

By Ultrasonic-Guided Erector Spinae Block, Thoracic Paravertebral Block versus Serratus Anterior Plane Block by Articaine with Adrenaline during Breast Surgery with General Anesthesia: A Comparative Study of Analgesic Effect Post-Operatively: Double Blind Randomized, Controlled Trial

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Abstract

Background and Aims: Erector spinae plane block, Paravertebral block and serratus anterior block are three formats for analgesia post-operatively following radical mastectomy. This study compares the analgesic efficacy of these modalities for analgesia post-operatively by articaine 2% with adrenaline. **Methods:** Seventy-five patients with ASA physical status I or II subjected to modified radical mastectomy with axillary clearance were enrolled for the study. After induction of general anaesthesia all patients received 20 mL 2% articaine with adrenaline in each technique of the study. Patients in Group 1 (Erector spinae block [ESB], $n = 25$), Group 2 paravertebral block [PVB] $n = 25$), Group 3 (serratus anterior plane block [SAPB] $n = 25$) were ultrasound-guided on ipsilateral side. Patients were estimated for pain scores at 0, 2, 4, 6, 12 and 24 h, and duration of analgesia post-operatively and relieve analgesic doses required of morphine up to 24 h. **Results:** Visual analogue scale scores post-operatively were lower in ESB and PVB group compared with SAPB at 4, 6, 12 and 24 h ($P < 0.05$). The first analgesic dose requirement was significantly longer in ESB (416 ± 68 min) than PVB group (371 ± 67 min) in compared with SAPB (343.5 ± 54.7 min). Mean duration of analgesia was significantly longer in ESB and PVB group ($P < 0.001$) in compared with SAPB. Total morphine dose of relieving analgesic was significantly lesser in ESB (4 ± 2 mg) than PVB group (6 ± 2 mg) compared with SAPB (7

± 2 mg) up to 24 h. ESB was easy technique and has less side effect on compared with PVB. As regard block-related complications including (accidental vascular puncture, pneumothorax, nerve damage, local anesthetics toxicity), there were no significant adverse effects noted in three groups. However, only a case of pneumothorax in (PVB) and a two patients' blood was aspirated when the paravertebral space was entered which required second trial at the blocks. **Conclusion:** Sonar-guided erector spinae block and thoracic paravertebral block minimize post-operative pain scores, prolongs the duration of analgesia and diminishes requirements for assigning analgesics in the first 24 h of post-operative period compared to ultrasound-guided serratus anterior plane block but, ESB technique was more potent, easily and less side effect in compared with PVB.

Keywords

Anesthesia, Pain, Analgesia, Post-Operative, Articaine, Mastectomy

1. Introduction

Regional anaesthesia has been believed as one of the formats for effective peri-operative pain control. Regional blocks using ultrasound-guide has become a perfect supplement to general anaesthesia for extending analgesia after modified radical mastectomy [1]. The advantage includes post-operative pain relief prolongation, a decrease in analgesic requirement post-operatively, a reduction in nausea and vomiting scores and probability for ambulatory discharge and hospital stay [1]. Hence, an efficient perioperative pain control of patients undergoing modified radical mastectomy is fundamental. Serratus anterior plane blocks have been used with changeable efficacy with GA but have its deficiencies as it disrupts surgical planes, and causes sparing of intercostobrachial nerve and also supraclavicular nerves [2]. Paravertebral block when used as the sole anaesthetic or with general anesthesia has been found to provide better post-operative pain relief but side effects such as vascular puncture and accidental pneumothorax are known problems [3]. In 2016 Forero *et al.* the first one described ESP block for managing thoracic neuropathic pain with hopeful results [4]. Erector spinae (ES) contains three layers of muscles: spinalis, longissimus and iliocostalis, which take place parallel to each other over the vertebra and expands from lower back of the skull base superiorly down to the pelvis caudally. ES facial Plane is a potential space deep to ES muscle, where the injected local anaesthetic (LA) diffuses cranio-caudally up to multiple levels as the ES fascia expands from nuchal fascia cranially to the sacrum caudally (C7 - T2 cranially and L2 - L3 caudally) [5]. LA effects gate into the thoracic paravertebral space by coming the costotransverse foramina and that way blocks dorsal rami, ventral rami of spinal nerves, and rami communicants that carry sympathetic fibers. In this way the block involves somatic and visceral pain during cancer breast surgery. With the present of ultrasound, novel interventions such as facial plane

blocks have been come for perioperative analgesia in cancer breast surgeries. Erector spinae plane (US-ESP) block guided by ultrasound is a newer analgesic technique, in which anaesthetic agents are injected into fascial plane between transverse process and erector spinae muscle. It is reasonable to block the ventral and dorsal rami of the nerve roots depending on the site of injection and volume of injected local anaesthetic. The drug spreads in superio-inferior way over multiple levels as the erector spinae facial plane extended from nuchal fascia cranially to the sacrum caudally [6]. Cadaveric studies have appeared that block at thoracic 5 level is adequate to have ipsilateral multidermatomal sensory block ranging from T1 to L3 [7]. This block does the purpose of a paravertebral block but erector spinae block is done without risk of pleural injury [8]. The serratus anterior block has been to cause anterolateral chest wall analgesia following breast surgery. It was also wonderful and low-risk technique to improve post-mastectomy acute pain management [9] [10]. Serratus anterior block ultrasound-guided can increase the safety and accelerate the procedure [11] [12]. They have an opioid-sparing effect, and give early mobilization and early come out from hospital.

Articaine hydrochloride (HCl) presents in 1969 with the name of Carticaine, was first derived in Germany in 1976. Articaine is as powerful as Lidocaine and offered as the same characters to Lidocaine (Gold standard) and best cardiac stability. In medically severely ill patients where the utilization of Lidocaine with adrenaline can be advised with caution, Articaine can be a best acceptable alternative. The pharmacological properties of this anesthetic drug are reliable for its main advantages. Change of the aromatic ring by a thiophenic ring augmented the liposolubility of the drug through with its capability (1.5 times more than that of lidocaine) [13]. Furthermore, Articaine is the only amide local anesthetic consists of an ester group in its molecular structure—thus permitting metabolism of the drug both by liver microsomal enzymes and plasma esterase.

This study compares the postoperative analgesic efficacy of these methods [Erector spinae block, Paravertebral block and serratus anterior plane block] for analgesia post-operatively by articaine 2% with adrenaline as a primary outcome and duration of analgesia and requests for rescue analgesics in the first 24 h of post-operative period as a secondary outcome.

2. Patient and Method

This randomized, double-blind, comparative study was performed, after obtaining approval from the Ethics Committee of hospital and written informed consent from seventy five adult females in Aswan and Benha university from October 2018 to February 2019, who were planned for elective MRM. The inclusion criteria were ASA Physical Status I or II, age 18 - 65 years and weight 40 - 85 kg. The exclusion criteria were contraindications to regional blocks, for example infection at the site of block, coagulopathy and anaesthetic allergy to articaine and significant cardiac, neurological, hepatic, renal or respiratory disease and patients scheduled for breast conservative surgery versus simple mastectomy with

axillary dissection.

The primary purpose of this study was to detect visual analogue scale (VAS) pain scores postoperative. The secondary targets were to determine the variation in the duration of analgesia of the three blocks, the morphine consumption in 24 h. After surgery, block-related side effects and morphine-related complication (nausea/vomiting).

The participants were randomly assigned into three groups 25 in each (ESB, PVB and SPB) by a random sequence number produced by the computer and kept in sealed envelopes. The closed envelopes were opened on the day of surgery after induction of anaesthesia, and participants received either ESB ($n = 25$) or PVB ($n = 25$) or SPB ($n = 25$) as per the envelope. The participants were blinded, as the blocks were done after induction of general anaesthesia. And blocks were done by a different anesthesiologist (who was a proficiently in these blocks).

Before surgery, the participants received learning about the VAS pain score (0 - 10) and the technique and details of the nerve block techniques. After a 6 h fast, the patients were brought into the operation room, where an 18-gauge intravenous (IV) cannula was secured and observations (pulse oximeter, electrocardiography and non-invasive blood pressure) were applied. General anaesthesia was done with midazolam 2 mg, fentanyl 2 mcg/kg and propofol 2.5 mg/kg treated IV, and the trachea was intubated after administering atracurium besylate 0.15 mg/kg IV for muscle relaxation. The lungs were ventilated to preserve an end-tidal carbon dioxide of 35 - 45 mmHg. Anaesthesia was preserved with oxygen, and 1% isoflurane. One gram paracetamol was administered IV after induction of anaesthesia. At the end of surgery, ondansetron 4 mg was treated IV, and muscle relaxation was reversed with IV neostigmine 40 mcg/kg and atropine 1 mg. Then trachea extubation, and the patients were transferred to post-anaesthetic care unit (PACU) for follow up.

Patient in Group 1 (ESPB) after induction of general anaesthesia, the patient was curved to the lateral decubitus position and the surgical side superiorly [Figure 1]. After proper skin sterilisation, By sonar guided with a linear probe (8 - 13 MHz) and an ultrasound machine (M-Turbo, SonoSite Inc., USA), the probe was put in a parasagittal plane over the transverse process of thoracic 4 or thoracic 5 vertebrae, approximately 2.5 cm lateral to the spinous processe. Under all aseptic precautions and sonar guided, ESP block was managed at T4 or T5 on the same surgical side using a high-frequency linear ultrasound probe. The transverse process has a square form contour as compared to rib which is rounded form contour. Then the three muscles layers or sheets with facial plane are distinguished from superficial to deep as trapezius, rhomboid major, and erector spinae with flickering pleura in between the transverse processes. The block was managed by in-plane technique using 22-gauge, 50 mm, echogenic needle was inserted in cranial-caudad orientation and the block needle was proceeded through the trapezius, rhomboid major, and erector spinae to smoothly contact transverse process. Needle location was confirmed by hydro dissection



Figure 1. Patient position.

on injecting 2 - 3 ml of normal saline. On injecting 20 ml of 2% articaine with adrenaline into interfascial plane below to erector spinae, a manifest linear pattern was visualized uplifting the muscle [Figure 2].

As regard the patient in Group 2 (PVB), for the ultrasound-guided thoracic PVB, with the patient in the lateral decubitus position and the side of surgery was superiorly, the probe was put in a parasagittal plane over the transverse process of thoracic four and thoracic five vertebrae, almost 2.5 cm lateral to the spinous processes. The thoracic paravertebral space was distinguished as a wedge-shaped hypoechoic space between the superior costotransverse ligament and the pleura [Figure 3(a)]. After proper skin sterilisation, a 22-gauge, 50 mm, echogenic needle was putted using in-plane approach from the superior side of the probe and proceeded in cranial-caudal direction and during needle progression, hydrodissection was used to determine the needle tip under ultrasound guidance, until the tip pierced the superior costotransverse ligament. The block was believed satisfactory when the pleural membrane was displaced downwards, during this time injection of 20 ml of 2% articaine with adrenaline [Figure 3(b)].

But Patients in group 3 (SPB) received serratus anterior plane block, this blocks were done after induction of general anaesthesia. After proper skin sterilisation, for the ultrasound-guided serratus plane block, with the patient in the lateral decubitus position and the side of surgery superiorly, the ultrasound probe was put longitudinally oblique just below the mid-clavicle. After distinguish the second rib, the probe was mobilised caudally and laterally (obliquely), towards the mid-axillary line to distinguish the third, fourth and fifth ribs, The ideal and definite probe position had its cephalad end at the anterior axillary line and the caudad end at posterior axillary line. The fascial plane between the serratus anterior muscle and ribs four and five was identified between the 4th and 5th rib in the mid-axillary region. Under sonar guided, a22-gauge, 50

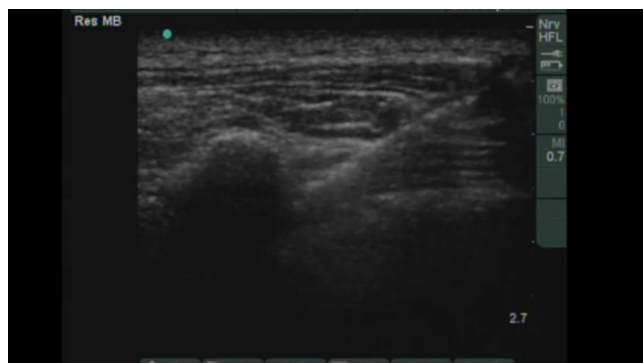


(a)

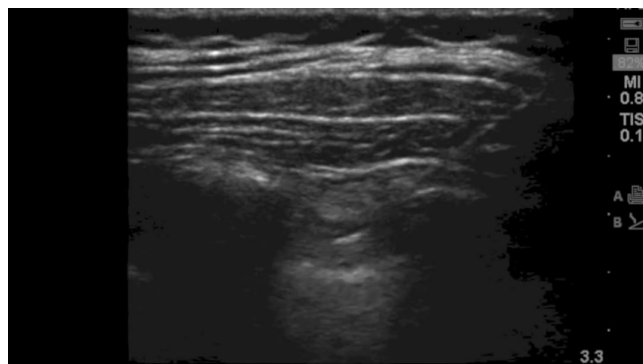


(b)

Figure 2. ESB (a) & (b).



(a)



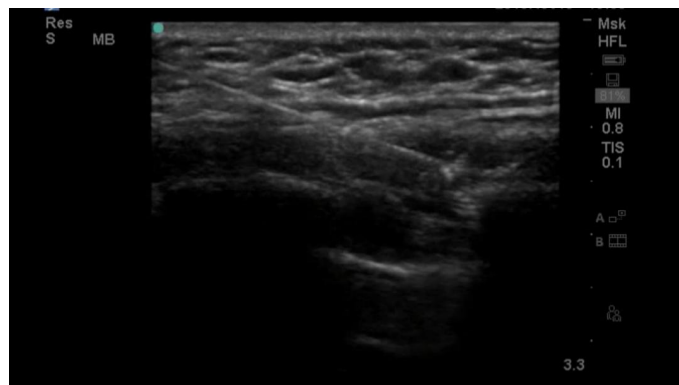
(b)

Figure 3. PVB (a) & (b).

mm echogenic needle was advanced in-plane to introduce this fascial plane in cranio-caudal direction. Once the needle was in perfect position, confirmed by hydrodissection on injecting 2 - 3 ml of normal saline then, 20 ml of 2% artecaine with adrenaline was injected. In such case, settling the drug below SA using rib as the end point is safer [Figure 4].

Vital signs (heart rate [HR], systolic, diastolic and mean blood pressure) were registered immediately before induction of anaesthesia, 10 min after induction, and then every 30 min, until the end of surgery. The patient was supposed to have pain, if HR or mean arterial pressure increased >20% from baseline (at the time just before induction), sufficient anaesthetic depth by inhalation anaesthesia and a bolus of 25 mcg fentanyl were treated IV if still high.

In the PACU, patient-controlled analgesia (PCA) pump was connected to the patient intravenously. The pump status was morphine (1 mg per ml) bolus dose 1 mg, lockout interval 10 min and maximum dose 4 mg per hour. Pain was observed by an autonomous investigator, who was blinded, as he was not knowing of the type of block (ESB, PVB or SAPB) done to the patient. He applied the VAS scale (0 = no pain and 10 = worst imaginable pain) to estimate the pain at 2, 4, 6, 12 and 24 h after surgery and registered this in a patient sheet. The patient was directed to press the PCA button, whenever pain VAS ≥ 4 . Duration of analgesia was from the time of administration of block to the first use of PCA



(a)



(b)

Figure 4. SAPB (a) & (b).

by the patient, as registered by the nurse. Morphine consumption and morphine-related side effects (nausea, vomiting, respiratory depression and itching) were registered at 2, 4, 6, 12 and 24 h after surgery. Ondansetron was managed IV for nausea/vomiting and diphenhydramine was given IV for itching. One gram paracetamol was administered IV every 8 h.

Our preparatory pilot study with ten participants in each group (ESB, PVB and SAPB) showed that the duration of analgesia (mean \pm standard deviation [SD]) of ESB was 45% higher than PVB which was 35% higher than SPB (ESB, 396 ± 63 PVB, 351 ± 62 min and SPB, 234 ± 61 min). On this data and finding, we calculated the minimum sample size with 90% power of the study and type I error of 0.05 to be 23 patients in each study group. Allowing for withdrawal of 8% of patients, we estimated a total sample size of 25 patients for each group.

The data were analyzed using Statistical Package for the Social Sciences version 21.0 (SPSS Inc. Chicago, Illinois, USA). The categorical variables are given in numbers and percentage (%), and the continuous variables are given as mean \pm SD. Normality of data was tested by Kolmogorov-Smirnov test. The quantitative variables were compared using the Unpaired *t*-test or Mann-Whitney test (when the data sets were not normally distributed) between the groups. The qualitative variables were compared using the Chi-square test or Fisher's exact test. $P < 0.05$ was considered statistically significant.

3. Result

The total number of patients registered during the study period was 75 in three groups 25 in groups Group 1 (ESP), Group 2 (PVB) and Group 3 (SAPB), respectively, being comparable to each other with respect to age, weight, side, duration of surgery and ASA status [Table 1], The number of patients who had incomplete blocks or failed blocks (patients having VAS scores > 8 at 0 min) were two in Group 1, two in Group 2 and one in Group 3 showed in Flow Diagram [Figure 5]. These patients were analyzed at 0 hrs, but came out from further VAS analysis because they received alternative methods of analgesia.

VAS was found to be lower in ESB group than PVB group at 2, 4, 6 and 12 h while values were lower in PVB group compared to SAPB group at 2, 4, 6, 12 and 24 h [Table 2] [Figure 6].

Table 1. Patient demographic data.

	(ESP) Group	(PVB) Group	(SAPB) Group	PValue
Age	55 ± 2.9	55.1 ± 3.2	50.2 ± 7.8	0.409
Body mass index	26.2 ± 1.8	24.8 ± 1.4	23.5 ± 3.2	0.560
Side of surgery right	15	12	14	0.582
Left	10	13	11	-
ASA Class I/II	14/11	9/16	12/13	0.409
Duration of surgery (min)	210 ± 19	206 ± 18	203 ± 14	0.582

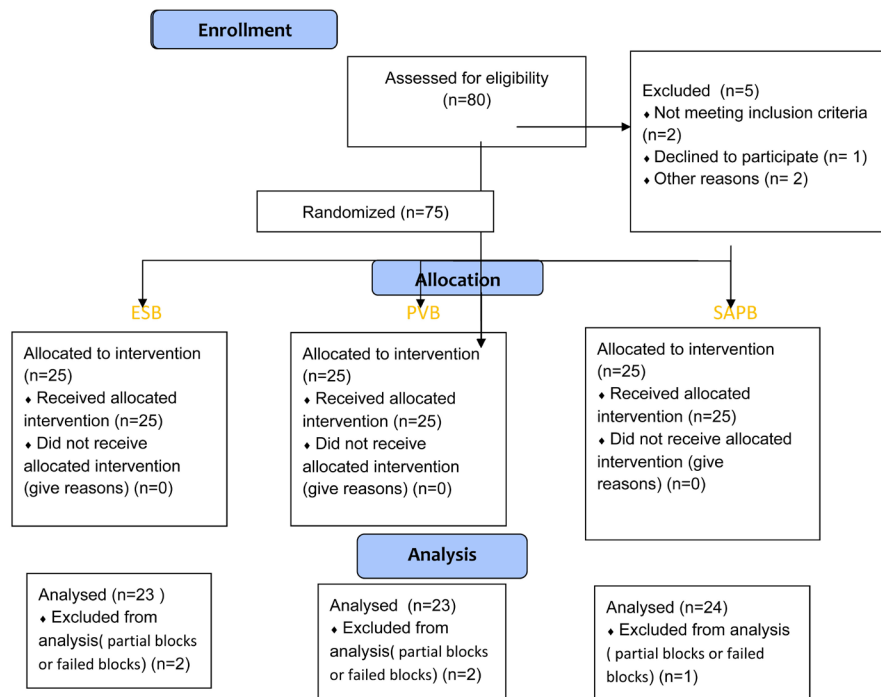


Figure 5. Consort flow diagram.

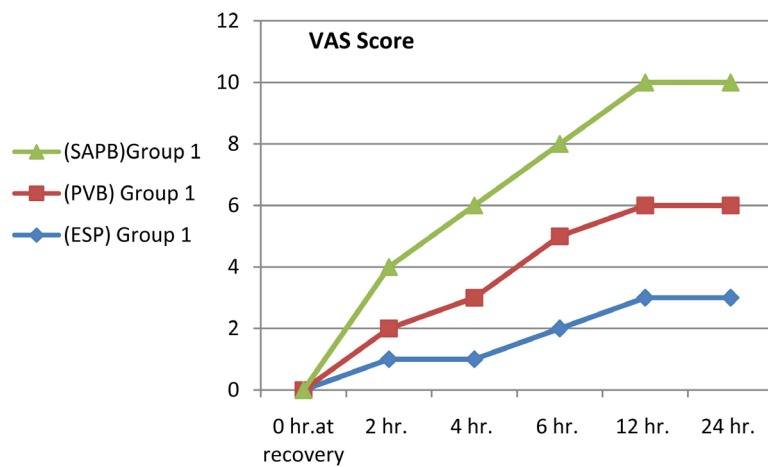


Figure 6. VAS score.

Table 2. VAS score.

	(ESP) Group	(PVB) Group	(SAPB) Group	PValue
VAS Scores				
0 hr. at recovery Median (Range)	1 (0 - 3)	1 (0 - 3)	1 (0 - 3)	0.135
2 hr. Median (Range)	1 (0 - 3)	1 (0 - 4)	2 (0 - 4)	0.135
4 hr. Median (Range)	1 (0 - 4)	2 (0 - 4)	3 (0 - 5)	(<i>P</i> < 0.05)
6 hr. Median (Range)	2 (1 - 4)	3 (1 - 4)	3 (1 - 5)	(<i>P</i> < 0.05)
12 hr. Median (Range)	3 (1 - 4)	3 (1 - 5)	4 (1 - 6)	(<i>P</i> < 0.05)
24 hr. Median (Range)	3 (1 - 5)	3 (1 - 5)	4 (1 - 6)	(<i>P</i> < 0.05)

Mean duration of analgesia, that is, duration to first analgesic requirement was found to be significantly prolonged in Group 1 (ESB) (416 ± 68 min) compared to Group 2 (PVB) (371 ± 67 min) and Group 3 (SAPB) (343 ± 54.7 min) ($P < 0.001$) [Table 3] [Figure 7].

Total dose of morphine(mg) in ESB group were 4 ± 2 , while in PVB group were 6 ± 2 and in SAPB group were 7 ± 2 ($P < 0.05$) [Table 3] [Figure 8].

No significant complications such as vascular puncture, hypotension, pleural puncture or pneumothorax were seen in any of the groups.

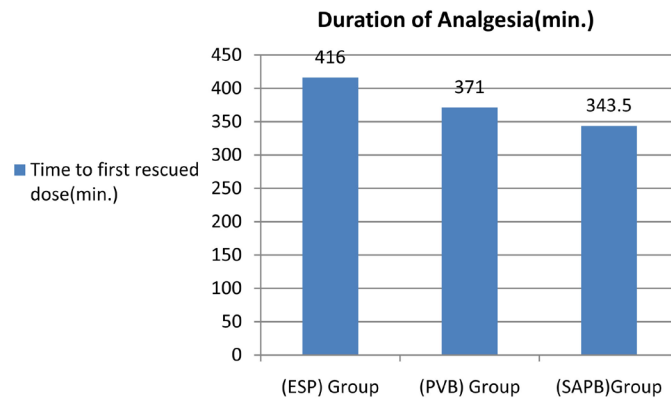


Figure 7. Duration of postoperative Analgesia (min).

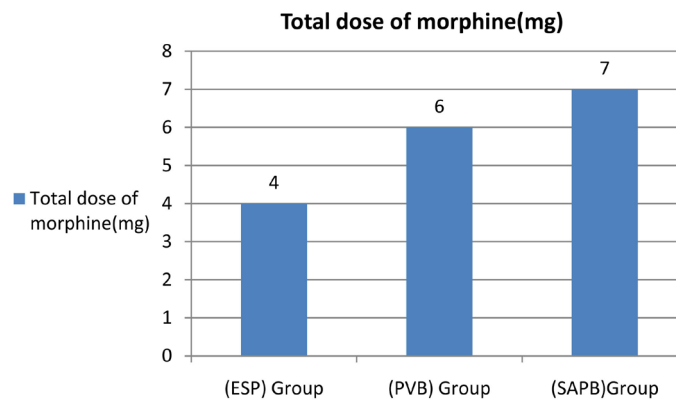


Figure 8. Total dose of morphine (mg).

Table 3. Time to first analgesic requirement and total dose.

	(ESP) Group	(PVB) Group	(SAPB) Group	Pvalue
Time to first rescued dose (min)	416 ± 68	371 ± 67	343.5 ± 54.7	$(P < 0.001)$
Total dose of morphine (mg)	4 ± 2	6 ± 2	7 ± 2	$(P < 0.05)$

4. Discussion

Different regional anaesthetic such as local wound infiltration, thoracic epidural and more recently, ultrasound-guided fascial plane blocks as serratus anterior plain block (SAPB), thoracic paravertebral block (PVB) and erector spinae plane block (ESB) have been utilized to prolong analgesia in cancer breast surgeries.

These procedures not only treat acute post-operative pain but also assist and prevent chronic post-surgical pain and may prevent cancer recurrence [14]. With the entrance of ultrasound in the operating theater; regional anaesthetic block training has undergone a wonderful change. PVB has long been believed the gold standard procedure in patients undergoing breast cancer surgery. The possible side effects and complications of PVB include pneumothorax, vascular puncture, intrathecal or epidural spread and sympathetic block leading to haemodynamic instability [15]. In breast surgeries, ultrasound-guided recent interfascial plane blocks as (ESB) have been appeared which are being used as efficient alternatives to more invasive and more side effects techniques such as PVB.

ESP block has elicited as an effective novel and recent regional technique with good analgesia with less opioid requirements, in addition to simplicity and safety [7] [8]. Since the description of these newer and safer interfascial plane blocks, different authors have studied their use in breast surgeries.

This randomized double-blind clinical trial compared the three main procedures of prolonged analgesia after mastectomy with axillary dissection and found that the post-operative VAS scores were better in the (ESB) group compared to the (PVB) and (SAPB) groups ($P < 0.05$). In addition, the duration of post-operative analgesia was significantly prolonged in the (ESB) group compared to the other groups ($P < 0.001$). And also, analgesic requirement significantly lower in the (ESB) group compared to the other groups ($P < 0.05$).

Ultrasound-guided PVB is an excellent analgesic procedures for breast surgery because not only does it decrease pain but also it decreases PONV and length of hospital stay due to less morphine requirement [16]-[21]. PVB is requiring a higher degree of skill; however the educational curve of ultrasound-guided rather declines. Moreover, a number of complications have priority been detected with PVB [3] [16]. Blanco *et al.* proposed SAPB as a substitution to PVB for surgeries on the anterior and lateral thoracic wall including breast surgeries [22]. SAPB is an easy block to teaching and performing because the serratus anterior muscle is an easy sonographic landmark to identify for this block also, pleura and ribs well defined.

Our supposition of a longer duration of analgesia of PVB in comparison to SAPB is based on the technicality of action of the two blocks. The breast is supplied by anterior and lateral cutaneous branches of the second to sixth thoracic intercostal nerves and supraclavicular nerves [23]. Supraclavicular nerves from the lower fibers of the cervical plexus innervate the upper and lateral parts of the breast but, anterior cutaneous branches of intercostal nerves (T2 - T4) innervate the parasternal area of breast. Because the anterior cutaneous branches of the intercostal nerves and supraclavicular nerves are escaped, SAPB is not predicted to produce complete analgesia of the chest wall [22] [24] [25]. Furthermore, SAPB may not realize sufficient somatic and sympathetic blockade in the axillary area, as would be predicted with thoracic PVB [22] [24] [26]. The local anaesthetic in PVB blocks the spinal nerves directly and expands laterally to

block the intercostal nerves and expands medially into the epidural space through the intervertebral foramina and influences the sympathetic chain, leading to strong analgesia but, in ESB is indirect by this way [26] [27] [28]. The local anaesthetic can also diffuse longitudinally cranially or caudally in PVB. This is supported by Hetta and Rezk [29] and also in ESB who compared SAPB and PVB block in patients with MRM and reported complete sensory blockade over T1 - T7 dermatome levels in 100% of the patients after PVB although 40% of the patients had incomplete sensory blockade in the axilla after SAPB [29].

In Hetta *et al.* Study also noted that the duration of analgesia of SAPB was significantly shorter compared to PVB [(median [range], 6 h [5 - 7 h] for SAPB vs. 11 h [9 - 13 h] for PVB)] by bupivacaine 25% [29]. In our study, we found a much longer duration of analgesia in groups ESB (means \pm SD), [396 \pm 63 min] group PVB [351 \pm 62 min]) vs. group SAPB [323.5 \pm 49.7 min] by articaine 2%. It is nice and pleasant to note that four or more intercostal spaces may be anaesthetised by a single level PVB injection,

The volume of local anaesthetic is also likely an important detection of the range and duration of analgesia for ESB, SAPB and thoracic PVB. In Hetta *et al.* study, a more volume of bupivacaine was injected in SAPB (30 ml vs. 20 ml in our study), and more efficient analgesia was detected than our study [29]. And so, SAPB is a fascial block, a larger volume is expected to enhance local anaesthetic spread in this technique. In Wahba SS *et al.* study, after injection of 15 - 20 ml of levobupivacaine 0.25% at thoracic fourth level for PVB [30], the duration of analgesia was shorter 137.5 [115 - 165 min) than in our study (371 \pm 67 min), again highlighting the influence of the local anaesthetic volume and type on duration of analgesia. Similar to our study, Klein SM *et al.* study found a 24 h post-operative morphine consumption higher in the SAPB group compared to PVB group and ESB (mg) [1] [30]. Similar to our study, a recent study of Abdallah FW *et al.* also found a lowered consumption of opioids intraoperatively and postoperatively, decreased PONV and increased duration of analgesia after ambulatory breast cancer surgery [31]. In our study both ESB, PVB and SAPB groups provide excellent post-operative recovery and lower the opioid requirement, as reflected by post-operative morphine consumption 4 \pm 2, 6 \pm 2 and 7 \pm 2 mg respectively up to 24 h postoperatively [31]. Our study results add to the limited amount of objective data available today as regarding the analgesic profile of these three new blocks after MRM. One of the powerful of our study is the use of a standardized and fixed volume and concentration of local anaesthetic in all blocks (20 ml of 2% articaine). Hence, our methodology has provided an equal analgesic comparison between groups as compared to other studies which administered unequal volume and/or concentration of local anesthetic [29] [30]. Limitations in our study were also present, we could not determine on set time of block or sensory level detection because both blocks were done after induction of general anaesthesia. We do a single level injection, realizing that multiple injection procedures may provide more effective analgesia in blocks. In our study did not put a catheter to provide continuous analgesia and we could nei-

ther comment on clinical safety nor the long-term impact (as regard, development of chronic pain) of the three modalities in this small study. We conclude that ESB can thus be considered better than PVB and SAPB for providing analgesia after breast surgery and ultrasound-guided ESP block is an excellent regional anaesthesia procedure on mastectomy and has wide applications in pain relief ranging from postoperative acute pain in breast surgeries. We hope that in the future studies will observing the remaining issues such as the duration of analgesia with and without adjuncts and also we hope a systematic review and meta-analyses are suggested comparing the post-operative analgesic techniques for cancer breast surgery.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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