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Effects of 0.25% Ropivacaine versus 0.25% Bupivacaine in Erector Spinae Plane Block on Interleukin-6 Levels in Post-Thoracotomy Patients

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KEYWORDS

thoracotomy; interleukin-6; erector spinae plane block; bupivacaine; ropivacaine

ABSTRACT:

Background: Thoracotomy induces a pronounced systemic inflammatory response, with interleukin-6 (IL-6) serving as a key mediator of the acute-phase reaction. Regional anesthesia techniques such as the erector spinae plane (ESP) block may modulate perioperative inflammation; however, whether different local anesthetics influence postoperative IL-6 levels remains unclear. This study compared the effects of 0.25% bupivacaine and 0.25% ropivacaine administered via ESP block on serum IL-6 levels in patients undergoing thoracotomy.

Methods: A double-blind randomized controlled trial was conducted at a tertiary referral hospital in Makassar, Indonesia. Thirty patients undergoing thoracotomy were randomly assigned to receive ultrasound-guided ESP block with either 15 mL of 0.25% bupivacaine (Group B) or 15 mL of 0.25% ropivacaine (Group R). Venous blood samples were collected at baseline (0 h), 12 h, and 24 h postoperatively for IL-6 measurement using ELISA. Data were analyzed using appropriate parametric or non-parametric tests, with $p < 0.05$ considered statistically significant.

Results: Baseline characteristics were comparable between groups. Mean IL-6 levels at 0 h were 6.13 ± 6.20 pg/mL in Group B and 6.27 ± 9.83 pg/mL in Group R ($p = 0.815$). At 12 h, levels were 5.27 ± 5.96 pg/mL and 2.25 ± 1.11 pg/mL, respectively ($p = 0.860$). At 24 h, IL-6 levels were 6.85 ± 8.08 pg/mL in Group B and 5.18 ± 10.02 pg/mL in Group R ($p = 0.880$). No statistically significant differences were observed at any time point.

Conclusion: Bupivacaine and ropivacaine administered via ESP block produce comparable postoperative IL-6 profiles following thoracotomy.

1. Introduction

Thoracotomy is among the most invasive surgical procedures and is associated with a pronounced systemic inflammatory response [1]. Surgical tissue injury activates complex neuro-immunological pathways that lead to the release of proinflammatory cytokines [2,3]. Among these mediators, interleukin-6 (IL-6) plays a pivotal role in orchestrating the acute-phase response following surgical trauma [4]. IL-6 is rapidly synthesized by macrophages, endothelial cells, and fibroblasts in response to tissue injury, and its circulating concentration increases proportionally to the magnitude of surgical stress [5].

IL-6 has been widely recognized as a reliable biomarker of surgical stress and systemic inflammation [6]. Serum IL-6 levels rise within hours after incision and typically peak in the early postoperative period [7]. In thoracic surgery, IL-6 concentrations have been reported to increase significantly as early as three hours after thoracotomy, reflecting the substantial inflammatory burden associated with this procedure. Elevated IL-6 levels are not only indicative of tissue injury severity but are also associated with postoperative complications and

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prolonged recovery, underscoring their clinical relevance [8,9].

Modulation of the perioperative inflammatory response has become an important consideration in anesthetic management [10]. Regional anesthesia techniques may attenuate the stress response to surgery by reducing afferent nociceptive input and sympathetic activation, thereby potentially influencing cytokine release, including IL-6 [11]. Thoracic epidural analgesia has traditionally been considered the standard approach for thoracotomy; however, newer interfascial plane techniques such as the erector spinae plane (ESP) block have emerged as promising alternatives [12]. The ESP block is technically simpler, performed under ultrasound guidance, and associated with a favorable safety profile. Beyond analgesic effects, its potential impact on systemic inflammatory markers warrants further investigation [13].

Bupivacaine and ropivacaine are long-acting amide local anesthetics commonly used in regional anesthesia. While both provide effective neural blockade, they differ in pharmacologic and toxicity profiles [14]. Whether these differences translate into varying effects on the perioperative inflammatory response, particularly IL-6 release, remains unclear [15]. Although previous studies have evaluated the analgesic efficacy of ESP block in thoracotomy, data examining its influence on systemic inflammatory biomarkers are limited. Furthermore, direct comparisons between bupivacaine and ropivacaine in ESP block with specific assessment of serum IL-6 levels remain scarce. Therefore, this study aims to compare the effects of 0.25% ropivacaine and 0.25% bupivacaine administered via ESP block on serum IL-6 levels in post-thoracotomy patients.

2. Methods

Study Design, Setting, and Period

The study was designed as a double-blind, randomized controlled clinical trial and was conducted at Dr. Wahidin Sudirohusodo Hospital, along with its affiliated teaching hospitals in Makassar, Indonesia, commencing in April 2024 and continuing until the required sample size was achieved.

Study Population and Sample

The study population included all patients undergoing thoracotomy at Dr. Wahidin Sudirohusodo Hospital and its affiliated teaching hospitals in Makassar. The study sample consisted of those patients who met the inclusion criteria and provided written informed consent to participate in the study.

Eligibility Criteria

Patients were included if they were scheduled to undergo elective or urgent thoracotomy, were aged between 19 and 65 years, had an acceptable body mass index, had an American Society of Anesthesiologists (ASA) physical status of I–III, and provided written informed consent to participate in the study. Patients were excluded if they had a history of hypertension, diabetes mellitus, dyspeptic disease, cardiovascular or heart disease, acute or chronic infection, or long-term steroid use. Additional exclusion criteria included local infection at the block site, coagulopathy, morbid obesity, allergy to local anesthetics, uncontrolled hypertension or ischemic heart disease, renal dysfunction, pre-existing neurological disorders, psychiatric illness, and pregnancy. Patients were withdrawn from the study if intraoperative or postoperative complications occurred, if blood samples for IL-6 analysis were hemolyzed or damaged, if the patient withdrew consent, or if the erector spinae plane block failed.

Study Procedures

Participants who met the inclusion criteria provided written informed consent and were randomly assigned to either the ropivacaine group (Group R) or the bupivacaine group (Group B). Upon arrival in the operating room, a venous blood sample was collected for baseline IL-6 measurement. General anesthesia was induced with sevoflurane in oxygen with or without nitrous oxide. After intravenous access and endotracheal intubation, fentanyl (0.2–0.5 µg/kg) was administered, and anesthesia was maintained with propofol, opioids, and sevoflurane. Intraoperative opioids were titrated to the minimum effective dose.

All patients received standardized multimodal analgesia, including intravenous dexamethasone (0.5 mg/kg, maximum 10 mg), ondansetron (0.1 mg/kg), and acetaminophen (15 mg/kg). Ultrasound-guided erector spinae plane (ESP) block was performed using 15 mL of 0.25% bupivacaine in Group B and 15 mL of 0.2% ropivacaine in Group R. Hemodynamic parameters were recorded every minute for 20 minutes after block administration and every five minutes thereafter. Hypotension (mean arterial pressure <65 mmHg) was treated with intravenous ephedrine (5–10 mg).

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Venous blood samples were collected at 6, 12, 24, and 48 hours postoperatively for IL-6 analysis. Adverse events, including nausea, vomiting, shivering, bradycardia, and agitation, were monitored and managed according to institutional protocols. All data were recorded prospectively.

Data Processing and Statistical Analysis

Data were analyzed using SPSS version 23.0 for Windows (IBM Corp., Armonk, NY, USA). Results are presented as narrative descriptions, tables, or figures. Normally distributed numerical variables are expressed as mean ± standard deviation (SD), while non-normally distributed numerical variables are presented as median (minimum–maximum). Categorical variables are reported as frequencies and percentages. Data normality was assessed using the Shapiro–Wilk test. Comparisons between two independent groups were performed using the independent samples t-test for normally distributed data and the Mann–Whitney U test for non-normally distributed data. Within-group comparisons were analyzed using the paired t-test for normally distributed data and the Wilcoxon signed-rank test for non-normally distributed data. Associations between categorical variables were evaluated using the chi-square test when all expected cell counts were ≥5; otherwise, Fisher's exact test was applied. A p-value <0.05 was considered statistically significant.

3. Results

Characteristics of Study Participants

The initial characteristics of patients receiving an erector spinae plane (ESP) block, categorized by the type of local anesthetic used, either bupivacaine or ropivacaine, with a total of 30 participants. The average age was 44.93 ± 13.20 years for those in the bupivacaine group and 42.60 ± 15.10 years for the ropivacaine group, suggesting a similar age range across both groups. The mean body weight was also comparable, with the bupivacaine group averaging 56.00 ± 6.85 kg and the ropivacaine group averaging 55.47 ± 7.13 kg, indicating relatively uniform anthropometric characteristics. The average ASA PS was 2.29 ± 0.47 for the bupivacaine group and 2.47 ± 0.52 for the ropivacaine group, showing that most patients in both groups had mild to moderate systemic disease. Overall, the baseline characteristics were well-matched between the groups, reducing the likelihood of confounding effects on the analgesic outcomes.

IL-6 Levels

Table 1 summarizes the perioperative interleukin-6 (IL-6) levels measured at 0, 12, and 24 hours in patients receiving an ESP block with either bupivacaine or ropivacaine. At baseline (0 hours), mean IL-6 levels were comparable between groups, measuring 6.13 ± 6.20 pg/mL in the bupivacaine group and 6.27 ± 9.83 pg/mL in the ropivacaine group. At 12 hours postoperatively, IL-6 levels decreased in both groups, with a more pronounced reduction observed in the ropivacaine group (2.25 ± 1.11 pg/mL) compared with the bupivacaine group (5.27 ± 5.96 pg/mL). At 24 hours, IL-6 levels increased again in both groups, reaching 6.85 ± 8.08 pg/mL in the bupivacaine group and 5.18 ± 10.02 pg/mL in the ropivacaine group.

Overall, both groups demonstrated a similar temporal pattern characterized by an initial postoperative decline at 12 hours followed by a rise at 24 hours, although the magnitude of change appeared greater in the ropivacaine group at 12 hours.

Table 2 and Figure 1 presents postoperative serum IL-6 levels at 0, 12, and 24 hours in patients receiving ESP block with bupivacaine or ropivacaine. Overall, no statistically significant differences in IL-6 levels were observed between the two groups at any time point.

At 0 hours, the median IL-6 level was 6.13 (6.20) in the bupivacaine group and 6.27 (9.83) in the ropivacaine group (p = 0.815). At 12 hours, median IL-6 levels were 5.27 (5.96) in the bupivacaine group and 2.25 (1.11) in the ropivacaine group (p = 0.860). At 24 hours, the median IL-6 level was 6.85 (8.08) in the bupivacaine group compared with 5.18 (10.02) in the ropivacaine group (p = 0.880).

Table 1. Postoperative IL-6 Levels (ELISA) in Patients Receiving ESP Block with Bupivacaine or Ropivacaine

Variables	Time	N	Erector spinae plane (ESP) block	
			Bupivacaine, mean ± SD	Ropivacaine, mean ± SD
IL-6 level	0 h	30	6.13 (6.20)	6.27 (9.83)
	12 h	30	5.27 (5.96)	2.25 (1.11)
	24 h	30	6.85 (8.08)	5.18 (10.02)

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Analysis of delta IL-6 values showed a decrease at 12 hours in both groups (−0.86 ± −0.24 for bupivacaine and −4.02 ± −8.72 for ropivacaine), followed by an increase at 24 hours (1.58 ± 2.12 and 2.93 ± 8.91, respectively). However, these changes were not statistically significant between groups.

Table 2. Postoperative IL-6 Levels at Three Time Points in Patients Receiving ESP Block with Bupivacaine or Ropivacaine

Variables	Time	N	Erector spinae plane (ESP) block				P value*
			Bupivacaine, median (min-max)	Delta Hours, mean ± SD	Ropivacaine, median (min-max)	Delta Hours, mean ± SD	
IL-6 level	0 h	30	6.13 (6.20)		6.27 (9.83)		0.815
	12 h	30	5.27 (5.96)	-0.86 (-0.24)	2.25 (1.11)	-4.02 (-8.72)	0.860
	24 h	30	6.85 (8.08)	1.58 (2.12)	5.18 (10.02)	2.93 (8.91)	0.880

**Analysis was performed using the Mann–Whitney test.*

These findings indicate that the type of local anesthetic used for ESP block did not significantly influence postoperative systemic IL-6 levels during the 24-hour observation period.

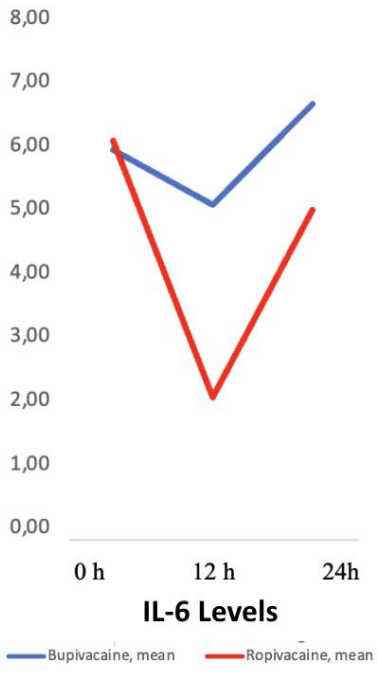

Figure 1. Summary of IL-6 Levels in the Bupivacaine and Ropivacaine Groups with ESP Block

4. Discussion

Baseline characteristics were comparable between the bupivacaine and ropivacaine groups, including age, body weight, and ASA physical status, supporting a balanced comparison of postoperative inflammatory responses. Similar ASA classification is particularly important, as perioperative systemic inflammation may be influenced by preoperative physical status and surgical stress burden [16]. The comparable baseline profiles in this study reduce the likelihood that differences in IL-6 levels were confounded by patient-related factors.

Systemic inflammatory response, assessed by serum IL-6 levels, did not differ significantly between the two groups at any measured time point (0, 12, and 24 hours postoperatively). Both groups demonstrated a similar temporal pattern of IL-6 changes, characterized by an initial postoperative value, a relative decrease at 12 hours, and a subsequent increase at 24 hours. However, these fluctuations were not statistically different between the bupivacaine and ropivacaine groups.

IL-6 is a key proinflammatory cytokine released in response to surgical tissue injury and plays a central role in mediating the acute-phase response [3,17]. Although regional anesthesia techniques have been proposed to attenuate surgical stress responses by reducing nociceptive input and sympathetic activation, the magnitude of their effect on systemic cytokine release remains variable and is influenced by factors such as surgical extent, timing of sampling, and individual inflammatory reactivity [18,19]. The absence of significant intergroup differences in IL-6 levels suggests that, when administered at equivalent concentrations for ESP block, both bupivacaine and ropivacaine provide a comparable modulatory effect on postoperative systemic inflammation.

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Overall, the findings indicate that the choice between 0.25% ropivacaine and 0.25% bupivacaine for ESP block does not result in differential systemic IL-6 responses within the first 24 hours after thoracotomy. This supports the notion that the inflammatory profile following surgery is more strongly influenced by surgical trauma and time-dependent physiological responses than by the specific local anesthetic agent used in the ESP block [20].

5. Conclusions

This study demonstrates that systemic inflammatory response, as assessed by serum interleukin-6 (IL-6) levels, did not differ significantly between patients receiving 0.25% ropivacaine and those receiving 0.25% bupivacaine for ESP block following thoracotomy. At 0, 12, and 24 hours postoperatively, IL-6 levels were comparable between groups, and no statistically significant differences were identified through descriptive or bivariate analyses.

Although temporal fluctuations in IL-6 levels were observed during the first 24 hours, these changes were similar in both groups, indicating that the type of local anesthetic used for ESP block did not significantly influence postoperative systemic inflammatory response. Overall, the findings suggest that 0.25% ropivacaine and 0.25% bupivacaine exert comparable effects on postoperative IL-6 profiles when administered for ESP block in thoracotomy patients.

6. Declarations

Consent for Publication

Consent for publication is not required, as the manuscript does not include any identifiable personal data or images of study participants.

Authors' Contributions

ANK was responsible for the implementation of the study, as well as the collection and analysis of data, and the drafting of the manuscript. AA and MDD were instrumental in conceiving and designing the study, conducting data analysis, supervising the research process, and critically revising the manuscript. ANK, AA, and MDD were involved in data interpretation and manuscript revision. All authors (ANK, AA, MDD, SKA, NSW, and CWT) critically reviewed the manuscript, contributed to its refinement, and approved the final version.

Ethical Approval and Consent to Participate

The study received ethical approval from the Health Research Ethics Committee of the Faculty of Medicine, Hasanuddin University, Makassar, Indonesia (Ethical Approval No. 719/UN4.6.4.5.31/PP36/2025; Protocol No. UH25080656), following a full board review conducted on 17 September 2025. The approved protocol (Version 2, dated 23 September 2025) was implemented at Dr. Wahidin Sudirohusodo General Hospital, Makassar. Prior to participation, all eligible patients were provided with a comprehensive explanation of the study procedures and objectives, and written informed consent was obtained from all participants before enrollment.

Data Availability

All data generated and analyzed in the course of this study are comprehensively included in the published article.

Conflict of Interest

The authors declare that there are no conflicts of interest pertaining to this work.

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