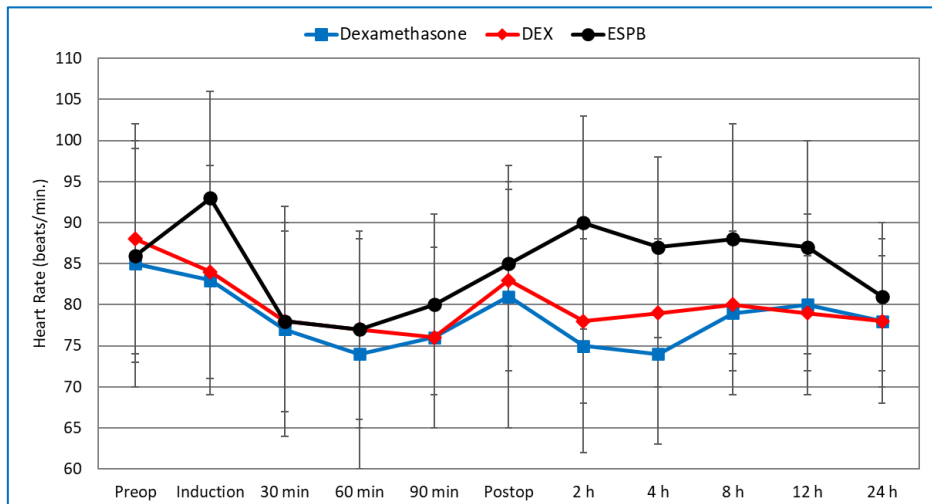
More patients were satisfied with the analgesic protocol in Dex [25(83.30%)] and Dexa Group [27(90%)] compared to ESPB Group [21(70%)]. However, the difference was not statistically significant ( $P = 0.133$ ).

No block-related complications were recorded in this study.

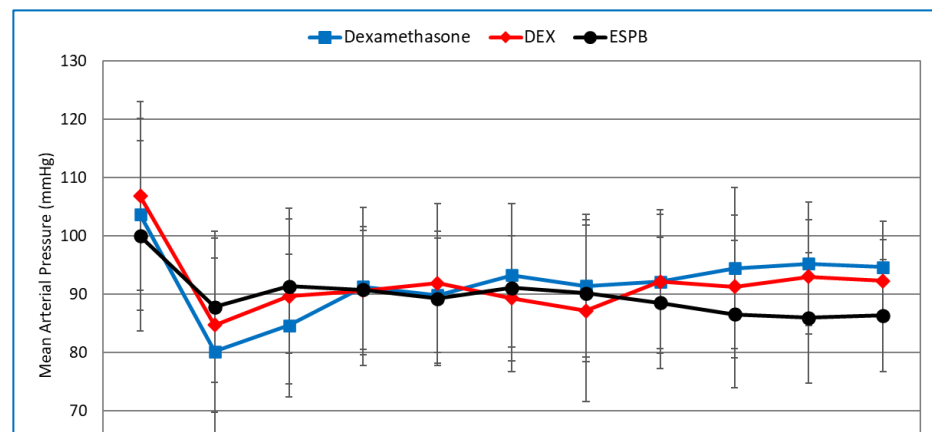
### 4. Discussion

This study demonstrated that Dex as an adjuvant to levobupivacaine in ESPB prolongs the analgesic duration and is associated with significantly reduced intraoperative fentanyl and postoperative morphine consumption. Dex was effective in pain reduction at rest and with movement up to 24 h postoperatively. Dex was superior to dexamethasone in pain reduction at rest at some time points. Dexamethasone was not associated with better pain

reduction compared to ESPB with levobupivacaine only. Dex and dexamethasone did not significantly affect sedation levels during the first postoperative 24 h. Dexamethasone can reduce postoperative nausea and vomiting compared to Dex and ESPB groups, but the difference was insignificant. The two adjuvants were hemodynamically stable as in cases with ESPB with levobupivacaine only.



**Figure 1: Intra- and postoperative changes of heart rate in the three studied**



**Figure 2: Intra- and postoperative changes of mean arterial pressure in the three studied groups**



The erector spinae plane block gained substantial popularity due to its simplicity of performance, with the transverse processes as an easily recognizable landmark for LA injection.<sup>18</sup> Several RCTs and systematic reviews constitute substantial evidence for its effectiveness in breast and thoracic surgery,<sup>19,20</sup> as well as newer clinical applications like abdominal,<sup>21</sup> upper limb,<sup>22</sup> and lower limb analgesia.<sup>23</sup>

The most probable basic mechanism of action of ESPB is through a direct action of LA on different neural targets, including nerves passing within the erector spinae muscle (as branches of the dorsal rami) and nerves within adjoining compartments like spinal nerve roots, ventral rami, and brachial plexus. A small part of the LA spreads into the paravertebral and epidural space exerting significant effects on nociceptive transmission and processing.<sup>24</sup> A comprehensive systematic review of 13 studies investigating ESPB in breast surgery reported a superior analgesic profile of ESPB with a reduction of pain intensity and opioid consumption. Pain reduction was more marked in the early postoperative period (up to 6 h) and decreased at 12 and 24 h postoperatively.<sup>20</sup>

Like other peripheral nerve blocks (PNB), the favorable effect of LA in ESPB is limited by its duration of action and dose-dependent adverse effects.<sup>25</sup> Thus, the use of adjuvants is a common practice to potentiate the effect of LA due to their synergistic effect that might prolong sensory block duration and limit the possible side effects. Many adjuvants were tried in this context, including alpha-2 adrenoreceptor antagonists such as clonidine and dexmedetomidine, steroids like dexamethasone, anti-inflammatory agents, and others.<sup>26</sup>

Previous studies have demonstrated the efficacy of perineural dexmedetomidine in prolonging analgesic duration in brachial plexus block,<sup>27</sup> lower limb block,<sup>28</sup> epidural block,<sup>29</sup> and paravertebral block.<sup>30,31</sup> On the other hand, few studies investigated the value of adjuncts to LA in interfascial plane block techniques.

Gao et al. compared dexmedetomidine to dexamethasone as an adjuvant to ropivacaine in ESPB in patients undergoing video-assisted thoracoscopic lobectomy (VATL). Dexmedetomidine addition was associated with lower pain scores, longer duration of sensory blockade, and lower opioid consumption compared to ropivacaine alone or with dexamethasone.<sup>32</sup> Dexmedetomidine was also comparable to nalbuphine as an adjuvant to ropivacaine in ESPB in terms of the analgesia duration and need for rescue analgesia in patients after VATL.<sup>33</sup> The addition of dexmedetomidine to ropivacaine for ESPB successfully prolonged the postoperative analgesic duration and reduced opioid consumption in patients subjected to open thoracotomy.<sup>34</sup> Dexmedetomidine also effectively reduced postoperative pain and opioid consumption in

patients undergoing posterior lumbar spine surgery.<sup>35</sup>

In different breast surgeries, adding dexmedetomidine to LA in the pectoral nerve block increased analgesia duration and reduced postoperative morphine consumption.<sup>36</sup> Similar findings were reported in patients who underwent MRM.<sup>37</sup> Also, adding dexmedetomidine to bupivacaine has been found to prolong the analgesic efficacy of the transversus abdominis plane (TAP) block.<sup>38,39</sup>

The exact mechanism by which dexmedetomidine potentiates the local anesthetic action is not well-known. Its local vasoconstrictive effect may prolong analgesia duration by decreasing the systemic absorption of the LA from the injection site.<sup>40,41</sup> Unlike clonidine, dexmedetomidine has been proposed to prolong sensory rather than motor block. This differential sensory motor effect may result from the greater inhibitory effect on A $\delta$  and C nerve fibers relative to motor neurons.<sup>42</sup>

Dexamethasone, as an additive to local anesthetics, is supposed to help in pain management by anti-inflammatory effects and suppressing potassium channel-mediated discharge of nociceptive C-fibers.<sup>43,44</sup> In the current study, dexamethasone was more effective in reducing postoperative nausea and vomiting than Dex and ESPB groups, but the difference was insignificant. Conversely, dexamethasone did not prolong sensory block or reduce pain compared to ESPB. Previous studies reported similar findings in ESPB for VATL,<sup>32</sup> and ulnar nerve block.<sup>45</sup> On the contrary, a meta-analysis found that perineural dexamethasone significantly prolonged the duration of analgesia compared with placebo.<sup>46</sup> Another meta-analysis provided moderate evidence that perineural dexamethasone combined with bupivacaine slightly prolongs analgesia duration compared with systemic dexamethasone. This effect was not found with ropivacaine.<sup>47</sup>

## 5. Conclusion

We can conclude that Dex is a valuable adjuvant to levobupivacaine in ESPB. It prolongs the analgesia duration and reduces intraoperative fentanyl and postoperative morphine consumption. It effectively reduces pain at rest and with movement up to 24 h postoperatively. Dex was superior to dexamethasone in pain reduction and duration of analgesia. Both adjuvants were hemodynamically stable.

## 6. Data availability

The numerical data generated during this research is available with the authors.

## 7. Acknowledgement

We gratefully thank Faculty of Medicine, Universitas Indonesia for the PUTI grant (NKB-2247/UN2.RST/HKP.05.00/2020) which helped fund this

project.

### 8. Conflict of interest

The study utilized a grant by Faculty of Medicine, Universitas Indonesia, and no external or industry funding was involved.

### 9. Authors' contribution

RM: Concept, conduct the study, data collection/ analysis. manuscript writing, editing and correction, final approval

DF, AA: Searched the literature, data analysis. manuscript writing, editing and correction, Final approval

## 10. References

1. Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer Statistics, 2021. *CA Cancer J Clin.* 2021 Jan;71(1):7-33. [PubMed] DOI: [10.3322/caac.21654](https://doi.org/10.3322/caac.21654)
2. Ibrahim AS, Khaled HM, Mikhail NN, Baraka H, Kamel H. Cancer incidence in egypt: results of the national population-based cancer registry program. *J Cancer Epidemiol.* 2014;2014:437971. [PubMed] DOI: [10.1155/2014/437971](https://doi.org/10.1155/2014/437971)
3. Jossa V, Olivier F, Lifrange E, Crevecœur A, Courtois A, Coibion M, et al. From modified radical mastectomy to infra-radical mastectomy: a phase I study for surgical de-escalation focusing on pathological analyses. *Gland Surg.* 2021;10:1931–40. [PubMed] DOI: [10.21037/gs-21-48](https://doi.org/10.21037/gs-21-48)
4. Cui L, Fan P, Qiu C, Hong Y. Single institution analysis of incidence and risk factors for post-mastectomy pain syndrome. *Sci Rep.* 2018;8:11494. [PubMed] DOI: [10.1038/s41598-018-29946-x](https://doi.org/10.1038/s41598-018-29946-x)
5. Bruce J, Thornton AJ, Powell R, Johnston M, Wells M, Heys SD, et al. Psychological, surgical, and sociodemographic predictors of pain outcomes after breast cancer surgery: a population-based cohort study. *Pain.* 2014;155:232–43. [PubMed] DOI: [10.1016/j.pain.2013.09.028](https://doi.org/10.1016/j.pain.2013.09.028)
6. Abraham A. Gold standards and anaesthesia. *Indian J Anaesth.* 2013;57:207–9. [PubMed] DOI: [10.4103/0019-5049.111876](https://doi.org/10.4103/0019-5049.111876)
7. Kumar S, Goel D, Sharma SK, Ahmad S, Dwivedi P, Deo N, et al. A randomised controlled study of the postoperative analgesic efficacy of ultrasound-guided pectoral nerve block in the first 24 h after modified radical mastectomy. *Indian J Anaesth.* 2018;62:436–42. [PubMed] DOI: [10.4103/ija.IJA\\_523\\_17](https://doi.org/10.4103/ija.IJA_523_17)
8. Garg R. Regional anaesthesia in breast cancer: Benefits beyond pain. *Indian J Anaesth.* 2017;61:369–72. [PubMed] DOI: [10.4103/ija.IJA\\_292\\_17](https://doi.org/10.4103/ija.IJA_292_17)
9. Freise H, Van Aken HK. Risks and benefits of thoracic epidural anaesthesia. *Br J Anaesth.* 2011;107:859–68. [PubMed] DOI: [10.1093/bja/aer339](https://doi.org/10.1093/bja/aer339)
10. Zhang J, He Y, Wang S, Chen Z, Zhang Y, Gao Y, et al. The erector spinae plane block causes only cutaneous sensory loss on ipsilateral posterior thorax: a prospective observational volunteer study. *BMC Anesthesiol.* 2020;20:88. [PubMed] DOI: [10.1186/s12871-020-01002-0](https://doi.org/10.1186/s12871-020-01002-0)
11. Jyothi B, Gowda S, Shaikh SI. A comparison of analgesic effect of different doses of intrathecal nalbuphine hydrochloride with bupivacaine and bupivacaine alone for lower abdominal and orthopedic surgeries. *Indian J Pain.* 2014;28:18. DOI: [10.4103/0970-5333.128881](https://doi.org/10.4103/0970-5333.128881)
12. Gupta A, Gupta N, Choudhury A, Agrawal N. Erector Spinae Plane Block using clonidine as an Adjuvant for Excision of Chest Wall Tumor in a Pediatric Patient. *Ann Card Anaesth.* 2020;23:221–3. [PubMed] DOI: [10.4103/aca.ACA\\_188\\_18](https://doi.org/10.4103/aca.ACA_188_18)
13. Fusco P, Volpe D, De Paolis V, De Sanctis F, Scimia P, Marinangeli F, et al. Dexamethasone as a local anesthetic adjuvant in bilateral ultrasound guided erector spinae plane block can provide a long-lasting analgesia in laparotomic abdominal surgery. *Minerva Anestesiol.* 2019;85:1144–5. [PubMed] DOI: [10.23736/S0375-9393.19.13798-4](https://doi.org/10.23736/S0375-9393.19.13798-4)
14. Wang Q, Li H, Wei S, Zhang G, Ni C, Sun L, et al. Dexmedetomidine Added to Ropivacaine for Ultrasound-guided Erector Spinae Plane Block Prolongs Analgesia Duration and Reduces Perioperative Opioid Consumption After Thoracotomy: A Randomized, Controlled Clinical Study. *Clin J Pain.* 2021;38:8–14. [PubMed] DOI: [10.1097/AJP.0000000000000992](https://doi.org/10.1097/AJP.0000000000000992)
15. Pehora C, Pearson AM, Kaushal A, Crawford MW, Johnston B. Dexamethasone as an adjuvant to peripheral nerve block. *Cochrane Database Syst Rev.* 2017;11(11):CD011770. [PubMed] DOI: [10.1002/14651858.CD011770.pub2](https://doi.org/10.1002/14651858.CD011770.pub2)
16. Kaur M, Singh PM. Current role of dexmedetomidine in clinical anesthesia and intensive care. *Anesth Essays Res.* 2011;5:128–33. [PubMed] DOI: [10.4103/0259-1162.94750](https://doi.org/10.4103/0259-1162.94750)
17. Sessler CN, Jo Grap M, Ramsay MA. Evaluating and monitoring analgesia and sedation in the intensive care unit. *Crit Care.* 2008;12:S2. [PubMed] DOI: [10.1186/cc6148](https://doi.org/10.1186/cc6148)
18. Chin KJ, Versyck B, Pawa A. Ultrasound-guided fascial plane blocks of the chest wall: a state-of-the-art review. *Anaesthesia.* 2021;76:110–26. [PubMed] DOI: [10.1111/anae.15276](https://doi.org/10.1111/anae.15276)
19. Saadawi M, Layera S, Aliste J, Bravo D, Leurcharusmee P, Tran DQ. Erector spinae plane block: A narrative review with systematic analysis of the evidence pertaining to clinical indications and alternative truncal blocks. *J Clin Anesth.* 2021;68:110063. [PubMed] DOI: [10.1016/j.jclinane.2020.110063](https://doi.org/10.1016/j.jclinane.2020.110063)
20. Leong RW, Tan ESJ, Wong SN, Tan KH, Liu CW. Efficacy of erector spinae plane block for analgesia in breast surgery: a systematic review and meta-analysis. *Anaesthesia.* 2021;76:404–13. [PubMed] DOI: [10.1111/anae.15164](https://doi.org/10.1111/anae.15164)
21. Hamed MA, Goda AS, Basiony MM, Fargaly OS, Abdelhady MA. Erector spinae plane block for postoperative analgesia in patients undergoing total abdominal hysterectomy: a randomized controlled study original study. *J Pain Res.* 2019;12:1393–8. [PubMed] DOI: [10.2147/JPR.S196501](https://doi.org/10.2147/JPR.S196501)
22. Kapukaya F, Ekinci M, Ciftci B, Atalay YO, Gölboyu BE, Kuyucu E, et al. Erector spinae plane block vs interscalene brachial plexus block for postoperative analgesia management in patients who underwent shoulder arthroscopy. *BMC Anesthesiol.* 2022;22:142. [PubMed] DOI: [10.1186/s12871-022-01687-5](https://doi.org/10.1186/s12871-022-01687-5)
23. Diwan S, Nair A. Lumbar erector spinae plane block obtunding knee and ankle reflexes. *Saudi J Anaesth.* 2021;15:222–4. [PubMed] DOI: [10.4103/sja.SJA\\_79\\_20](https://doi.org/10.4103/sja.SJA_79_20)
24. Chin KJ, El-Boghdady K. Mechanisms of action of the erector spinae plane (ESP) block: a narrative review. *Can J Anesth.* 2021;68:387–408. [PubMed] DOI: [10.1007/s12630-020-01875-2](https://doi.org/10.1007/s12630-020-01875-2)

25. Swain A, Nag DS, Sahu S, Samaddar DP. Adjuvants to local anesthetics: Current understanding and future trends. *World J Clin Cases.* 2017;5:307–23. [PubMed] DOI: [10.12998/wjcc.v5.i8.307](https://doi.org/10.12998/wjcc.v5.i8.307)
26. Desai N, Albrecht E, El-Boghdady K. Perineural adjuncts for peripheral nerve block. *BJA Educ.* 2019;19:276–82. [PubMed] DOI: [10.1016/j.bjae.2019.05.001](https://doi.org/10.1016/j.bjae.2019.05.001)
27. Liu W, Guo J, Zheng J, Zheng B, Ruan X, Addition of Dexmedetomidine to Ropivacaine-Induced supraclavicular Block (ADRIb) Investigator. Low-dose dexmedetomidine as a perineural adjuvant for postoperative analgesia: a randomized controlled trial. *BMC Anesthesiol.* 2022;22:249. [PubMed] DOI: [10.1186/s12871-022-01791-6](https://doi.org/10.1186/s12871-022-01791-6)
28. Helal SM, Eskandr AM, Gaballah KM, Gaarour IS. Effects of perineural administration of dexmedetomidine in combination with bupivacaine in a femoral-sciatic nerve block. *Saudi J Anaesth.* 2016;10:18–24. [PubMed] DOI: [10.4103/1658-354X.169469](https://doi.org/10.4103/1658-354X.169469)
29. Shukla U, Singh D, Singh J, Yadav JBS. Comparative Study of Epidural Dexmedetomidine, Fentanyl, and Tramadol as Adjuvant to Levobupivacaine for Lower Limb Orthopedic Surgeries. *Cureus.* 2022;14:e25225. [PubMed] DOI: [10.7759/cureus.25225](https://doi.org/10.7759/cureus.25225)
30. Mohamed SA, Fares KM, Mohamed AA, Alieldin NH. Dexmedetomidine as an adjunctive analgesic with bupivacaine in paravertebral analgesia for breast cancer surgery. *Pain Physician.* 2014;17:E589-598. [PubMed]
31. Alimian M, Imani F, Rahimzadeh P, Faiz SHR, Bahari-Sejahrood L, C Hertling A. Adding Dexmedetomidine to Bupivacaine in Ultrasound-guided Thoracic Paravertebral Block for Pain Management after Upper Abdominal Surgery: A Double-blind Randomized Controlled Trial. *Anesth Pain Med.* 2021;11:e120787. [PubMed] DOI: [10.5812/aapm.120787](https://doi.org/10.5812/aapm.120787)
32. Gao Z, Xiao Y, Wang Q, Li Y. Comparison of dexmedetomidine and dexamethasone as adjuvant for ropivacaine in ultrasound-guided erector spinae plane block for video-assisted thoracoscopic lobectomy surgery: a randomized, double-blind, placebo-controlled trial. *Ann Transl Med.* 2019;7:668. [PubMed] DOI: [10.21037/atm.2019.10.74](https://doi.org/10.21037/atm.2019.10.74)
33. Rao J, Gao Z, Qiu G, Gao P, Wang Q, Zhong W, et al. Nalbuphine and dexmedetomidine as adjuvants to ropivacaine in ultrasound-guided erector spinae plane block for video-assisted thoracoscopic lobectomy surgery: A randomized, double-blind, placebo-controlled trial. *Medicine.* 2021;100:e26962. [PubMed] DOI: [10.1097/MD.00000000000026962](https://doi.org/10.1097/MD.00000000000026962)
34. Wang Q, Li H, Wei S, Zhang G, Ni C, Sun L, et al. Dexmedetomidine Added to Ropivacaine for Ultrasound-guided Erector Spinae Plane Block Prolongs Analgesia Duration and Reduces Perioperative Opioid Consumption After Thoracotomy: A Randomized, Controlled Clinical Study. *Clin J Pain.* 2021;38:8–14. [PubMed] DOI: [10.1097/AJP.0000000000000992](https://doi.org/10.1097/AJP.0000000000000992)
35. Yi-Han W, Rong T, Jun L, Min W, Yan Z, Yi L, et al. Dexmedetomidine combined with ropivacaine for erector spinae plane block after posterior lumbar spine surgery: a randomized controlled trial. *BMC Musculoskelet Disord.* 2022;23:235. [PubMed] DOI: [10.1186/s12891-022-05198-9](https://doi.org/10.1186/s12891-022-05198-9)
36. Kaur H, Arora P, Singh G, Singh A, Aggarwal S, Kumar M. Dexmedetomidine as an adjunctive analgesic to ropivacaine in pectoral nerve block in oncological breast surgery: A randomized double-blind prospective study. *J Anaesthesiol Clin Pharmacol.* 2017;33:457–61. [PubMed] DOI: [10.4103/joacp.JOACP\\_298\\_16](https://doi.org/10.4103/joacp.JOACP_298_16)
37. Bakr MA, Mohamed SA, Mohamed MF, Mohamed MA, El Sherif FA, Mosad E, et al. Effect of Dexmedetomidine Added to Modified Pectoral Block on Postoperative Pain and Stress Response in Patient Undergoing Modified Radical Mastectomy. *Pain Physician.* 2018;21:E87–96. [PubMed]
38. Talebi G, Moayeri H, Rahmani K, Nasseri K. Comparison of Three Different Doses of Dexmedetomidine Added to Bupivacaine in Ultrasound-Guided Transversus Abdominis Plane Block; A Randomized Clinical Trial. *Anesth Pain Med.* 2021;11:e113778. [PubMed] DOI: [10.5812/aapm.113778](https://doi.org/10.5812/aapm.113778)
39. Madangopal RM, Dang A, Aggarwal M, Kumar J. A comparative evaluation of different doses of dexmedetomidine as an adjuvant to bupivacaine in transversus abdominis plane block for postoperative analgesia in unilateral inguinal hernioplasty. *J Anaesthesiol Clin Pharmacol.* 2020;36:398–406. [PubMed] DOI: [10.4103/joacp.JOACP\\_26\\_19](https://doi.org/10.4103/joacp.JOACP_26_19)
40. Kosugi T, Mizuta K, Fujita T, Nakashima M, Kumamoto E. High concentrations of dexmedetomidine inhibit compound action potentials in frog sciatic nerves without alpha(2) adrenoceptor activation. *Br J Pharmacol.* 2010;160:1662–76. [PubMed] DOI: [10.1111/j.1476-5381.2010.00833.x](https://doi.org/10.1111/j.1476-5381.2010.00833.x)
41. Masuki S, Dinenna FA, Joyner MJ, Eisenach JH. Selective alpha2-adrenergic properties of dexmedetomidine over clonidine in the human forearm. *J Appl Physiol (1985).* 2005;99:587–92. [PubMed] DOI: [10.1152/jappphysiol.00147.2005](https://doi.org/10.1152/jappphysiol.00147.2005)
42. Abdallah FW, Dwyer T, Chan VWS, Niazi AU, Ogilvie-Harris DJ, Oldfield S, et al. IV and Perineural Dexmedetomidine Similarly Prolong the Duration of Analgesia after Interscalene Brachial Plexus Block: A Randomized, Three-arm, Triple-masked, Placebo-controlled Trial. *Anesthesiology.* 2016;124:683–95. [PubMed] DOI: [10.1097/ALN.0000000000000983](https://doi.org/10.1097/ALN.0000000000000983)
43. Barnes PJ. Anti-inflammatory actions of glucocorticoids: molecular mechanisms. *Clin Sci (Lond).* 1998;94:557–72. [PubMed] DOI: [10.1042/cs0940557](https://doi.org/10.1042/cs0940557)
44. Johansson A, Hao J, Sjölund B. Local corticosteroid application blocks transmission in normal nociceptive C-fibres. *Acta Anaesthesiol Scand.* 1990;34:335–8. [PubMed] DOI: [10.1111/j.1399-6576.1990.tb03097.x](https://doi.org/10.1111/j.1399-6576.1990.tb03097.x)
45. Marhofer D, Kettner SC, Marhofer P, Pils S, Weber M, Zeitlinger M. Dexmedetomidine as an adjuvant to ropivacaine prolongs peripheral nerve block: a volunteer study. *Br J Anaesth.* 2013;110:438–42. [PubMed] DOI: [10.1093/bja/aes400](https://doi.org/10.1093/bja/aes400)
46. Albrecht E, Kern C, Kirkham KR. Perineural vs intravenous administration of dexamethasone: more data are available. *Br J Anaesth.* 2015;114:160. [PubMed] DOI: [10.1093/bja/aeu421](https://doi.org/10.1093/bja/aeu421)
47. Baeriswyl M, Kirkham KR, Jacot-Guillarmod A, Albrecht E. Efficacy of perineural vs systemic dexamethasone to prolong analgesia after peripheral nerve block: a systematic review and meta-analysis. *Br J Anaesth.* 2017;119:183–91. [PubMed] DOI: [10.1093/bja/aex191](https://doi.org/10.1093/bja/aex191)