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PECS II block vs. local infiltration anesthesia on postoperative neutrophil-lymphocyte ratio and pain intensity in modified radical mastectomy: a randomized controlled trial

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BACKGROUND: Optimal postoperative pain management is required to improve the quality of life of patients after modified radical mastectomy (MRM). PECS II block and local infiltration anesthesia (LIA) are multimodal analgesia modalities that can be used in MRM patients. Neutrophil-lymphocyte ratio (NLR) is an affordable, widely available marker, and has been shown to be useful in assessing therapeutic response. This study compared PECS II block with ALI on postoperative NLR and pain intensity in MRM patients.
METHODS: This study used a single-blind randomized trial design. The subjects were divided into group 1 (PECS II block) and group 2 (LIA). Neutrophil-lymphocyte ratio were examined 1 hour preoperatively (T0), 2 hours (T1) and 12 hours (T2) postoperatively in both groups. Pain intensity was assessed at 0 (T0), 2 (T1), 4 (T2), 6 (T3), 12 (T4), and 24 (T5) hours postoperatively using the Numeric Rating Scale (NRS).
RESULTS: The NLR was higher in group 2 at T2 and T0-T2 ($p=0.015$ and $p=0.013$). The resting NRS was higher in group 2 at T4 ($p=0.009$) and T0-T4 ($p=0.046$). Total fentanyl requirement in 24 hours was higher in group 2 ($p=0.011$).
CONCLUSIONS: PECS II block can be used as one of the multimodal analgesia regimens for postoperative pain management of MRM patients, and LIA can be an alternative option in conditions where no ultrasound modality is available.

Key words: interleukin-6, local anesthetic, modified radical mastectomy, pectoralis muscle, postoperative pain

Introduction

Breast cancer is the most common malignancy in women, with over 2 million new cases worldwide in 2016. Mastectomy is a common oncologic surgery, causing moderate to severe acute postoperative pain.[1] Approximately 36% of women undergoing mastectomy experience acute nociceptive pain, while between 25% and 60% experience chronic pain known as postmastectomy pain syndrome.[2,3] Postoperative pain management is essential to reduce metabolic and endocrine stress responses, protect cognitive function, shorten mobilization and rehabilitation time, reduce costs and hospital stay, and prevent chronic pain development.[4,5]

Pectoralis nerve (PECS) block is a safe and simple regional anesthesia technique, superior to systemic analgesia alone. PECS block and modified PECS block (PECS II block) are

ultrasound-guided blocks that target the inter-fascial plane between the pectoralis major and pectoralis minor muscles.[3] Postoperative pain occurs as an inflammatory reaction to surgical trauma, leading to increased nociceptor sensitivity and hyperalgesia.[4] The neutrophil-lymphocyte ratio (NLR) is a marker that has recently increased in use as a prognostic factor related to immune system relationships and several diseases.[4,6]

There has been no study comparing PECS II block with ALI in modified radical mastectomy (MRM) patients in Indonesia. The researcher hypothesized that PECS II block yielded lower postoperative NLR and pain intensity in MRM patients than ALI.

Materials and methods

This study was a single-blind randomized trial conducted at Dr. Wahidin Sudirohusodo Hospital in Makassar, Indonesia, from February to May 2024. The population included patients who underwent elective MRM procedures. The inclusion criteria included age (18-60 years), body weight (BW) 50-70 kg, height (TB) 150-170 cm, BMI 18.5-29.9 kg/m2, and American Society of Anesthesiologists physical status (ASA PS) class I-II. Exclusion criteria included patients with contraindications to PECS II block, LIA, coagulation disorders or receiving anticoagulant therapy, chronic pain, allergies to the study material, history of breast surgery, or refusal to participate in the study.

The study subjects were randomly divided into two groups: group 1 (received PECS II block) and group 2 (received LIA). Demographic data were recorded upon subject entry into the study. Subjects were given gabapentin 300 mg/orally 2 hours before surgery, ketorolac 30 mg/IV, paracetamol 1 g/IV, and dexamethasone 8 mg/IV 1 hour before surgery. A peripheral blood sample of 3 mL was taken to check NLR levels 1 hour before surgery (T0) in both groups. General anesthesia was performed in both groups.

In group 1, a PECS II block was performed before surgery, with the patient in the supine position. The needle insertion area was disinfected using 70% alcohol and 10% povidone iodine. The transducer was placed at the midclavicula line and angled inferolaterally to visualize the axillary artery, axillary vein, and second costa. A 22G block needle was inserted between the pectoralis major and pectoralis minor muscles, and the first injection was made with 0.25% isobaric bupivacaine 10 mL (25 mg). The needle was advanced toward the axilla

using ultrasound guidance until it was between the pectoralis minor and serratus anterior muscles, then a second injection with 0.25% isobaric bupivacaine 10 mL (25 mg) was performed.

In group 2, LIA was performed after surgery using 0.25% isobaric bupivacaine 20 mL (50 mg) at the subdermal area at the incision site. The duration of surgery was recorded. After surgery, the patient was transferred to the post-anesthesia care unit. All subjects were given postoperative pain management with ketorolac 30 mg/8 h/IV and paracetamol 1 g/8 h/IV.

Pain intensity was observed during resting and moving at hours 0 (T0), 2 (T1), 4 (T2), 6 (T3), 12 (T4), and 24 (T5) postoperatively assessed by the Numeric Rating Scale (NRS). Rescue analgesics were given if pain intensity was obtained with an NRS score >4, using 0.5-1 µg/kg/IV fentanyl. Peripheral blood samples were taken to check NLR levels 2 hours (T1) and 12 hours (T2) postoperatively in both groups.

Ethical clearance was obtained from the Ethics Committee for Biomedical Research on Humans, Faculty of Medicine, Hasanuddin University, with ethical recommendation number 173/UN4.6.4.5.31/PP36/2024 and protocol number UH24020118. The clinical trial has been prospectively registered in the trial registry of ClinicalTrials.gov under the identifier NCT06451705.

The data obtained were processed using SPSS 25.0 for Windows. The data normality test used the Kolmogorov Smirnov test. Data per group were analyzed by paired t-test if the distribution was normal, or analyzed by Wilcoxon test if the distribution was not normal. Numerical data between groups were analyzed by unpaired t-test if the distribution was normal, or Mann-Whitney U test if the distribution was not normal. Categorical data were analyzed by Chi-Square test, if there were <5 cells, Fisher's exact test was performed. To test the comparison of the difference in NLR, resting NRS, and moving NRS between the two groups, repeated ANOVA test was performed. P value <0.05 was considered significant.

Results

The comparison of the characteristics of the two groups of study subjects was shown in Table 1. There was no significant difference in demographic data between the two groups (p>0.05). All subjects in this study were ASA PS class 2.

The comparison of NLR at the three measurement times between the two groups was shown in Table 2. There was a significant difference in NLR values between the two groups, at T2 and T2-T0 (p=0.015 and p=0.013).

Comparison of the difference in resting and moving NRS between the two groups was shown in Table 3 and 4, respectively. There was a significant difference in the resting NRS at T4 (p=0.009) and T4-T0 (p=0.046) between the two groups, where the moving NRS in group 1 was lower than group 2. There was no significant difference in the moving NRS between the two groups.

The time until the first rescue analgesic requirement was shown in Table 5. The total number of rescue opioid requirements was shown in Table 6. There was no significant difference in the time until first rescue fentanyl requirement between the two groups (p=0.869). There was a significant difference in the total requirement for fentanyl in 24 hours between the two groups (p=0.011), where the requirement for rescue opioids in group 1 was lower than group 2.

Discussion

In this study, there was an increase in NLR values at 2 hours and 12 hours postoperatively compared to 1 hour preoperatively. In addition, there was a significant difference in NLR values between the two groups at the 12th hour postoperatively. These findings are consistent with those reported by Alkan et al. who discussed the impact of different anesthesia and analgesia techniques after thoracotomy on NLR.[9] The study found that intravenous analgesia led to a significant increase in NLR compared to thoracic epidural anesthesia (TEA). In addition, patients in the epidural analgesia group with higher preoperative NLR required less additional analgesics, possibly due to the effective analgesia produced by TEA.[7] In previous studies, it was reported that increased NLR was associated with increased pain scores and postoperative analgesic requirements.[4]

In this study, the PECS II block group had better postoperative analgesia than the LIA group. This was indicated by a significant difference in the resting NRS 12 hours post-surgery, where the resting NRS in the PECS II block group was lower than the LIA group. This finding is consistent with previous studies, where pain scores in the PECS II block group were lower than

the LIA group.[2,8] The LIA technique has been proven to be easy and safe to perform as it is less invasive, but has the disadvantage of a shorter duration of postoperative analgesia when compared to PECS II block.[3] PECS II block has an advantage in MRM surgery due to its analgesic effect that covers up to the axilla. PECS II block is a combination of motor and sensory nerve blockade that includes the pectoralis, intercostobrachial, intercostal 3 to 6, and thoracic longus nerves. Blockade of these nerves produces adequate analgesia effects for MRM patients.[2] However, in conditions where the anesthesiologist is unable to perform ultrasound-guided nerve blocks, the LIA technique will have an important role in improving the quality of life of MRM patients.[9]

In this study, the requirement for rescue opioids 24 hours postoperatively in the PECS II block group was lower than the LIA group. This finding is consistent with that reported by Ng et al. where the need for rescue opioids after mastectomy surgery in the PECS II block group was lower than the LIA group.[9] However, Argun et al. reported a different result, where there was no significant difference in the need for rescue opioids after surgery between the PECS II block group and the LIA group.[10]

This study has several limitations. Firstly, the relatively small sample size may result in the statistical test being insignificant. Secondly, in this study, the LIA was conducted after surgery, while the PECS II block was conducted before surgery. This could be a factor affecting the results of the study. Third, the measurement of NLR values was only carried out at 3 specific times, thus making the data on changes in NLR values were less varied.

Conclusions

PECS II block can be used routinely as one of the multimodal analgesia regimens for postoperative pain management of MRM patients, but LIA can be an alternative choice in conditions where no ultrasound modality is available. Further research can be conducted with a larger sample size and using other biomarkers of pain neurotransmitters such as TNF-α, IL-10, substance P, NGF, and glutamate.

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Conflicts of interest

The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

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Authors' contributions

Jokevin Prasetyadhi, Muhammad Ramli Ahmad, and Syafruddin Gaus have given substantial contributions to the conception or the design of the manuscript, Jokevin Prasetyadhi, Syafri Kamsul Arif, Haizah Nurdin, and Andi Adil to the acquisition, analysis and interpretation of the data. All authors have participated to drafting the manuscript, Muhammad Ramli Ahmad and Syafruddin Gaus revised it critically. All authors read and approved the final version of the manuscript.

All authors contributed equally to the manuscript and read and approved the final version of the manuscript.

TABLES

Table 1. Demographic data.

Variables	Group 1 (n=15)	Group 2 (n=15)	p
Age (years)	49,07 ± 8,16	48,80 ± 6,44	0,209^{ns}
Body weight (kg)	57,20 ± 7,67	63,13 ± 5,85	0,383^{ns}
Height (cm)	157,27 ± 5,97	158,20 ± 5,66	0,942^{ns}
BMI (kg/m)^2	23,18 ± 3,19	25,32 ± 3,06	0,682^{ns}
ASA PS class 2	15 (100)	15 (100)	-
Surgery duration (minutes)	112,13 ± 10,23	114,00 ± 11,28	0,496^{ns}

Numerical data (age, weight, height, BMI, length of surgery) are displayed as mean ± standard deviation and analyzed by unpaired t-test if normal distribution, or displayed as median (min-max) and analyzed by Mann-Whitney U test if abnormal distribution. Categorical data (ASA PS) are displayed as frequencies (n) and percentages. Data were analyzed by Chi-Square test, if there were <5 cells, Fisher's exact test was performed. ns: no significant difference. BMI: body mass index; ASA PS: American Society of Anesthesiologists physical status.

Table 2. Comparison of NLR values between groups 1 and 2.

Measurement time	Group	NLR	p
T0	1	2,56 ± 0,10	0,072^{ns}
	2	2,62 ± 0,24	
T1	1	4,28 ± 0,71	0,830^{ns}
	2	5,06 ± 0,72	
T2	1	4,41 ± 0,30	0,015*
	2	6,65 ± 0,42	
T0-T1	1	1,72 ± 0,66	0,902^{ns}
	2	2,43 ± 0,62	
T0-T2	1	1,85 ± 0,26	0,013*
	2	4,03 ± 0,32	

Data are presented as mean ± standard deviation. Data were analyzed by repeated ANOVA test. *: significantly different; ns: no significant difference. NLR: neutrophil-lymphocyte ratio.

Table 3. Comparison of resting NRS difference between groups 1 and 2.

Measurement time	Group	Resting NRS	p
T0	1	0,20 ± 0,41	0,345^{ns}
	2	0,13 ± 0,35	
T1	1	0,60 ± 0,74	0,101^{ns}
	2	0,47 ± 0,52	
T2	1	0,40 ± 0,63	0,732^{ns}

Measurement time	Group	Resting NRS	p
	2	0,53 ± 0,64	
T3	1	0,93 ± 0,80	0,378^{ns}
	2	1,73 ± 1,10	
T4	1	1,13 ± 0,83	0,009*
	2	1,47 ± 1,30	
T5	1	1,60 ± 1,24	0,733^{ns}
	2	2,93 ± 1,49	
T0-T1	1	0,40 ± 0,51	0,488^{ns}
	2	0,33 ± 0,62	
T0-T2	1	0,20 ± 0,77	0,748^{ns}
	2	0,40 ± 0,74	
T0-T3	1	0,73 ± 0,88	0,600^{ns}
	2	1,60 ± 1,06	
T0-T4	1	0,93 ± 0,96	0,046*
	2	1,33 ± 1,29	
T0-T5	1	1,40 ± 1,30	0,432^{ns}
	2	2,80 ± 1,57	

Data are presented as mean ± standard deviation. Data were analyzed by repeated ANOVA test. *: significant difference; ns: no significant difference. NRS: numeric rating scale.

Table 4. Comparison of moving NRS difference between groups 1 and 2.

Measurement time	Group	Moving NRS	p
T0	1	0,20 ± 0,41	0,345^{ns}
	2	0,13 ± 0,35	
T1	1	0,60 ± 0,74	0,101^{ns}
	2	0,47 ± 0,52	
T2	1	0,47 ± 0,83	0,727^{ns}
	2	0,53 ± 0,64	
T3	1	1,07 ± 0,96	0,857^{ns}
	2	1,87 ± 1,06	
T4	1	1,33 ± 1,05	0,053^{ns}
	2	1,67 ± 1,63	
T5	1	2,27 ± 1,03	0,921^{ns}
	2	2,80 ± 1,26	
T0-T1	1	0,47 ± 0,64	0,791^{ns}
	2	0,33 ± 0,62	
T0-T2	1	0,27 ± 0,96	0,826^{ns}
	2	0,40 ± 0,74	

Measurement time	Group	Moving NRS	p
T0-T3	1	0,87 ± 1,06	0,767^{ns}
	2	1,73 ± 1,03	
T0-T4	1	1,13 ± 1,19	0,078^{ns}
	2	1,67 ± 1,84	
T0-T5	1	2,07 ± 1,03	0,940^{ns}
	2	2,40 ± 0,99	

Data are displayed as mean ± standard deviation. Data were analyzed by repeated ANOVA test. ns: no significant difference. NRS: numeric rating scale.

Table 5. Time to first rescue analgesic requirement.

Group	Time until first rescue fentanyl requirement (minutes)	p
1	192 ± 506,69	0,869^{ns}
2	264 ± 440,21	

Data are presented as mean ± standard deviation. Data were analyzed by unpaired t-test if distribution was normal, or Mann-Whitney U test if distribution was not normal. ns: no significant difference.

Table 6. Requirement for rescue opioids.

Group	Total rescue fentanyl requirement in 24 hours (µg)	p
1	4 ± 10,56	0,011*
2	10 ± 14,64	

Data are presented as mean ± standard deviation. Data were analyzed by unpaired t-test if distribution was normal, or Mann-Whitney U test if distribution was not normal. *: significantly different.