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Comparison of the effect of erector spinae plane block for postoperative analgesia on neutrophil/lymphocyte ratio and platelet/lymphocyte ratio in patients operated for breast cancer

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ABSTRACT

Objectives: It was seen that recurrence and metastasis after breast cancer surgery are related to the immune response of the host. Anesthetic agents modulate the surgical stress response or directly impair the functions of immune system cells. In our study, we aimed to compare the effects of nonsteroidal anti-inflammatory drugs and erector spinae plane block, which are among the methods we use for postoperative analgesia, on the neutrophil/lymphocyte ratio and platelet/lymphocyte ratio in patients undergoing breast cancer surgery.

Methods: One hundred female patients aged 18-75 years, scheduled for unilateral breast cancer surgery, and who agreed to participate were included in our study. These cases were divided into two groups of the analgesia method: Those with erector spinae plane block (Group E) and those who were administered nonsteroidal anti-inflammatory drugs (Group N). According to the results, preoperative and postoperative neutrophil/lymphocyte ratio and platelet/lymphocyte ratio values were calculated and recorded.

Results: Neutrophil/lymphocyte ratio and platelet/lymphocyte ratio were statistically higher in both groups in the postoperative period. No statistically significant difference was found when the preoperative and postoperative measurement changes of the laboratory parameters between the groups were compared. Postoperative VAS scores were statistically significantly lower in Group E.

Conclusions: We concluded that when erector spinae plane block and nonsteroidal anti-inflammatory drug use were compared in managing postoperative analgesia in breast cancer surgery, their effects on the neutrophil/lymphocyte ratio and platelet/lymphocyte ratio were not superior to each other. However, the erector spinae plane block was superior for adequate pain control.

Keywords: Breast cancer, neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), erector spinae plane block (ESPB), stress response

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Women's breast cancer is the fifth leading cause of worldwide cancer deaths and constitutes 11.7 % of all cancer cases [1]. The reactions of immune system cells to breast cancer are associated with the prognosis and mortality of cancer. Although immune surveillance provides an important first defense against cancer cells, it can be associated with tumor growth by changing tissue microchexes [2]. It is suggested that the increase in the number of neutrophils in these patients is correlated with poor prognosis. Neutrophils remodel the tumor microenvironment and suppress the cytolytic activity of the host immune system. It has been shown that neutrophils in peripheral blood secrete inflammatory mediators that cause tumor growth. Unlike neutrophils, the presence of lymphocytes in tumor tissue is associated with healing and good prognosis in breast cancer patients. Lymphocytes in the tumor microenvironment are thought to fight tumor cells in the host by inhibiting the growth and migration of tumor cells [3]. It is known that platelets directly interact with tumor cells and secrete the factors contributing to tumor growth, invasion, and angiogenesis. Thrombocytes can protect tumor cells from natural lethal cell-mediated lysis and facilitate metastasis [4].

It is known that surgical procedures and anesthesia practices indirectly affect the inflammatory response process by modifying the stress response or directly disrupting the functions of immune system cells. It has been reported that intravenous anesthetics, inhalation anesthetics and opioids used in general anesthesia induction and maintenance suppress the immune system and increase cancer recurrence in oncological surgery [5].

Recently, oncological surgery, there is a positive effect on survival and metastasis, but has been ordered to regional anesthesia and analgesia techniques that have not yet been consensive [6, 7]. It is thought that the sympathetic blockage formed after the erector spinae plane block (ESPB) for postoperative analgesia of breast cancer surgery suppresses the hemodynamic response of surgical stress [8].

Neutrophil/lymphocyte ratio (NLR) is used as a marker of subclinical inflammation. The stress of leukocytes in the organism, the increase in the number of neutrophils, the number of lymphocytes in the form of a decrease in the physiological response has been shown as a result of the researches. Cellular immunity has an important place in tumor progression. The presence of T lymphocytes in tumor tissue is a significant indicator of the immune response to the tumor. The number of high neutrophils shows the activation of the proinflammatory immunity pathway, and low number of low lymphocytes reflects that cellular immunity is suppressed [9].

Platelet/lymphocyte ratio (PLR) has recently been associated with inflammatory response and immune system like NLR, and has become a prognostic marker in many solid organ tumors. High PLR values were found to be directly related to survival in solid organ tumors such as breast, pancreas and ovarium [10]. As a result of all this, NLR and PLR have taken its place in the literature as cheap, and easy accessible biobelirts.

Our aim in our study; in patients with breast cancer surgery, general anesthesia and nonsteroid antiinflammatory drugs (NSAID) and ESPB, which we use routine for analgesia, to compare the effect of ESPB on NLR and PLR.

METHODS

The study was started with the approval of Namık Kemal University Hospital Clinical Research Ethics Committee (dated 27.10.2020 and decision number 2020.234.10.02). The study was planned as prospective, randomized and single-blind in female patients aged 18-75 who would undergo unilateral elective breast surgery, with the consent of the patients. Anticipating a large effect size (effect size=0.8) difference between the groups, the alpha (α) significance level was 0.05 and the sample size for 95% Power was calculated as 100 people. Patients planned for bilateral mastectomy and lymph node dissection, those with known hematological malignancies, those in pregnancy and puerperium, patients with evidence of active infection in the planned block area, existing coagulopathy, emergency cases, severe organ failure and local anesthetic allergy were excluded from the study.

Randomization was achieved by sealed envelope method. The patients were divided into two: cases to be administered intravenous NSAID (Tenoxicam), one of the methods routinely used for postoperative analgesia (Group N, n=50), and cases to be subjected to ESPB (Group E, n=50). In both groups, demographic data (age, weight, height, BMI), operation time and ASA score were recorded. A tube of blood was taken from all cases into a purple-capped hemogram tube before the operation. In the hemogram analysis, the patients' white blood cell (WBC), leukocyte, lymphocyte, platelet, hemoglobin, hematocrit, mean body volume (MCV), and mean platelet volume (MPV) measurements were recorded. According to the results, NLR and PLR values were calculated and recorded. The patients who would undergo ESPB (Group E) were taken to the waiting room 30 minutes before the operation. All cases were monitored with electrocardiography (ECG), pulse oximetry (SpO_2) and noninvasive blood pressure (NIBP) measurement cuff before general anesthesia, and their vital parameters [heart rate peak (HR), SpO_2, NIBP] were recorded before the operation.

Anesthesia Technique

Routine monitoring (ECG, NIBP and SpO_2) was applied to all patients taken to the operating table. General anesthesia was induced with Propofol 2-3 mg/kg, Fentanyl 1-2 mcg/kg, Rocuronium 0.6 mg/kg intravenously. After muscle relaxation, all patients were orotracheally intubated with an appropriate size laryngoscope. After induction, anesthesia was maintained with 2 L/min flow, 50% oxygen-air mixture, Sevoflurane 2%. Tenoxicam 20 mg was administered intravenously to patients in Group N after anesthesia induction and intubation. At the end of the operation, Atropine 0.01 mg/kg and Neostigmine 0.03 mg/kg were administered intravenously to both groups to reverse the neuromuscular blockade effect.

Analgesia Technique

The block application was performed by an experienced anesthesiologist (who had performed this block at least 20 times), independently of the study, under the guidance of an ultrasonography device (Esaote MyLabX7, United Kingdom). The level of the 4th thoracic vertebra was taken as the block level. The peripheral nerve block needle (Stimuplex Ultra 360® Braun, Germany, 22 gauge, 50 mm) was directed from cranial to caudal under ultrasonography guidance, and when it passed the erector spinae muscle and contacted the transverse process, it was withdrawn slightly and 20 ml 0.25% bupivacaine was injected into the confirmed space (Fig. 1). At the 30th minute after the block, dermatome mapping was performed with a hot-cold test and the patients were taken to the operating table.

Visual analoug scale (VAS) scores of all patients taken to the recovery unit for postoperative care were recorded. Patients were sent to the surgery service when the Modified Aldrete score was 9. A tube of blood was collected from both groups in a purple-capped hemogram tube at the 2nd postoperative hour. Hemogram parameters (WBC, leukocyte, lymphocyte, platelet, hemoglobin, hematocrit, MCV, MPV, NLR, PLR) were recorded. VAS scores of all patients participating in the study were recorded at 0, 2, 4 and 6 hours.

Statistical Analysis

NCSS (Number Cruncher Statistical System) 2007 (Kaysville, Utah, USA) program was used for statistical analysis. Descriptive statistical methods (mean, standard deviation, median, frequency, percentage, minimum, maximum) were used when evaluating the study data. The suitability of quantitative data for normal distribution was tested using the Shapiro-Wilk test and graphical analysis. Independent groups t test was used to compare normally distributed quantitative

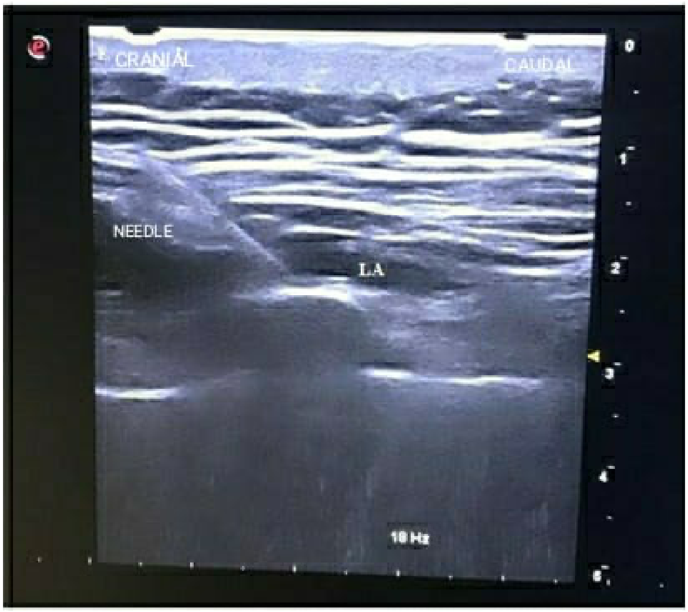

Fig. 1. Erector spinae plane block block needle placement and local anesthetic spread. LA=Local anesthetic.

Table 1. Demographic (Age, weight, height, bmi) data of the cases according to analgesia types

		Group E (n = 50)	Group N (n = 50)	P value
Age (years)		52.54 (25-75)	51.92 (26-75)	0.784[a]
Weight (kg)		76.36 (44-115)	77.06 (47-109)	0.820[a]
Height (m)		1.61 (1.52-1.75)	1.61 (1.50-1.72)	0.639[a]
BMI (kg/m^2)		30.16 (17.2-49.8)	29.23 (18.4-39.4)	0.459[a]
Surgical side	**Right**	23 (46.0)	26 (52.0)	0.548[e]
	Left	27 (54.0)	24 (48.0)	
Surgery time (min)		113.42 (45-175)	118.34 (70-195)	0.883[a]

Descriptive statistics are given as mean (minimum-maximum) depending on the distribution for numerical variables, and as number (%) for categorical variables. Group E=those with erector spinae plane block, Group=those who were administered nonsteroidal anti-inflammatory drugs, BMI=Body Mass Index.

[a]Student t test, [e]Pearson Chi-Square test

variables between two groups, and Mann-Whitney U test was used to compare non-normally distributed quantitative variables between two groups. Friedman Test was used for intragroup comparisons of quantitative variables that did not show normal distribution, and Wilcoxon signed-ranks test with Bonferroni correction was used for evaluation of pairwise comparisons. Dependent groups t test was used for intragroup comparisons of normally distributed quantitative variables. Wilcoxon signed-ranks test was used for intragroup comparisons of quantitative variables that did not show normal distribution. Pearson chi-square test was used to compare qualitative data. Pearson correlation analysis and Spearman correlation analysis were used to evaluate the relationships between quantitative variables. Statistical significance was accepted as $P<0.05$.

RESULTS

The average age of the cases participating in the study was 52.23±11.21, average body weight was 76.71±15.25 kg, average height was 1.61±0.06 m, average BMI was 29.69±6.23 kg/m2. has been determined. The distribution of age, weight, height and BMI between the groups was found to be statistically insignificant (P=0.784, P=0.820, P=0.639 and P=0.459, respectively) (Table 1).

Fourty-nine percent (n=49) of the cases had surgery for right breast cancer, and 51% (n=51) had surgery for left breast cancer (Table 1). The average operation time was 113.42 minutes in Group E (n=50) and 118.34 minutes in Group N (n=50), and there was no significant difference between the groups (P=0.883) (Table 1).

Table 2. Comparison of vital parameters of patients in group E and group N in the preoperative period

Preoperative period	Group E (n=50)	Group N (n=50)	P value[a]
HR	72.22 (53-96)	72.12 (53-98)	0.695
SpO_2	97.92 (94-100)	97.88 (94-100)	0.706
MAP	77.66 (64-95)	78.92 (60-96)	0.162

Descriptive statistics are given as mean (minimum-maximum) depending on the distribution for numerical variables. Group E=those with erector spinae plane block, Group=those who were administered nonsteroidal anti-inflammatory drugs, HR=Heart rate peak, SpO_2=Oxygen saturation, MAP=Mean arterial pressure.

[a]Student t test

Table 3. **Evaluation of laboratory parameters according to analgesia types**

	Group E (n = 50)	Group N (n = 50)	P value
WBC (/µL)			
Preoperative	7485.60 (4330-28620)	6458.66 (2900-10650)	0.334[b]
Postoperative	10127.60 (4810-19300)	9836.80 (4530-21500)	0.738[b]
P value	[c]**0.001****	[c]**0.001****	
Δ(Preop-Postop)	2642.00 (35.20)	3378.14 (52,30)	0.918[b]
Leukocyte (/µL)			
Preoperative	4586.72 (2140-24500)	4110.00 (850-7470)	0.754[b]
Postoperative	8313.00 (3360-17300)	8257.60 (3550-18600)	0.929[a]
P value	[c]**0.001****	[c]**0.001****	
Δ(Preop-Postop)	3726.28 (81.20)	4147.60 (100,90)	0.989[b]
Lymphocyte (/µL)			
Preoperative	2082.26 (610-4620)	2061.80 (700-4580)	0.310[b]
Postoperative	1249.72 (530-2530)	1382.20 (450-2560)	0.424[b]
P value	[c]**0.001****	[c]**0.001****	
Δ(Preop-Postop)	-832.54 (39,90)	-679.60 (32.96)	0.442[b]
Platelet (×10^9/L)			
Preoperative	276300.0 (153000-452000)	264500.0 (154000-400000)	0.067[a]
Postoperative	240960.0 (138000-446000)	239780.0 (105000-424000)	0.099[b]
P value	[c]**0.001****	[c]**0.001****	
Δ(Preop-Postop)	-35340.0 (12.79)	-24720.0 (9.34)	0.637[b]
MPV (fL)			
Preoperative	8.51 (7.3-10,1)	8.72 (3-10.8)	0.114[b]
Postoperative	8.47 (7-10.2)	8.91 (6.9-11.5)	**0.049***[b]
P value	0.800[c]	0.166[c]	
Δ(Preop-Postop)	-0.03 (0.35)	0.19 (2.17)	0.269[b]
NLR			
Preoperative	2.53 (0.8-10.4)	2.65 (0.6-8.8)	0.122[b]
Postoperative	7.81 (1.7-27)	9.00 (2.1-22.7)	0.182[a]
P value	[c]**0.001****	[c]**0.001****	
Δ(Preop-Postop)	5.28 (208.69)	6.35 (239.62)	0.212[b]
PLR			
Preoperative	155.28 (64.7-616.4)	155.86 (91.1-431)	0.497[b]
Postoperative	223.67 (84.6-564.6)	245.13 (65.2-533.9)	0.236
P value	[c]**0.001****	[c]**0.001****	
Δ(Preop-Postop)	68.39 (44.04)	89.26 (57.26)	0.279[b]

Descriptive statistics are average (minimum-maximum) depending on the distribution for numerical variables; for categorical variables, it was given as number (%). Group E=those with erector spinae plane block, Group=those who were administered nonsteroidal anti-inflammatory drugs, WBC=White blood cell, MPV=Mean platelet volume, NLR=Neutrophil/Lymphocyte ratio, PLR=Platelet/Lymphocyte ratio, Preop=Preoperative, Postop=Postoperative.

[a]Student t test, [b]Mann Whitney U test, [c]Wilcoxon Signed Rank test, *$P<0.05$, **$P<0.01$.

The vital parameters of all cases were measured when they were taken to the waiting room before the operation, and there was no statistically significant difference between the mean arterial pressure calculated from the HR, SpO2 and NIBP measurements of the groups (P=0.695, P=0.706 and P=0.162, respectively) (Table 2).

When the laboratory data of the cases are examined; Postoperative WBC and leukocyte counts increased statistically significantly in both groups (P=0.001 and P=0.001, respectively). When the postoperative WBC and leukocyte count increases were compared between the groups, although the increase observed in Group N was numerically higher than the patients who underwent ESPB, no statistically significant difference was found between the two groups (P=0.918 and P=0.989, respectively) (Table 3).

A decrease in postoperative lymphocyte and platelet counts was detected in both groups, and it was found to be statistically significant (P=0.001 and P=0.001, respectively). When the decrease in the lymphocyte and platelet counts of the cases in the postoperative period was compared between the groups, no statistically significant difference was found (P=0.442 and P=0.637, respectively) (Table 3).

Postoperative MPV measurements of those who received analgesia with ESPB were found to be statistically significantly lower than those who received analgesia with NSAIDs (P<0.05). No statistically significant difference was detected between the MPV measurement changes of the cases according to analgesia types (P=0.269) (Table 3).

Preoperative and postoperative period NLR measurements of the cases do not show a statistically significant difference according to analgesia types (P=0.122 and P=0.182, respectively). The average increase of 5.28±4.01 units in the postoperative NLR measurements of the patients in Group E compared to the preoperative period was found to be statistically significant (P=0.001; P<0.01). The average increase of 6.35±4.66 units in the postoperative NLR measurements of the patients in Group N compared to the preoperative period was found to be statistically significant (P=0.001; P<0.01). Although the increase in NLR that we observed in patients who received analgesia with nonsteroidal anti-inflammatory drugs

Table 4. Evaluation of postoperative visual analog scale measurements according to analgesia types

Postoperative	Group E (n=50)	Group N (n=50)	P value
VAS 0	4.16 (1-7)	5.50 (2-8)	**[a]0.001****
VAS 2	3.64 (1-6)	4.62 (2-7)	**[a]0.001****
VAS 4	3.32 (1-6)	4.16 (2-8)	**[a]0.003****
VAS 6	2.92 (1-6)	3.56 (2-6)	**[a]0.013***
P value	**[c]0.001****	**[c]0.001****	
Δ			
0-2	-0.52	-0.88	[b]0.171
P value	[ee]0.199	**[ee]0.004****	
0-4	-0.84	-1.34	**[b]0.031***
P value	**[ee]0.001****	**[ee]0.001****	
0-6	-1.24	-1.94	**[b]0.005****
P value	**[ee]0.001****	**[ee]0.001****	

Descriptive statistics for numerical variables were provided in terms of distribution, including the mean (minimum-maximum) format. Group E=those with erector spinae plane block, Group=those who were administered nonsteroidal anti-inflammatory drugs, VAS=Visual Analog Scale, VAS 0=Visual Analog Scale score at 0 hours, VAS 2=Visual Analog Scale score at 2 hours, VAS 4=Visual Analog Scale score at 4 hours, VAS 6=Visual Analog Scale score at 6 hours.

[a]Student T Test, [b]Mann Whitney U Test, [c]Friedman Test & [ee]Wilcoxon tet, *P<0.05, **P<0.01

was numerically higher than in patients who underwent ESPB, no statistically significant increase was detected (P=0.212) (Table 3).

Preoperative and postoperative period PLR measurements of the cases do not show a statistically significant difference according to analgesia types (P=0.497 and P=0.236, respectively). The average increase of 68.39±108.89 units in the postoperative PLR measurements of the patients in Group E compared to the preoperative period was found to be statistically significant (P=0.001 and P<0.01, respectively). The average increase of 89.26±110.17 units in the postoperative PLR measurements of the patients in Group N compared to the preoperative period was found to be statistically significant (P=0.001and P<0.01, respectively). No statistically significant difference was detected between the PLR measurement changes of the cases according to analgesia types (P=0.279) (Table 3).

The VAS measurements at 0, 2, 4, and 6 hours in Group E patients were statistically significantly lower compared to those in Group N patients (P=0.001, P=0.001, P=0.003, P=0.013 and P<0.05, respectively). The changes in VAS measurements at 4 hours and 6 hours compared to hour 0, for patients provided analgesia with nonsteroidal anti-inflammatory drugs (NSAIDs), were statistically significantly higher than those undergoing analgesia with Erector Spinae Plane Block (ESPB) (P=0.031, P=0.005 and P<0.05, respectively) (Table 4).

DISCUSSION

Breast cancer is the second most common cause of cancer-related deaths worldwide. [1]. The primary reason for this high mortality rate is local recurrence and metastases, despite the best surgical treatment. Surgery is generally the preferred and curative method in breast cancer treatment. However, tumor cells have a tendency to undergo micrometastasis in the blood and lymphatic circulation that cannot be controlled during surgery. At this point, the host immune defense becomes crucial. It is believed that analgesic and anesthetic methods minimizing the stress response and suppressive effects on the immune system of surgery may have a positive impact on recurrence and metastases.

The immune system cells present in the tumor microenvironment undergo reshaping in response to surgical stress-induced inflammation. As a result of inflammation, the number of neutrophils increases, while the counts of lymphocytes and natural killer cells decrease within the tumor microenvironment. It is believed that the decreased cytotoxic-effective cells and the cytokines released by inflammatory mediators trigger tumor growth and metastasis [11].

In a study where Lombardi *et al*. [12] investigated postoperative inflammatory parameters, hematological parameters in the postoperative period were examined. White blood cell (WBC) count, leukocyte percentage, lymphocyte percentage, and mean corpuscular volume (MCV) were found to be statistically significantly higher compared to the preoperative period in all cases. In the same study, hemoglobin, hematocrit, and platelet count were found to be statistically significantly lower compared to the preoperative period in all cases. Consistent with this study, in our study, a statistically significant increase in WBC and leukocyte counts was observed in all cases during the postoperative period, while a statistically significant decrease in lymphocyte, platelet, hemoglobin, and hematocrit levels was also found. We believe that the increase in WBC and leukocyte counts and the decrease in lymphocyte and platelet counts observed in the postoperative period are related to immune modulation resulting from the surgical stress response.

Studies have demonstrated the immunosuppressive role of general anesthesia. Anesthetic agents can suppress cell-mediated immunity or induce an alteration in the balance between proinflammatory and anti-inflammatory cytokines. Additionally, acute pain also plays a suppressive role on the immune system [13].

Breast cancer surgery is one of the surgeries where postoperative pain incidence and opioid consumption increase due to the complex innervation network of the breast. The intensity of postoperative pain has a significant effect on the chronicization of pain. Increased opioid dependence due to pain is an undesirable behavior in cancer patients. The suppressive effect of opioids on cellular and humoral immunity has been known for many years. Because of these effects, the use of regional blocks in breast cancer surgery and postoperative analgesia management has gained a significant place [14]. Regional anesthesia can reduce surgical stress and pain in the perioperative period, improving neuroendocrine function and cytokine-associated stress response.

The implementation of an effective analgesia method can reduce the stress response to surgery in the perioperative period and is known to have a certain protective effect on the patient's immune system function. Hu *et al*. [8], in their study comparing the effects of ESPB and Paravertebral Block (PVB) on immune functions and postoperative recovery in breast cancer patients, observed lower VAS scores and higher levels of serum CD4, CD8, and IFNɣ in the ESPB group. CD4+ T lymphocytes have a regulatory role over other lymphocytes. The preservation of the levels of CD4+ T lymphocytes, which are expected to decrease due to the stress response to surgery, in patients treated with ESPB compared to those treated with PVB, suggests that ESPB has less impact on immune functions.
To date, there is no precisely defined clinical threshold value for NLR in the studies conducted. Since the values found in current studies are associated with patient prognosis, we did not utilize these values in our study. Parallel to our literature review, we have come to the conclusion that high values of NLR may be associated with the immunosuppressive effect of the analgesic method we used.

For the Platelet/Lymphocyte Ratio (PLR), there is no clinically established critical threshold value. Krenn-Pilko *et al*. [15] and Gündüz *et al*. [16] have explained that a high PLR value is associated with poor prognosis. In our study, we believe that high PLR values may be related to the negative impact of the analgesia method on the immune system.

Erector spinae plane block's effectiveness is dependent on inter-compartmental spread and the distribution of local anesthetic near the targeted nerves. The absorption and diffusion of local anesthetic are crucial in determining the quality of the block. This is because the mechanism of action of ESPB is thought to involve the diffusion of the administered local anesthetic from the intertransverse ligament to the thoracic paravertebral space and its spread anteriorly, exerting an effect on the dorsal and ventral rami of the spinal nerves. The craniocaudal distribution of the local anesthetic is also important in terms of covering the surgical area. This distribution in the interfascial plane is dependent on the volume of the administered local anesthetic.

In studies conducted to date, various volumes of local anesthetic have been tested for Erector Spinae Plane Block (ESPB); however, the optimal volume, concentration, and dermatomal distribution have not been defined yet. Abdella *et al*. [17], comparing the analgesic efficacy and patient satisfaction between two groups of patients undergoing ESPB with different volumes of local anesthetic, did not observe a statistically significant difference. However, when they visualized the craniocaudal spread of the local anesthetic using computed tomography with simultaneous administration of radiopaque contrast, they observed that bupivacaine applied in a high volume spread 22% more levels than the standard volume. Nevertheless, in the study, there was no statistically significant difference in the spread of the local anesthetic to the paravertebral space, epidural space, or spinal nerve roots with high volume application. However, the spread to the paravertebral space was observed in 30% of patients with a standard dose and 40% of patients with a high dose. Altıparmak *et al*. [18] conducted a study comparing different doses with the same volume. The group receiving a high dose of bupivacaine showed a greater decrease in postoperative Numerical Rating Scale (NRS) scores and opioid consumption.

In our study, we administered 20 ml of 0.25% concentration bupivacaine with 50 mg in standard volume at the T4 level to the group undergoing the block. We ensured control of the dermatomal region necessary for postoperative analgesia within the surgical area using a hot-cold test. In our study investigating the effect of the administered Erector Spinae Plane Block (ESPB) on postoperative NLR and PLR values, we did not find a statistically significant difference. We believe that the lack of statistically significant results may be associated with the standard volume we applied. The immunomodulatory effect of ESPB is known to be associated with the spread of the local anesthetic to the paravertebral and epidural spaces [19]. Therefore, we believe that by applying a higher volume, both increasing the spread to the paravertebral and epidural spaces and expanding the dermatomal area in the craniocaudal direction to reduce postoperative pain may lead to more effective results on the immune system.

Opioids are among the most frequently prescribed medications for cancer patients. There is a controversial relationship between opioids and the immune system. Several studies have shown that opioids inhibit the activity of immune cells [20, 21]. Chen *et al*. [22], in a study examining the impact of perioperative opioid use on the immune system, administered opioid-based analgesia to one group and thoracic paravertebral block (PVB) to another group in 80 patients undergoing thoracoscopic lobectomy. They compared postoperative NLR values between the two groups. In the PVB group, the NLR value was significantly reduced on the 3rd day compared to the 1st day of surgery, which was statistically significant when compared to the opioid group.

When examining nonsteroidal anti-inflammatory drugs (NSAIDs), recent studies suggest a significant decrease in the development of breast cancer associated with these drugs [23, 24]. Forget *et al*. [25], who investigated the effect of NSAIDs in breast cancer patients with NLR > 4, found that perioperative NSAID use extended survival time and reduced the risk of recurrence by two-fold. In our study, although postoperative NLR and PLR values in the group where ESPB was applied showed a less pronounced increase compared to the other group, this was found to be statistically insignificant. Unlike many other practices, we believe that the limited perioperative opioid use in our study and the follow-up of patients with NSAIDs intraoperatively and perioperatively might result in the immune system being less affected compared to situations involving opioid use.

The erector spinae plane block (ESPB), in terms of its technique, is considered a safer block for providing analgesia to the breast compared to other blocks due to the absence of vascular and neural structures near the application site and its distance from the pleura. In our study, we did not observe any complications associated with ESPB application.

It is believed that analgesics and anesthesia methods used during the perioperative period play a significant role in the immune system and indirectly affect tumor progression. In our study, where we used easily accessible and cost-effective NLR and PLR values as parameters to observe this effect, although there was no statistically significant difference, we found that ESPB resulted in less neutrophilia and lymphopenia. We are of the opinion that further studies are needed to observe the reflection of this effect on the tumor microenvironment and the evasion of tumor cells from the immune system more clearly.

In our study, we believe that our preference for non-steroidal anti-inflammatory drugs (NSAIDs) in analgesic drug selection for patients compared with ESPB in our study is a limiting factor due to the significant effects of this drug group on cytokines associated with surgical stress response and inflammation. Additionally, we have come to the conclusion that other limiting factors may include not making a distinction between patients who have received neoadjuvant chemotherapy and those who have not, as well as not knowing the long-term outcomes of patients when selecting them for the study.

CONCLUSION

As a result, we observed that the use of ESPB in postoperative analgesia management in breast cancer surgery, compared to NSAIDs, did not create a significant difference in the surgical stress response. We observed that the effects on NLO and PLO, which we used as biomarkers for surgical stress response, did not show a significant difference. Although both analgesia options are effective methods in the postoperative period, we observed that ESPB provides more effective pain control.

Authors' Contribution

Study Conception: KŞK, AG; Study Design: KŞK, AG, CA; Supervision: AŞ, İY; Funding: AŞ, SÖG, İY; Materials: KŞK, AG; Data Collection and/or Processing: KŞK, AG; Statistical Analysis and/or Data Interpretation: KŞK, AG, AŞ, SÖG, İY, CA; Literature Review: KŞK, AG, CA; Manuscript Preparation: KŞK, AG, CA and Critical Review: KŞK, AG, AŞ, İY, CA.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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