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EFFECTIVENESS OF PERIOPERATIVE INTRAVENOUS LIDOCAINE ON SERUM LEVELS OF SUBSTANCE P, NEUTROPHIL-TO-LYMPHOCYTE RATIO AND PAIN INTENSITY FOLLOWING POSTERIOR VERTEBRAL DECOMPRESSION AND STABILIZATION SURGERY

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Abstract

Background: Posterior vertebral decompression and stabilization surgery addresses spinal instability and other conditions but can cause significant pain if not managed well. This can lead to hemodynamic disturbances and chronic pain. Opioids are common for pain management but have side effects like drowsiness and nausea. Low-dose intravenous lidocaine during surgery can reduce opioid use and postoperative pain. This study aims to assess its effect on serum substance P levels, neutrophil-lymphocyte ratio, and pain intensity.

Methods: This study used a double-blind randomized clinical trial conducted from April to June 2024. Patient who underwent decompression and posterior vertebral stabilization surgery were selected via consecutive sampling. Participants were split into two groups: the intervention group received intravenous lidocaine, while the control group received a placebo. Data were analyzed using SPSS 25, with results presented as narratives, tables, or graphs. Statistical tests included t-tests and Mann-Whitney U tests, with significance set at $p < 0.05$.

Results: A total of 30 patients were included in this study with 15 patients in each groups. At 6h, 12h, and 24h postoperatively, pain intensity was significantly lower in the lidocaine group compared to the control group ($p<0.05$). Additionally, the neutrophil-lymphocyte ratio (NLR) decreased significantly in the lidocaine group at 6h postoperatively compared to the control group. However, no significant difference in substance P levels was found between the two groups.

Conclusion: Lidocaine can lower postoperative NRS scores, decrease postoperative NLR values, and reduce the difference in substance P levels between postoperative and preoperative measurements.

Keyword: lidocaine, substance P, neutrophil-to-lymphocyte ratio, pain management

INTRODUCTION

Posterior vertebral decompression and stabilization surgery is a procedure performed to correct spinal instability, spinal stenosis, herniated discs, spinal trauma, infections, and tumors.

This surgery involves significant dissection of subcutaneous tissues, bones, and ligaments, resulting in moderate to severe pain. If not managed, intraoperative pain can lead to sympathetic stimulation, causing hemodynamic disturbances such as tachycardia, elevated blood pressure and heart rate, and increased cardiac oxygen consumption, which can result in ischemia or intraoperative myocardial infarction. Poorly managed acute postoperative pain can negatively impact patient health, recovery, hospitalization duration, and overall patient experience, potentially leading to chronic pain.[1–3]

While opioids are commonly used for perioperative pain management and are generally safe, they come with risks such as drowsiness, CO_2 retention, postoperative nausea and vomiting, and prolonged postoperative ileus, which can extend hospital stays.[1–3] To improve patient outcomes and minimize postoperative physiological stress, the enhanced recovery after surgery (ERAS) approach is frequently used. ERAS guidelines recommend a multimodal pain management strategy, which includes using various analgesics targeting different mechanisms in the peripheral and central nervous systems, employing regional anesthesia, avoiding opioids when possible, and switching to oral medications as soon as possible.[2–4]

Lidocaine is an anesthetic drug that can be used for local anesthesia, nerve blocks, intrathecal anesthesia, general anesthesia, and long-term treatment for ventricular arrhythmias. Recent studies have shown that low-dose intravenous lidocaine during and/or after surgery can reduce opioid use, inhibit hyperalgesia, alleviate acute or chronic postoperative pain, reduce nausea and vomiting, shorten bowel paralysis duration, inhibit inflammatory responses, shorten hospital stays, and reduce postoperative cognitive dysfunction.[3,5–9]

Pain involves several stages: transduction, conduction, transmission, modulation, and perception, initiated by the stimulation of nociceptors. Pain is a key sign of inflammation, with mediators such as prostaglandins, histamine, bradykinin, and substance P, the most dominant pain mediator, playing roles in the pain process.[10–12]

The stress response to tissue damage during surgery can be measured using various tests, including a complete blood test to evaluate neutrophils and lymphocytes, which indicate the inflammatory process. The neutrophil-lymphocyte ratio is a valuable prognostic marker and can diagnose acute conditions.[13,14]

This study aims to determine the effectiveness of perioperative intravenous lidocaine administration on serum substance P levels, the neutrophil-lymphocyte ratio, and pain intensity following posterior vertebral decompression and stabilization surgery.

METHODS

Study design and patient selection

This study utilizes an experimental design, specifically a double-blind randomized clinical trial. It was conducted at our center from April to June 2024. The sample consisted of orthopedic surgery patients who underwent decompression and posterior vertebral stabilization and met the inclusion criteria. Participants were selected using a consecutive sampling method.

The inclusion criteria were: patients scheduled for decompression and posterior vertebral stabilization surgery under general anesthesia; those with American Society of Anesthesiologists (ASA) Physical Status 1-2; aged 18-60 years; BMI between 18.50-25 kg/m²; surgery duration of less than 6 hours; and patients who signed the informed consent.

Exclusion criteria included: patients or families who refused participation; contraindications to decompression and posterior vertebral stabilization; history of allergies to opioids, NSAIDs, or other anesthetics used in the study; patients with communication limitations due to impaired consciousness or cognitive issues; patients requiring reoperation due to postoperative complications such as bleeding resulting in shock; and those experiencing major anesthesia complications.

The dropout criteria included patients who developed severe allergies to research materials, patients who died during surgery, patients who experienced severe complications leading to a significant decline in hemodynamic status, and surgeries lasting longer than 6 hours.

The study was approved by the our center ethics committee (Approval number: 271/UN4.6.5.31/PP36/2024. Written informed consent was obtained from all participants prior to enrollment.

Treatment groups

Participants in the intervention group (lidocaine group) received intravenous lidocaine perioperative analgesics, which included an intravenous lidocaine bolus of 1.5 mg/kg at 1 minute before endotracheal intubation and followed by intravenous lidocaine infusion of 1.5 mg/kg/hour/iv until surgery was completed and continued at 1 mg/kg/hour/IV up to 6 hours

postoperatively. Participants in the control group received placebo with an intravenous 0.9% NaCl bolus with the same procedure.

Intervention methods

At first, both groups received ketorolac 30 mg/iv and paracetamol 1 gr/iv 60 minutes before the scheduled surgery. For general anesthesia, both groups were given premedication with Fentanyl 2 mcg/kg, induction with Propofol 2 mg/kg/iv, and Atracurium 0.5 mg/kg/iv before intubation. The lidocaine group received an intravenous lidocaine bolus of 1.5 mg/kg 1 minute before endotracheal intubation, followed by an intravenous lidocaine infusion of 1.5 mg/kg/hour until the operation was completed and then 1 mg/kg/hour for up to 6 hours postoperatively. The control group received an intravenous 0.9% NaCl placebo bolus following the same procedure. Anesthesia maintenance was achieved using volatile anesthesia with Isoflurane 1-1.5 vol% MAC, O2 60% at 4 liters per minute, and Fentanyl 1 mcg/kg/hour/iv via syringe pump in both groups. Atracurium 0.1 mg/kg was administered intravenously every 30 minutes to maintain relaxation and controlled ventilation. In cases of hypotension (MAP <20% of baseline), an intravenous bolus of Ephedrine 5-10 mg was given. For bradycardia (HR <50 beats per minute), Atropine Sulphate 0.5 mg was given intravenously, with a maximum dose of 2 mg. During surgery, Fentanyl was used as a rescue analgesic if there was an increase in pulse and blood pressure by 20% from the baseline. Hemodynamic status was recorded throughout the surgery. Postoperative analgesia included Ketorolac 30 mg intravenously every 8 hours, starting 8 hours after the first dose, and Fentanyl 1 mcg/kg intravenously as a rescue analgesic if NRS >6. The use of opioid analgesics and postoperative complications such as nausea, vomiting, and sedation were recorded. The second blood sample was taken 6 hours postoperatively and sent to the laboratory for analysis of substance P levels and NLR.

Statistical analysis

The data obtained were processed and the results were presented in the form of narratives, tables, or graphs, showing averages, standard deviations, frequencies, and percentages, using SPSS 25 for Windows. Depending on the type and form of data obtained, the appropriate statistical test method was determined. Categorical data such as gender, ASA PS, and NRS were presented as frequencies (n) and percentages. Numerical data, including age, BMI, and total opioid use, were presented as mean ± standard deviation (mean ± SD). The data normality was tested using the Kolmogorov-Smirnov test. For normally distributed data, the unpaired t-test was used, and for

non-normally distributed data, the Mann-Whitney U test was employed. A p value of ≤0.05 was considered significant.

RESULTS

Data analysis was conducted on 30 samples divided into two groups: the Lidocaine group (15 subjects) and the Control group (15 subjects). The characteristics of the research sample are presented in Table 1. In both groups, the majority of subjects were male (66.7% in the lidocaine group and 33.7% in the control group) and had ASA 2 status (93.3% in the lidocaine group, 86.7% in the control group). The average age of the study subjects was between 44-47 years, with a BMI of 22.4-22.54 kg/m². The average duration of surgery was 189 minutes for the lidocaine group and 178.75 minutes for the control group.

Pain intensity was assessed using the NRS score at 2, 4, 6, 12, and 24 hours post-surgery. Table 2 shows that at 2 hours post-surgery, there was no significant difference in pain intensity between the two groups (p = 0.148). At 4 hours post-surgery, there was still no significant difference in pain intensity between the two groups (p = 0.472). At 6 hours post-surgery, a significant difference in pain intensity was observed between the two groups (p = 0.005), with the Lidocaine group (2.07) experiencing significantly lower pain intensity than the Control group (2.61). At 12 hours post-surgery, there was a significant difference in pain intensity between the two groups (p = 0.045), with the Lidocaine group (2.00) reporting lower pain intensity than the Control group (2.36). At 24 hours post-surgery, the difference in pain intensity remained significant (p = 0.031), with the Lidocaine group (1.71) experiencing lower pain intensity than the Control group (2.07).

Table 3 shows no significant differences in mean preoperative substance P levels between the two groups (p = 0.26). At 6 hours post-surgery, there was no significant difference in substance P levels between the Lidocaine group and the Control group (p = 0.9). However, the mean level of substance P at 6 hours post-surgery decreased in the Lidocaine group compared to the preoperative level, suggesting that perioperative intravenous lidocaine administration can reduce postoperative substance P levels.

Table 4 shows no significant difference between the preoperative NLR values of the Lidocaine group and the Control group (p = 0.173), indicating that preoperative NLR values were relatively similar between the groups. At 6 hours post-surgery, a significant difference in NLR values was observed between the Lidocaine group and the Control group (p = 0.003), indicating

that perioperative intravenous lidocaine can reduce NLR values compared to the control group at 6 hours post-surgery.

DISCUSSION

In this study, it was found that the numeric rating scale (NRS) measurements at 2 hours and 4 hours postoperatively showed no significant difference in pain intensity between the two groups. However, at 6 hours postoperatively, there was a significant difference in pain intensity ($p<0.01$), with the lidocaine group experiencing significantly lower pain than the control group. Similarly, at 12 hours and 24 hours postoperatively, pain intensity was significantly lower in the lidocaine group compared to the control group. These findings align with previous research by Peng et al.,[15] which demonstrated that continuous intraoperative intravenous lidocaine administration improved postoperative analgesia, with lower NRS scores in the lidocaine group than in the placebo group. Additionally, Rachman et al.,[2] reported that perioperative continuous intravenous lidocaine reduced both pain intensity and total opioid consumption after posterior vertebral decompression and stabilization surgery. This study results showed a significant decrease in pain intensity at 6 hours postoperatively in the lidocaine group compared to the control group, corresponding with a significant change in the neutrophil-to-lymphocyte ratio (NLR) at 6 hours postoperatively. This effect may be due to intravenous lidocaine's ability to inhibit neutrophil priming, affecting cytokine release and reducing postoperative pain.

This study found that NLR ratio at 6 hours postoperatively decreased significantly in the lidocaine group compared to the control group. These findings align with previous research by Memary et al.,[16] which showed that intraoperative intravenous lidocaine reduced postoperative NLR more effectively than the control group in women undergoing breast cancer surgery. Similarly, Surhonne et al.,[17] found that general anesthesia increased NLR compared to regional anesthesia in infraumbilical surgery, suggesting that intravenous lidocaine could help reduce NLR in surgeries involving general anesthesia.

Neutrophil-to-lymphocyte ratio is an immunosuppressive and inflammatory biomarker involved in the cellular immune response to trauma and the acute phase. Neutrophils are granulocytes that play a crucial role in the body's defense and are the earliest inflammatory cells to infiltrate traumatized or damaged tissues.[18] NLR is widely studied due to its easy and accessible measurement. While higher NLR is generally associated with worse outcomes, it cannot be used as a single biomarker. The significant decrease in NLR observed in this study may occur because

lidocaine can prevent the priming of polymorphonuclear leukocytes (PMNs) and neutrophils at very low concentrations (0.1 μM) during prolonged exposure. This mechanism is due to the inhibition of certain intracellular G protein (Gq) signaling pathways, allowing intravenous lidocaine to be effective at low doses and have a prolonged effect of up to 8.5 hours after administration is stopped.[7]

Postoperative pain arises as an inflammatory response to surgical trauma. Incision, dissection, retraction, and other surgical interventions trigger a local inflammatory mediator response, increasing nociceptor sensitivity and hyperalgesia, which leads to postoperative pain.[19] Innate immune cells, including neutrophils, can produce and respond to IL-6, amplifying inflammation and worsening pain.[20] Several previous studies have reported that an increased neutrophil-to-lymphocyte ratio is associated with higher pain scores and greater postoperative analgesic requirements.[19]

Lidocaine is a local anesthetic that works by inhibiting nerve conduction and interrupting pain transmission in C and Aδ nerve fibers. Pharmacologically, local anesthetics selectively block Na^+ channels. Additionally, lidocaine has significant effects on other targets, such as K^+ and Ca^{2+} channels, and exhibits anti-inflammatory properties by binding to G proteins, which inhibits the adhesion of polymorphonuclear leukocytes, macrophages, and monocytes. It also increases glutamate release and interferes with several intracellular signaling pathways. Postoperative pain is primarily caused by local inflammation and activation of C nerve fibers which can be mitigated by reducing cytokine production, thereby limiting the inflammatory response after tissue trauma. Reducing the inflammatory response decreases injury-induced immunosuppression and is associated with better functional recovery.[21,22]

This study found no significant difference in substance P levels between the control group and the lidocaine group at 6 hours postoperatively ($p > 0.05$). However, perioperative intravenous lidocaine reduced the mean substance P levels in the lidocaine group compared to the control group, indicating better analgesia with lidocaine. The study also observed that serum substance P levels increased at 6 hours postoperatively in both groups. This aligns with a case study which reported that serum substance P levels begin to rise after 4 hours and peak at 12-18 hours post-trauma. Longer trauma durations correlate with higher substance P levels.[23]

Additionally, the control group had higher postoperative substance P levels than the lidocaine group, despite the lidocaine group having a longer surgery duration (187 minutes vs. 178

minutes for the control group). The duration of trauma or surgical stress impacts blood substance P levels, with longer wound incisions increasing substance P levels. This aligns with Papp et al.,[23] who found that substance P release occurs with tissue trauma and is related to the length and severity of the trauma. Their study suggest that perioperative intravenous lidocaine can suppress substance P release more effectively than the control group at 6 hours postoperatively, even with a greater degree of trauma. This inhibition is likely due to intravenous lidocaine blocking Na^+ channels, preventing Na+ conduction and action potential generation.

This study has limitations, as it does not describe postoperative pain outcomes in patients given perioperative intravenous lidocaine, which may vary by race and education level. It also did not assess patients' NRS scores before surgery. The study only objectively observed postoperative pain outcomes, inflammation as characterized by NLR, and substance P levels as pain markers. Additionally, the study did not examine blood levels of lidocaine, which has an analgesic effect. These aspects can be explored in future research to determine the effective analgesic blood levels of lidocaine and to monitor postoperative pain in patients. Therefore, further studies should include preoperative pain assessments for both patient groups, consider racial and educational factors for homogeneity, and measure blood lidocaine levels.

CONCLUSION

In conclusion, perioperative intravenous lidocaine can lower postoperative NRS scores, decrease postoperative NLR values, and reduce the difference in substance P levels between postoperative and preoperative measurements. And in this study, there was no intravenous lidocaine side effects.

REFERENCES

1. Regev GJ, Leor G, Ankori R, et al. Long-Term Pain Characteristics and Management Following Minimally Invasive Spinal Decompression and Open Laminectomy and Fusion for Spinal Stenosis. *Medicina (Kaunas, Lithuania)*. 2021;57(10). doi:10.3390/medicina57101125

2. Rachman F, R R, Musba AMT. Efektivitas Lidokain Intravena Kontinyu Perioperatif Terhadap Intensitas Nyeri Dan Total Konsumsi Opioid Pasca Bedah Dekompresi Dan Stabilisasi Posterior Vertebra. *NMSJ*. Published online April 3, 2021:33-43. doi:10.20956/nmsj.v5i1.10154

3. Anshori T, Takdir Musba AM, Ratnawati. Efek Pemberian Lidokain Intravena Kontinu Intraoperasi terhadap Kebutuhan Isofluran dan Pemakaian Fentanil pada Operasi Dekompresi dan Stabilisasi Posterior Vertebra. *MACC*. 2021;39(1):35-45. doi:10.55497/majanestcricar.v39i1.208

4. Pędziwiatr M, Kisialeuski M, Wierdak M, et al. Early implementation of Enhanced Recovery After Surgery (ERAS®) protocol - Compliance improves outcomes: A prospective cohort study. *Int J Surg*. 2015;21:75-81. doi:10.1016/j.ijsu.2015.06.087

5. Firdhaus R, Rosita Tantri A, Kurniawan T, et al. Penggunaan Lidokain Intravena untuk Adjuvan Obat Analgesik pada Operasi Bedah Saraf. *JNI*. 2022;11(2):121-126. doi:10.24244/jni.v11i2.448

6. Foo I, Macfarlane AJR, Srivastava D, et al. The use of intravenous lidocaine for postoperative pain and recovery: international consensus statement on efficacy and safety. *Anaesthesia*. 2021;76(2):238-250. doi:10.1111/anae.15270

7. Hermanns H, Hollmann MW, Stevens MF, et al. Molecular mechanisms of action of systemic lidocaine in acute and chronic pain: a narrative review. *Br J Anaesth*. 2019;123(3):335-349. doi:10.1016/j.bja.2019.06.014

8. Lee IWS, Schraag S. The Use of Intravenous Lidocaine in Perioperative Medicine: Anaesthetic, Analgesic and Immune-Modulatory Aspects. *J Clin Med*. 2022;11(12):3543. doi:10.3390/jcm11123543

9. Yue H, Zhou M, Lu Y, Chen L, Cui W. Effect of Intravenous Lidocaine on Postoperative Pain in Patients Undergoing Intraspinal Tumor Resection: Study Protocol for a Prospective Randomized Controlled Trial. *J Pain Res*. 2020;13:1401-1410. doi:10.2147/JPR.S249359

10. Small C, Laycock H. Acute postoperative pain management. *Br J Surg*. 2020;107(2):e70-e80. doi:10.1002/bjs.11477

11. Valentin-Hansen L, Park M, Huber T, et al. Mapping Substance P Binding Sites on the Neurokinin-1 Receptor Using Genetic Incorporation of a Photoreactive Amino Acid. *J Biol Chem*. 2014;289(26):18045-18054. doi:10.1074/jbc.M113.527085

12. Chang CT, Jiang BY, Chen CC. Ion Channels Involved in Substance P-Mediated Nociception and Antinociception. *Int J Mol Sci*. 2019;20(7):1596. doi:10.3390/ijms20071596

13. Sudiartha IPG, Wiargitha IK, Mahadewa TGB. Perbedaan nilai Neutrophil Lymphocyte Ratio (NLR) terhadap pemeriksaan kultur darah dalam mendiagnosis sepsis pada pasien peritonitis di RSUP Sanglah, Bali, Indonesia. *Intisari Sains Medis*. 2020;11(1):165-171. doi:10.15562/ism.v11i1.571

14. Paliogiannis P, Deidda S, Maslyankov S, et al. Blood cell count indexes as predictors of anastomotic leakage in elective colorectal surgery: a multicenter study on 1432 patients. *World J Surg Oncol*. 2020;18(1):89. doi:10.1186/s12957-020-01856-1

15. Peng Y, Zhang W, Kass IS, Han R. Lidocaine Reduces Acute Postoperative Pain After Supratentorial Tumor Surgery in the PACU: A Secondary Finding From a Randomized, Controlled Trial. *Journal of Neurosurgical Anesthesiology*. 2016;28(4):309-315. doi:10.1097/ANA.0000000000000230

16. Memary E, Mirkheshti A, Ghasemi M, Taheri M, Arhami Dolatabadi A, Kaboudvand A. The Effect of Lidocaine Infusion during General Anesthesia on Neutrophil-Lymphocyte-Ratio in Breast Cancer Patients Candidate for Mastectomy; a Clinical Trial. *Journal of Cellular & Molecular Anesthesia*. 2016;1(4). doi:10.22037/jcma.v1i4.13519

17. Surhonne N, Hebri C, Kannan S, Duggappa DR, RS RR, Mapari CG. The effect of anesthetic techniques on neutrophil to lymphocyte ratio in patients undergoing infraumbilical surgeries. *Korean J Anesthesiol*. 2019;72(5):458-465. doi:10.4097/kja.d.19.00022

18. Nguyen A, Nguyen A, Hsu TI, et al. Neutrophil to Lymphocyte Ratio as a Predictor of Postoperative Outcomes in Traumatic Brain Injury: A Systematic Review and Meta-Analysis. *Diseases*. 2023;11(1):51. doi:10.3390/diseases11010051

19. Joshi GP, Ogunnaike BO. Consequences of inadequate postoperative pain relief and chronic persistent postoperative pain. *Anesthesiol Clin North Am*. 2005;23(1):21-36. doi:10.1016/j.atc.2004.11.013

20. Dureja GP, Iyer RN, Das G, Ahdal J, Narang P. Evidence and consensus recommendations for the pharmacological management of pain in India. *J Pain Res*. 2017;10:709-736. doi:10.2147/JPR.S128655

21. Beecham GB, Nessel TA, Goyal A. Lidocaine. In: *StatPearls*. StatPearls Publishing; 2024. Accessed August 12, 2024. http://www.ncbi.nlm.nih.gov/books/NBK539881/

22. Silva A, Mourão J, Vale N. A Review of the Lidocaine in the Perioperative Period. *Journal of Personalized Medicine*. 2023;13(12):1699. doi:10.3390/jpm13121699

23. Papp A, Valtonen P. Tissue substance P levels in acute experimental burns. *Burns*. 2006;32(7):842-845. doi:10.1016/j.burns.2006.01.018

TABLES

Table 1. Characteristics of study

Variables	Lidocaine Group	Control Group	P value
Gender			
Male	7 (46.6)	10 (66.7)	0.269[a]
Female	8 (53.2)	5 (33.7)	
ASA Physical Status			
Class I	1 (6.7)	2 (13.3)	0.543[a]
Class II	14 (93.3)	13 (86,7)	
Age	44.29±12.96	46.82±11.33	0.439[b]
BMI	22.541±2.93	22.377±2.25	0.816[b]
Duration of surgery (mins)	187±24.73	178±28.92	0.258[b]

Data on gender and ASA physical status are presented as number (n) and percentage (%)
Age, BMI, and length of surgery are presented as mean±standard deviation (SD).
[a]Chi-square test; [b]Unpaired T-test.

Table 2. Comparison of pain intensity based on groups

Variables	Groups	N	Mean±SD	P value
NRS 2h	Lidocaine	15	2.54±0.69	0.148
	Control	15	2.82±0.61	
NRS 4h	Lidocaine	15	2.68±0.55	0.472
	Control	15	2.57±0.74	
NRS 6h	Lidocaine	15	2.07±0.54	0.005*
	Control	15	2.61±0.79	
NRS 12h	Lidocaine	15	2.00±0.67	0.045*
	Control	15	2.36±0.62	
NRS 24h	Lidocaine	15	1.71±0.46	0.031*
	Control	15	2.07±0.66	

Mann-Whitney U test
*p < 0.05 is statistically significant

Table 3. Effectiveness of perioperative intravenous lidocaine on Substance P values (ng/L)

Parameter	Lidocaine (Mean±SD)	Control (Mean±SD)	P value
Preoperative Substance P	259.69±144.92	175.69±57.89	0.26
6h-postoperative Substance P	243.57±122.65	221.37±103.7	0.9

Mann-Whitney U test
*p < 0.05 is statistically significant

Table 4. Effectiveness of perioperative intravenous lidocaine on NLR values

Parameter	Lidocaine Median (min-max)	Control Median (min-max)	P value
Preoperative NLR	1.5 (22.12 – 1.35)	3.73 (4.51 – 0.54)	0.173
6h-postoperative NLR	10.01 (19.50 – 2.14)	12.65 (23.10 – 10.43)	0.003*

Mann-Whitney U test
*p < 0.05 is statistically significant