ORIGINAL RESEARCH

Comparative evaluation of two different concentrations of levobupivacaine on analgesic efficacy of ultrasound guided erector spinae block for breast surgery

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Abstract

Background &Aims: Erector Spinae Plane (ESP) block has been proven to be an effective component of multimodal analgesic regimens for breast surgeries with fewer side effects. Here, we aimed to compare the analgesic efficacy of two different concentrations of levobupivacaine in ultrasound guided ESP block for breast surgery in terms of duration, quality of analgesia and postoperative analgesic consumption.

Methodology: This prospective randomized comparative trial was done on 60 adult female patients aged between 20-65 years who were scheduled for unilateral modified radical mastectomy and randomly divided into two groups (30 each). In group A, 0.25% levobupivacaine and in group B, 0.375% levobupivacaine in same volume (20 mL) was given in ultrasound (US)-guided ESP block. Duration, quality of analgesia and adverse effects were noted. Statistical analysis was performed using student's t-test and chi-square test.

Result: The duration of analgesia was significantly prolonged in group B as compared to group A (907.7 ± 53.8 minutes and 711 ± 68.9 minutes respectively). The postoperative VNRS scores remained persistently less than 3 in both the groups except at 12th hours in group A and 18th hours in Group B. Postoperative rescue analgesic consumption was also higher in Group A (230 ± 46.6 mg) as compared to Group B (136.7 ± 49.0 mg).

Conclusion: Although use of both concentrations of levobupivacaine (0.25% and 0.375%) in ESP block can provide effective postoperative analgesia but the 0.375% levobupivacaine has significantly prolonged analgesia and lesser postoperative analgesic consumption without any significant adverse effects in unilateral breast surgery.

Keyword-: Erector spinae plane block; Levobupivacaine 0.25%; Levobupivacaine 0.375%; Analgesia.

Introduction

Breast surgery has become one of the most common cancer surgeries among the female population all over the world due to increase in incidence and detection tool of breast cancer. However, postoperative pain management following modified radical mastectomy (MRM) remains a great challenge and more than 60% of the patients categorize their acute pain as moderate to severe intensity [1]. Moreover, inadequate acute pain management has increased the incidence of chronic pain as high as 25–50% after mastectomy and is well validated with conditions like paraesthesia, intercostobrachial neuralgia and phantom breast pain [2,3]. Therefore, multimodal analgesic technique is of paramount importance in order to reduce the incidence of adverse effects of acute pain and

progression to chronic pain syndromes Multimodal analgesia model includes intravenous analgesics, local wound infiltration and different regional anaesthetic techniques like thoracic epidural block (TEA), ipsilateral thoracic paravertebral block (TPVB) and interfascial blocks [4-6]. Although regional anaesthesia techniques provide good perioperative analgesia, decreases opioid use and reduces the incidence of chronic pain but performance of these blocks using anatomical landmark technique may be associated with potentially serious complications like vascular puncture, nerve damage, accidental pneumothorax and epidural spread of local anaesthetic necessitating the development of alternative techniques [7,8]. Therefore, ultrasound (US) guided interfascial nerve blocks like pectoral nerve block and serratus anterior plane block have now become a part of the multimodal postoperative analgesic strategy. Erector spinae plane (ESP) block is a recent addition to US guided interfascial plane block technique proposed by Forero et al. (2016) which was initially used for thoracic neuropathic pain [9]. Erector spine plane is a potential space deep to erector spinae muscle (ESM), where the injected local anesthetic (LA) spreads cranio-caudally up to several levels from the point of injection to block both dorsal and ventral rami. The dermatomes covered by ESP block depend on the point of entry, concentration, and the volume of LA used as with other interfascial plane block. The choice of local anesthetic agent has been reported to be ropivacaine, levobupivacaine, bupivacaine (at concentrations of 0.5%, 0.25%, or 0.375%), and lidocaine (1% or 2% concentration) for ESP block [10,11]. Recently, several studies have reported the effectiveness of ESP blocks for breast cancer surgery with ease of performance and good analgesia but the data on the optimum local anaesthetic concentration and volume for this block has not been established till now. As the comparative data regarding analgesic efficacy of different concentrations of levobupivacaine for ESP block is still lacking, we planned this prospective, randomized trial to evaluate the efficacy of two different concentrations of levobupivacaine (0.25% vs 0.375%) with similar volume in US guided ESP block for breast surgery in terms of duration of analgesia (primary outcome), quality of analgesia, and total postoperative analgesic consumption in 24 hours (secondary outcome).

Material & Methods

This prospective, randomized, and double-blind clinical trial was conducted over a period of 18 months after the institutional ethical committee approval (ECR/836/Inst/PB/2016) dated 27/02/20 as per guidelines of the Indian Council of Medical Research for biomedical research. After registering the trial with the Clinical Trial Registry of India (CTRI/2020/11/029140), this study was planned on adult female patients aged between 20-65 years with American society of Anaesthesiologist (ASA) status I or II who were posted for unilateral modified radical mastectomy for breast cancer under general anaesthesia. Patient who refused for block, any contraindication to regional block like coagulopathies, obesity with body mass index (BMI) > 30 kg/m^2, any cardiopulmonary or hepatorenal dysfunction and with known allergy to study drugs were excluded from study. A systematic preoperative assessment of all the patients was done by an anesthesiologist and required detailed information about trial including verbal numeric rating scale (VNRS) used for postoperative pain measurement was explained to them. Each patients received oral premedication of Tab alprazolam 0.25 mg and Tab ranitidine 150 mg at night before surgery and were instructed nil per orally for six hours. After obtaining written informed consent, standard ASA monitors including electrocardiography (ECG), pulse oximeter (SpO2) and noninvasive blood pressure (NIBP) were attached in operation room and baseline parameters were recorded. Intravenous (IV) line with 18G cannula secured on the arm of nonoperating side and ringer lactate infusion at 10 ml/kg was started. All the selected patients were randomly assigned into two groups (30 patients each) by simple random method with computer generated randomization programme and allocation concealed by opaque sealed envelope containing code. All patients received 20 mL of 0.25 % levobupivacaine in group A and 0.375% levobupivacaine in group B for ESP block. The study drug was prepared in identical 20 mL syringe as per randomisation list by independent anaesthetist who was not involved in subsequent part of study. Similarly, anesthesiologist performing block and assessing postoperative pain were also blinded to drug prepared and injected in ESP block The ESP block on the side of surgery was performed by senior anaesthesiologist at T4 level in sitting position under all aseptic conditions and after local skin infiltration by using linear high frequency (5-10MHz) probe of ultrasound machine (Esaote my lab). Initially, probe was placed in transverse orientation to identify spinous process and then moved 3cm laterally and rotated 90° on transverse process in a parasagittal plane. After identification of erector spinae plane, 23G Quincke spinal needle (Becton Dickinson [BD], Franklin Lakes, NJ, USA) attached to 10 cm extension tubing for drug infusion was inserted craniocaudally using in plane technique. After confirming exact location of needle tip (by forming a well-defined hypo echoic elliptical shape deeper to erector spinae muscle), the study drug was injected. Sensory effect was confirmed by pin prick sensation after injection of study drugs from dermatomal level T1-T8. Standard general anesthesia technique involving intravenous morphine (0.1 mg/kg), IV propofol (1.5-2.5 mg/kg) and IV vecuronium (0.1mg/kg) was followed for every patient and airway was secured. Anes the sia was maintained with oxygen & nitrous oxide mixture (50:50) and

isoflurane (0.2-1 MAC) along with maintenance doses of vecuronium. All the patients were monitored intraoperatively for vital parameters at every 5 minutes for first 30 minutes then every 10 minutes interval till end of the surgery. Hypotension (fall in mean arterial pressure of > 20% of baseline values) and bradycardia (heart rate of ≤ 50 beats/min) was managed as per standard protocol. Intravenous paracetamol 15 mg/kg was administered 30 minutes before the end of surgery as a part of multimodal analgesia. After completion of surgery and successful extubation, the patients were transferred to post anesthesia care uni Postoperatively, all patients were observed for vital parameters and quality of analgesia at every 15 mins for first hour and then at 2, 4, 8, 12, 18 and 24 hours. Quality of analgesia was assessed by using 11-point verbal numeric rating scale (VNRS scale) as 0= no pain and 11= worst pain. Any patient having VNRS > 3 postoperatively, was given rescue analgesia in the form of tramadol 100 mg intravenously. If the patient still had VNRS>3, then injection morphine 0.1mg/kg IV was given as second rescue analgesic drug. Total analgesic consumption and total number of rescue analgesic doses given postoperatively over first 24 hours were recorded. Duration of analgesia as primary outcome of the study was defined as time taken from the completion of injection to the request of first rescue analgesia and was noted. Patient satisfaction score was assessed with a five-point numerical scale (1=very satisfied, 2=satisfied, 3=undecided, 4=dissatisfied, 5=very dissatisfied) at the end of 24 hours postoperatively. Any adverse effects like nausea and vomiting, hypotension, sedation and block related complication were noted and managed accordingly.

Statistical Analysis

Based on previous studies and considering duration of analgesia as primary outcome, we calculated the sample size of 27 patients in each group to detect the minimum difference of 20% between two means of the study groups with 80% power along with 5% probability of type one error. So, we enrolled total 60 patients (30 in each group) to cover 10% drop out rate. Statistical analysis was done using IBM SPSS Statistics version 22.0 and Medcalc Statistical software version 19 (MedCalc Software bvba, Ostend, Belgium). After completion of study, data were compiled and presented as mean ± standard deviation for continuous variable and as percentages for categorical variables. Unpaired t test was used to compare parametric data and chi square test was used for categorical variables. p-value of less than 0.05 was considered statistically significant and less than 0.001 as highly significant.

Results

In present study, total 66 patients were assessed but six patients did not meet inclusion criteria (four patients were above age of 65 and two patients were of ASA III status). So, finally 60 patients were enrolled for study and divided into two groups of 30 patients each (figure 1). Both the groups were comparable in terms of age, weight, BMI, ASA status and duration of surgery (table 1). Regarding perioperative hemodynamic parameters (HR, MAP, SpO2 and temperature), both the groups had no statistically significant difference. Duration of analgesia was longer in Group B as compared to Group A with mean duration of 907.7 ± 53.8 minutes in group B and of 711 ± 68.9 minutes in group A which was statistically highly significant ($p < 0.001$) (table 2). Postoperatively, quality of analgesia was better in group B in comparison to group A as the mean VNRS score were statistically significantly low in group B as always compared to group A except before 30 minutes. The VNRS scores remained persistently less than 3 in both the groups postoperatively except at 12 hrs in group A and 18 hrs in group B that correlates well with duration of analgesia in our present study (figure 2). Mean postoperative analgesic consumption in first 24 hrs was significantly lower in group B (136.7 ± 49.0 mg) as compared to group A (230.0 ± 46.6 mg) and this difference was highly significant ($p <0.001$) (table 2). Mean number of rescue analgesics doses required were significantly lesser in group B than group A (1.4 ± 0.5 vs 2.2 ± 0.4 respectively). Patients in group B have better satisfaction score than group A patients, which was statistically significant (p value < 0.05) and they were more satisfied with quality of analgesia in group B than group A (figure 3). Only nine patients (30%) in group A and seven patients (23.5%) in group B had reported nausea/vomiting as adverse effects in postoperative period. None of the patients had reported any other adverse effects like pneumothorax, vascular puncture, local anesthetic toxicity, vomiting, hypotension or bradycardia and pain at injection site.

Table 1:Demographic variable and Duration of surgery among both the groups

Parameters	Group A (n=30)	Group B (n=30)	p value*
Age (years)	49.7 ± 9.5	48.5 ± 12.5	0.669 (NS)
Weight (Kg)	69.0 ± 4.8	68.5 ± 4.9	0.689 (NS)
BMI (kg/m^2)	25.5 ± 1.9	25.1 ± 1.7	0.370 (NS)
ASA I/II	13/17	14/16	0.795 (NS)
Duration of Surgery (minutes)	78.3±10.2	77.0±12.6	0.665 (NS)

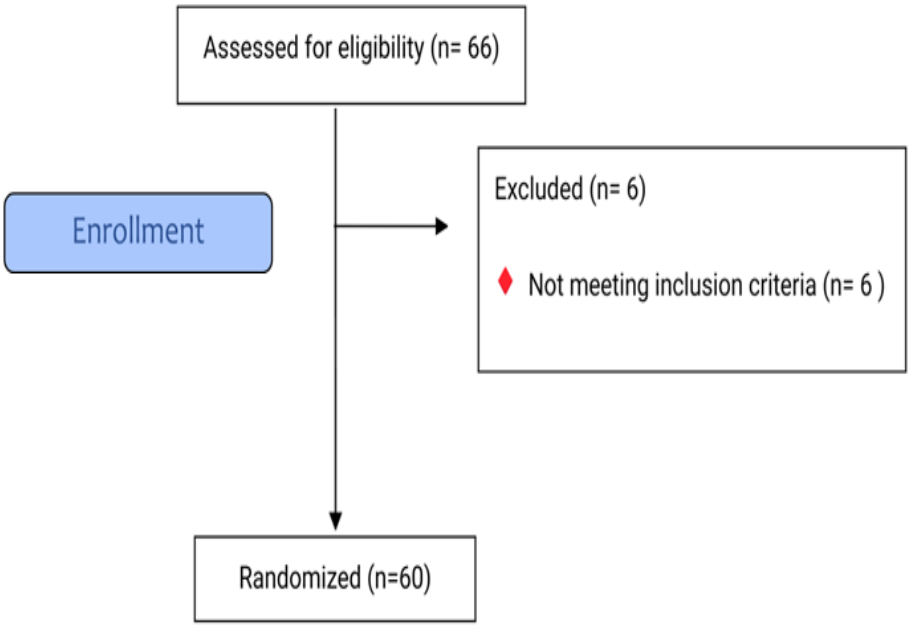
P value *<0.05 is considered significant, NS- non significant.

Table 2 :Mean duration of analgesia and Analgesic consumption among two groups

Variable	Group A (n=30)	Group B (n=30)	p-value
	Mean ± SD	Mean ± SD	
Mean duration of analgesia (minutes)	711 ± 68.9	907.7 ± 53.8	<0.001*
Total analgesic consumption (mg)	230 ± 46.6	136.7 ± 49.0	<0.001*
Mean number of analgesic doses	2.2± 0.4	1.4 ± 0.5	<0.001*

p value <0.05 is considered significant, *<0.001 is highly significant.

Figure 1- CONSORT Flow Diagram



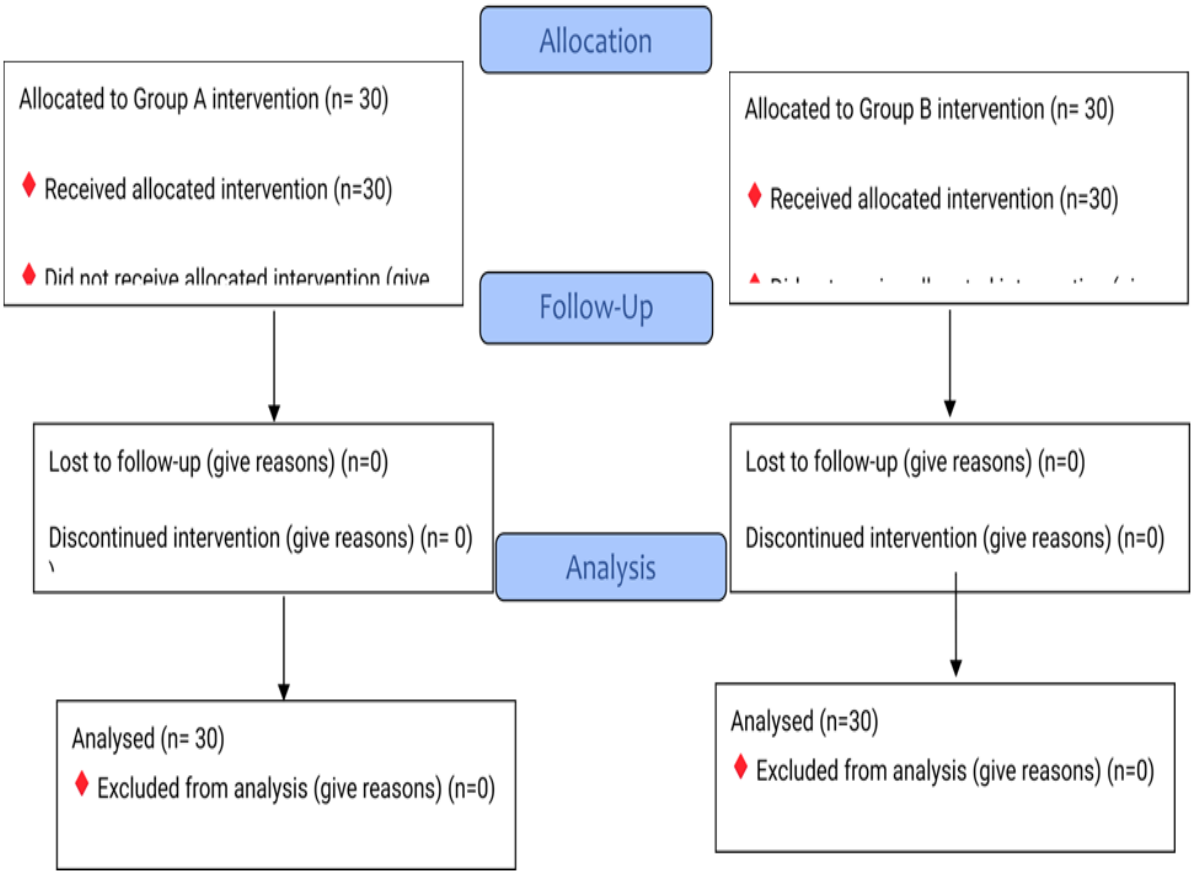


Figure 2: Postoperative mean verbal numeric rating scale trends in study group

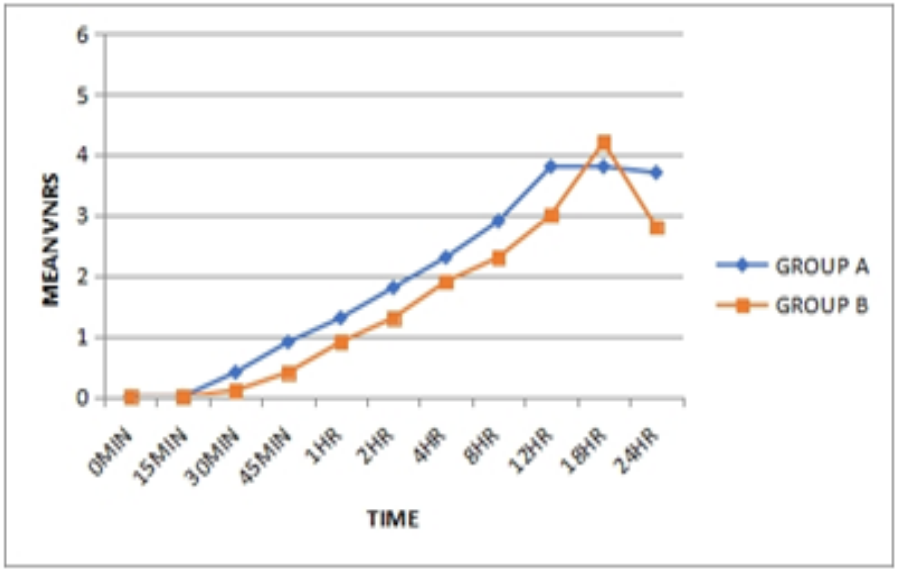
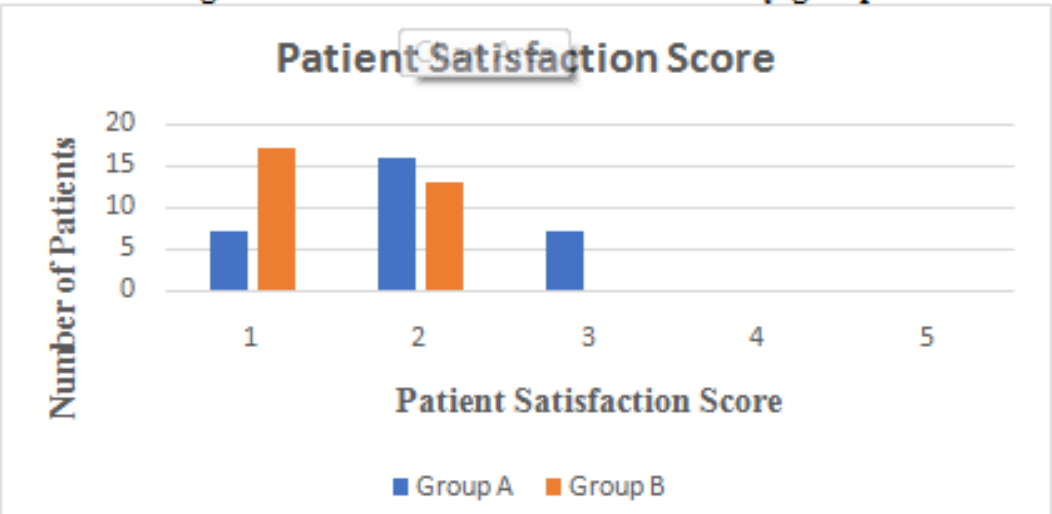


Figure 3: Patient satisfaction score in study group



Discussion

Breast surgery is usually performed for conditions like benign lump excision, drainage of abscess or cosmetic reasons, but the most common indication is breast cancer. Postoperative analgesia has always been difficult in radical mastectomy due to complex anatomy and innervation of the chest and armpit [12]. The development of ultrasonography led to the establishment of ultrasound (US) guided peripheral nerve blocks recently, including intramuscular, compartment, and interfascial plane blocks. One of the newest techniques that has been described recently is the ESP block that has been found to be safer than epidural or paravertebral block as the injection was administered into a tissue plane distant from major blood vessels, pleura and spinal cord nerves [13].In current literature, many researchers used different concentrations of bupivacaine, ropivacaine, levobupivacaine and lidocaine during ESP block procedures and found to be effective [11,12,14]. Veiga et al. performed ESP block using 20 ml of 0.5% levobupivacaine for postoperative analgesia in unilateral mastectomy surgery [15]. Similarly, another two recent studies evaluated the effect of ESP block by using 20 ml of 0.25% bupivacaine [16,17]. All these studies reported the effectiveness of ESP block for postoperative analgesia after unilateral breast surgery. Due to association of local anesthetic systemic toxicity (LAST) with use of higher concentration of local anes the tics, use of a larger volume and lower concentration of local anesthetic has been advised by many researchers as a larger volume solution tended to cover a greater number of segments for better postoperative analgesia [18]. However, two cases of failed ESP block to provide complete analgesia on T2-T6 intercostal nerves after radical mastectomy with use of 25 ml of 0.25% bupivacaine had been reported [19]. The authors asserted that provided concentration with given volume was insufficient to affect the anterior branches of the T2-T5 spinal nerves. This finding was also confirmed by Ivanusic et al., who showed that ESP block performed with 20 ml of 0.25% methylene blue dyed only the posterior and lateral branches of the thoracic nerve [20]. While on the other hand, a higher local anesthetic concentration is known to allow better diffusion into the paravertebral space, thereby result in more effective nerve block [21]. Therefore, in the current study we compared the efficacy of ESP block using two different concentrations of the levobupivacaine (0.25% vs 0.375%) in the similar volume of solution. Although both the concentrations provided effective analgesia in the postoperative period in our study but the ESP block with higher concentration of levobupivacaine (0.375%) had prolonged duration and better quality of analgesia than 0.25% levobupivacaine. The postoperative VNRS scores remained persistently less than 3 in both the groups postoperatively except at 12hrs in group A and 18hrs in Group B, that correlates well with duration of analgesia. The requirement time for rescue analgesia was earlier in group A as compared to group B. Besides the above advantages of performing ESP block using a higher concentration of local anesthetic agent, there might some disadvantages as well. Like, levobupivacaine overdose and systemic toxicity must be considered in surgeries that require bilateral ESP block and in low body weight patients. In the present study, we performed unilateral ESP block and used a total dose of 100 mg of levobupivacaine maximum in each patient. Our results coincide with the study conducted by Altiparmak et. al., where ESP block was performed with 0.375% bupivacaine in group I and with 0.25% bupivacaine in group II in 42 patients scheduled for unilateral modified radical mastectomy surgery [22]. Here, NRS scores were significantly lower at every time points in group I as compared to group II. The postoperative rescue analgesic requirements were also significantly higher in group II as compared to group I. Kamel et. al., compared the US-guided ESP block versus TAP block for open total

abdominal hysterectomy in which erector spinae (ES) group received bilateral ESP block with 20 mL of bupivacaine 0.375% plus 5 ug/mL adrenaline (1:200000) and transversus abdominis (TA) group received bilateral TAP block with the same volume of bupivacaine plus adrenaline [23]. The time for requirement of first rescue analgesic was similar to our study and significantly prolonged in the ES group (14.81 ± 3.52 hours) compared with the TA group (10.58 ± 2.35 hours) and the total amount of morphine consumption in 24 hours postoperatively was also significantly decreased in the ES group. Regarding side effects, our study observed incidence of nausea as 30% in group A and 23.5% in group B during 24 hours postoperative period and these results were supported by other studies [22,24]. Although multiple risk factor factors like young female, breast surgery, previous history of nausea/ vomiting and postoperative opioid use can be responsible for higher incidence of nausea/vomiting here but the difference in adverse effects among both groups was statistically insignificant. The present study has certain limitation. Firstly, we have performed this ESP block in awake patient to check and confirm the sensory effect of block before induction of general anesthesia. We did not notice any failure of block and probable reason for 100% success was ultrasound guidance and experienced anesthesiologist. Secondly, we used only 20 ml volume of local anesthetic for ESP block but there are studies who had used 25-30 ml volume for ESP block [25]. However, optimum volume of local anesthetics for peripheral blocks is still debatable. Thirdly, we did not assess dynamic VNRS during coughing and arm abduction postoperatively.

Conclusion

We conclude that use of both 0.25% and 0.375% levobupivacaine in ESP block can provide effective postoperative analgesia in the unilateral breast surgery but 0.375% levobupivacaine had prolonged duration and better quality of analgesia. However, risk of overdose and systemic toxicity must be considered while using higher concentration of local anesthetics especially during bilateral blocks.

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