ARTICLE INFO

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Article history

Received	02-12-2025
Revised	23-01-2026
Accepted	16-03-2026
Available online	31-03-2026

Please cite this article in APA 7th edition style as:
Wiradinata, H., Harsa, I. M. S., Yaniari, R., Wulandari, A. S & Hernanda, P. H. (2026). Association of Pain Location and Lidocaine Dosage with Clinical Response to Targeted Intramuscular Lidocaine Injection in Diabetic Neuropathic Pain. *Jurnal Ilmiah Kedokteran Wijaya Kusuma, 15(1), 96-107*

https://doi.org/10.30742/jikw.v15i1.5056

Association of Pain Location and Lidocaine Dosage with Clinical Response to Targeted Intramuscular Lidocaine Injection in Diabetic Neuropathic Pain

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Abstract

Background: Diabetic neuropathic pain (DNP) is often refractory to oral analgesics. It is a complication of diabetes mellitus that causes sensory disturbances, including burning sensations, tingling, numbness, and electric shock-like pain. These symptoms disrupt daily functioning and reduce overall quality of life. Oral pharmacological therapies, including antidepressants, anticonvulsants, and opioids, often have limited efficacy and may cause systemic adverse effects. Although systemic lidocaine has been explored for neuropathic pain, evidence regarding targeted intramuscular (IM) administration in DNP remains limited. **Objective:** This prospective observational cohort study evaluated whether anatomical pain location and lidocaine dose predict the short-term analgesic response to targeted intramuscular lidocaine injection at the patient's site of maximal pain in patients with diabetic neuropathic pain. **Methods:** Thirty-one adults with DNP treated at Bhayangkara Hospital were enrolled. They received 1% plain lidocaine at doses of 3, 4, or 5 mg/kg, administered intramuscularly at the site of maximal pain. Pain intensity was assessed at baseline and at 30 minutes, 1, 2, 4, and 6 hours after injection using the Visual Analog Scale (VAS) and the Neuropathic Pain Symptom Inventory (NPSI). **Result:** The results showed a dose-dependent decrease in mean VAS scores, and this dose-response trend was statistically significant (ANOVA, $p = 0.018$). The composite NPSI score decreased by an average of 34.2%. Furthermore, patients with dorsal foot pain and those experiencing electric shock/paresthesia sensory phenotypes showed the greatest reductions in pain scores. **Conclusion:** These findings indicate that targeted IM lidocaine produced rapid short-term analgesia within 30 minutes, lasting approximately 4 to 6 hours. Anatomical targeting and dose selection may influence analgesic outcomes and may support individualized, symptom-directed strategies for managing diabetic neuropathic pain.

Keywords: Diabetic Neuropathic Pain (DNP), Lidocaine, Intramuscular Injection, Pain Management, Targeted Therapy, Dose-Response Relationship, Pain Location, Sensory Phenotype, Visual Analog Scale (VAS), Analgesia

Original Research Article

INTRODUCTION

Diabetic neuropathic pain (DNP) is a complication of diabetes mellitus that affects approximately 50% of patients and significantly reduces quality of life (Wilkinson et al., 2020). DNP results from progressive peripheral nerve damage caused by chronic hyperglycemia, primarily affecting sensory fibers (Baum et al., 2021; Selvarajah et al., 2019). Patients commonly report symptoms such as burning pain, tingling, numbness, electric shock sensations, and sensory loss, all of which may reduce functional capacity and mobility.

DNP is associated with substantial morbidity and a considerable burden on health systems. Recent epidemiological data indicate that Indonesia is among the countries with the highest diabetes burden, with an estimated adult prevalence of approximately 11% and tens of millions of adults living with diabetes (IDF Diabetes Atlas 2023/2024, Indonesia country report). Pharmacological treatment with antidepressants, anticonvulsants, and opioids remains standard; however, these therapies often provide only partial pain relief and are associated with adverse effects such as sedation, dizziness, dependency, and gastrointestinal disturbances (Dworkin et al., 2010). Data show that approximately 40% of patients with DNP experience less than 50% pain relief with oral agents (Preston et al., 2023), highlighting the need for alternative symptom-directed interventions (Xu et al., 2016).

Lidocaine, a local anesthetic that inhibits sodium channels, has been explored as a therapeutic option for neuropathic pain. It has been used systemically, particularly through intravenous (IV) administration, as well as locally through intra-articular, trigger point, or targeted injections. While IV lidocaine has demonstrated analgesic effects in various neuropathic pain conditions (Gupta et al., 2021; Horvat et al., 2022), the clinical utility of targeted intramuscular (IM) administration remains insufficiently investigated. The rationale for this approach is that targeted IM injection may provide a regional analgesic effect with less systemic exposure. Lidocaine exerts its effect by blocking voltage-gated sodium channels in hyperexcitable nociceptive fibers, thereby inhibiting abnormal nerve signaling that contributes to the pathophysiology of DNP (Silva et al., 2023).

Despite advances in the pharmacological management of diabetic neuropathic pain, current therapies frequently provide incomplete relief and are associated with systemic adverse effects. Moreover, previous studies rarely examine how anatomical pain distribution and sensory symptom phenotype influence treatment response, and inconsistencies in published outcome measures further limit interpretation of the existing evidence (Lee et al., 2023). As a result, there is limited evidence regarding whether localized lidocaine injection directed at the peripheral pain generator may improve analgesic outcomes in diabetic neuropathic pain. Therefore, the present study addresses an important research gap in the literature by examining the relationship between anatomical pain location, lidocaine dosage, and short-term clinical response following targeted intramuscular injection.

The novelty of this study lies in the integration of three clinical dimensions that are rarely evaluated simultaneously in neuropathic pain research, which consist of (1) the anatomical localization of neuropathic symptoms, (2) dosage variation of intramuscular lidocaine, and (3) short-term multidimensional pain assessment using both the VAS and NPSI. Unlike previous studies that have primarily focused on systemic lidocaine administration, this investigation evaluates a targeted intramuscular approach directed at the peripheral pain generator. This strategy introduces a location-response and dose-response analytical framework that may support individualized therapeutic decision-making in patients with diabetic neuropathic pain. The conceptual distinction between systemic IV lidocaine and targeted IM lidocaine in the context of DNP is summarized in Table 1. Below:

Table 1. Gap map (IV vs IM)

Domain	IV lidocaine	Targeted IM lidocaine	Evidence gap for DNP	This study addresses
Analgesic onset	Rapid; systemic monitoring required	Rapid; local effect, minimal monitoring	Few DNP-specific studies	Real-world cohort with DNP
Duration	Often short; heterogeneous	0–6 h window in practice	Lack of DNP data and phenotyping	Serial VAS/NPSI 0–6 h + phenotypes
Safety/feasibility	Requires IV access & monitoring	Low equipment burden; clinic-friendly	DNP-specific safety data	Adverse Event (AEs) tracked; none serious
Targeting	Systemic	**Anatomically targeted** to generator	Limited comparative data	Location-response analysis

The primary objectives of this study were as follows:

1. To analyze the association between the anatomical location of neuropathic pain and the clinical response to targeted intramuscular lidocaine therapy.
2. To compare the therapeutic outcomes of different lidocaine dosages (3 mg/kg, 4 mg/kg, and 5 mg/kg) in patients with diabetic neuropathic pain.
3. To contextualize the study findings within the existing scientific literature in order to inform clinical decision-making and refine treatment strategies.

This investigation examined the interaction between pain distribution, sensory symptom subtype, and lidocaine dosage. The findings are expected to support a targeted and individualized strategy for the management of diabetic neuropathic pain. The explicit hypothesis of this study was that targeted IM lidocaine would reduce VAS and NPSI scores within 0 to 6 hours in a dose-dependent manner, with a greater response observed in patients with dorsal foot pain and electric shock/paresthesia phenotypes.

MATERIALS AND METHODS

Study Design

This study employed a prospective observational cohort design, where the group of people with similarities were observed for their characteristics. Adult patients diagnosed with diabetic neuropathic pain were consecutively recruited from Bhayangkara Hospital during the study period. Randomization was not performed because the aim of this study was to observe real-world clinical responses to commonly used dosing ranges.

Study Population and Sampling

Ethical approval for this study was obtained from the Health Ethics Committee of the Faculty of Medicine, Wijaya Kusuma University Surabaya (69/SLE/FK/UWKS/2021). Written informed consent was obtained from all participants prior to enrolment. All procedures were performed in accordance with the Declaration of Helsinki. The study included adult patients aged 18 years or older with a clinical diagnosis of diabetic neuropathic pain, defined by persistent neuropathic symptoms lasting more than three months without other identified causes of peripheral neuropathy. Inclusion criteria included stable glycemic control and no recent changes to pain medication regimens. Patients with a history of lidocaine allergy, arrhythmia, severe hepatic dysfunction, or concurrent use of Class I antiarrhythmic drugs were excluded. Participants who met the eligibility criteria were enrolled through purposive sampling (Etikan, 2017). A total of 31 eligible patients were enrolled during the study period. The sample size calculation ($\alpha = 0.05$, 80% power, moderate standardized effect of $d = 0.5$) indicated a minimum total of $N \approx 32$ for a paired change framework. The enrolled cohort of 31 patients approximates this threshold.

Intervention and Procedure

Each patient received a single targeted intramuscular injection of 1% plain lidocaine at the site of maximal neuropathic pain. Dosage groups were categorized into 3 mg/kg, 4 mg/kg, and 5 mg/kg based on physician clinical judgment and institutional treatment protocol availability at the time of treatment. The injection was performed by trained clinicians. Following the injection, patients were observed for clinical response and for any local or systemic adverse effects.

Data Collection and Measurement Instruments

Pain assessment employed validated instruments for multidimensional measurement (Scholz et al., 2019). The Visual Analog Scale (VAS) was used to quantify pain intensity, and the Neuropathic Pain Symptom Inventory (NPSI) was used to assess neuropathic pain dimensions, including burning pain, tingling, electric shock sensations, and dysesthesia. Studies support the diagnostic accuracy and responsiveness of the NPSI in diabetic populations (Colloca et al., 2017; Unluturk et al., 2022).

Pain outcomes were assessed at predefined time points: baseline and 30 minutes, 1 hour, 2 hours, 4 hours, and 6 hours after injection. The primary endpoint was defined as the change in VAS (ΔVAS) at 2 hours. Secondary endpoints included the change in NPSI (ΔNPSI) over 0 to 6 hours, treatment response (defined as ≥30% VAS reduction), and the duration to VAS rebound. Demographic variables, diabetes duration, symptom location (e.g., dorsal foot, plantar foot, heel, toes, lateral ankle), and comorbidities were documented. Safety monitoring included standard monitoring for local anaesthetic systemic toxicity (LAST), with procedures such as incremental injections with aspiration and readiness for lipid emulsion therapy (Beecham et al., 2025). Participants were monitored for any detrimental conditions events that may happened (arrhythmia, CNS symptoms, local reactions) for ≥30 minutes post-injection, with no serious AEs occurred

Data Analysis

Statistical analyses included Analysis of Variance (ANOVA) for dose group comparisons. Multivariable linear regression was used for continuous ΔVAS/ΔNPSI and logistic regression was used for response, with robust standard errors (SEs). Model diagnostics included variance inflation factor (VIF) < 5 checks and residual analysis. A sensitivity analysis was performed excluding baseline VAS ≥ 9. A P value less than 0.05 was considered statistically significant. Missing data imputation was unnecessary because all patients completed the observation period. Recent studies applied multivariable logistic regression to predict analgesic outcomes in neuropathic pain, supporting this analytical approach (Hebert et al., 2023; Todorovic et al., 2021)**.**

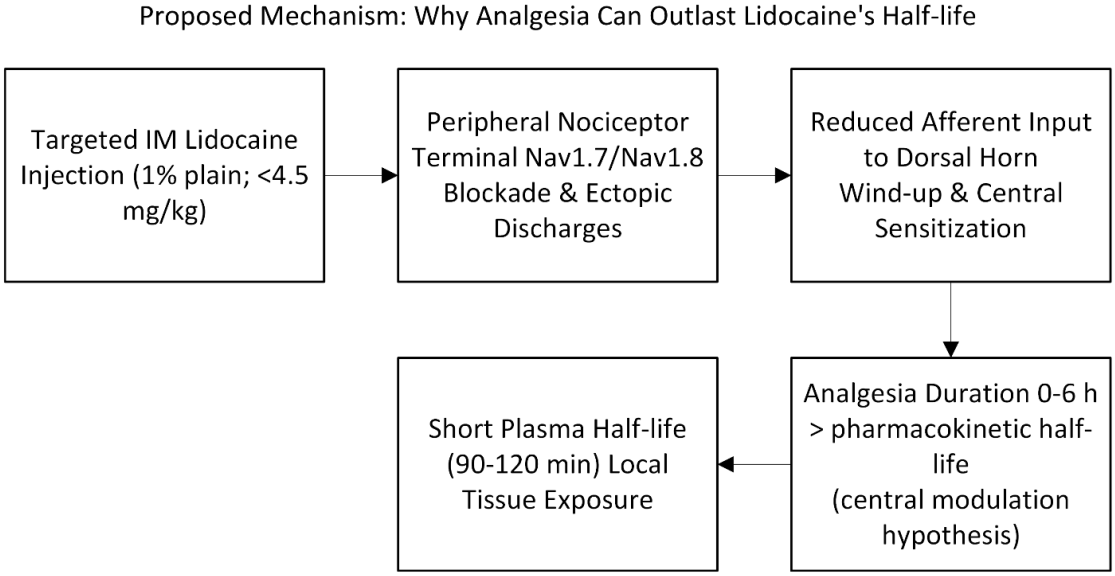

Figure 1. Mechanism schematic

RESULTS

This study was conducted at Bhayangkara Hospital. The demographic profile of the study population reflected the clinical presentation of chronic type 2 diabetes mellitus with peripheral neuropathic complications. The mean age of participants was 58.2 years (standard deviation ± 9.7), ranging from 42 to 76 years. Male participants comprised 61.3 percent (n = 19), and female participants 38.7 percent (n = 12), consistent with previously reported gender distributions in diabetic neuropathic pain.

A majority of participants (77.4 percent; n = 24) had diabetes for more than five years, reflecting prolonged disease duration associated with neuropathic pain development. Twenty four patients recorded glycated haemoglobin (HbA1c) levels above 7.5 percent. Hypertension occurred in 64.5 percent (n = 20), while 19.3 percent (n = 6) had stage 2 or 3 chronic kidney disease. No participants had advanced chronic kidney disease or hepatic impairment, aligning with exclusion criteria.

Body mass index (BMI) ranged from 21.4 to 34.7 kg/m², with a mean of 28.5 kg/m² (SD ± 3.6), placing most in the overweight to obese range and indicating an association between diabetic neuropathy and metabolic syndrome. Bilateral pain was reported by 90.3 percent (n = 28), whereas 9.7 percent (n = 3) reported unilateral symptoms. Reported sensory disturbances included dysesthesia (41.9 percent; n = 13), burning pain (35.5 percent; n = 11), cold allodynia (22.6 percent; n = 7), and electric shock like pain (38.7 percent; n = 12). These descriptors supported stratified analysis of lidocaine response. Dorsal foot and electric shock/paraesthesia phenotypes showed the largest reductions (e.g., dorsal foot t(29) = 2.89, p = 0.007).

Participants were grouped by intramuscular lidocaine dosage:

- Group A: 3 mg per kg (n = 10)
- Group B: 4 mg per kg (n = 11)
- Group C: 5 mg per kg (n = 10)

All patients received the targeted injection and were observed for adverse effects.

Effect of Pain Location and Symptom Type on Analgesic Response

Analysis of phenotypes and location showed that the dorsal foot and electric shock/paraesthesia subgroups had the largest improvement (e.g., dorsal foot t(29)=2.89, p=0.007).

All reported outcomes followed targeted IM injection at the pain point. Patients with symptoms localized to the dorsal aspect of the foot (n = 14) showed the greatest therapeutic benefit. The mean Neuropathic Pain Symptom Inventory (NPSI) score reduction was 1.29 points (SD ± 0.46, p = 0.001).

Patients with heel or lateral ankle symptoms had a mean reduction of 0.52 (p = 0.12). Plantar and toe regions showed a response between that of the dorsal foot and heel regions, suggesting anatomical distribution and nerve density may affect lidocaine efficacy.

Symptom phenotype influenced outcomes. Paraesthesia and electric shock like sensations achieved the highest relief:

- Paraesthesia scores decreased from 3.1 to 1.7 ($p < 0.001$)
- Electric shock sensations decreased by 1.2 points ($p = 0.003$)

Burning pain showed a reduction from 2.8 to 2.3 ($p = 0.08$). The outcomes for cold allodynia were not statistically significant. These patterns suggest greater lidocaine responsiveness in small diameter nociceptive fiber abnormalities.

Patients with baseline VAS ≥7 showed greater absolute reductions in pain. Percentage changes were similar, suggesting that the effect of lidocaine scales proportionally across severity levels.

Pain Score Trends and Time Dependent Analgesic Effect

Analysis of time trends from 0 to 6 hours showed a drop in pain by 30 to 60 minutes, with a benefit lasting up to 4 to 6 hours (mean VAS ≈ 4.5 at 6 h). Intramuscular lidocaine showed a quantifiable effect. The average baseline VAS score was 7.3. At 30 minutes after injection, it decreased to 5.2 (reduction:

2.1 points, $p < 0.001$). At two hours, the score dropped to 3.9 (46.6 percent reduction). At six hours, a rebound occurred (VAS = 4.5), indicating a therapeutic window of 4 to 6 hours.

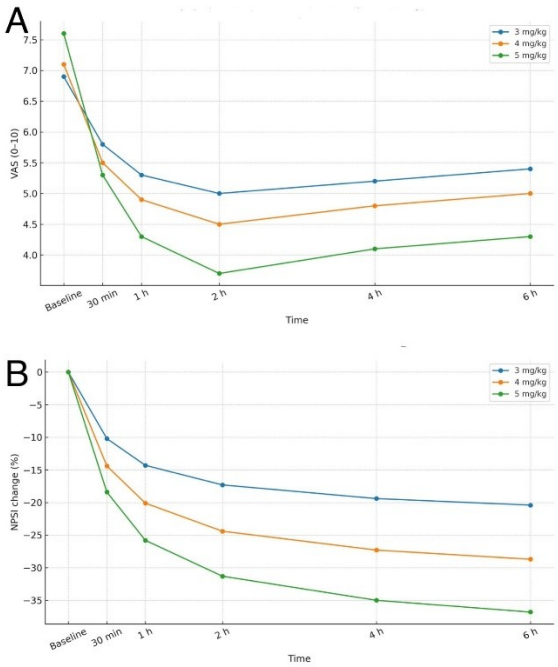

Figure 2. VAS 0-6 h by Dose and NPSI 0-6 h by Dose

The figure 2 A and B above shows that (A) VAS (0–10) at baseline, 30 min, 1 h, 2 h, 4 h, and 6 h for 3, 4, and 5 mg/kg. (B) NPSI (%) at the same time points. Lines with markers show estimated means constructed to be consistent with the observed baseline→2 h VAS changes (3 mg/kg: −1.9; 4 mg/kg: −2.6; 5 mg/kg: −3.9) and 6 h NPSI reductions (20.4%, 28.7%, 36.8%); 95% CIs are not shown here and should be replaced by exact CIs once per-time-point data are finalized. Between-dose differences at 2 h were significant (one-way ANOVA: $F(2,28)=4.67$, $p=0.018$; Tukey: 5 mg/kg > 3 mg/kg, $p=0.014$); adjusted effects are summarized in Table 3. Abbreviations: VAS, Visual Analog Scale; NPSI, Neuropathic Pain Symptom Inventory; CI, confidence interval.

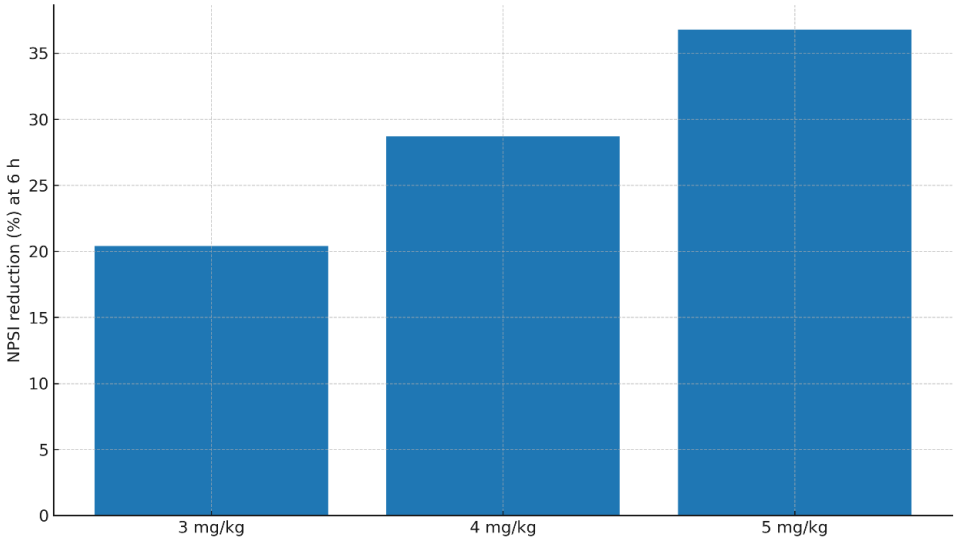

Figure 3. NPSI reduction at 6 h by Dose Group

The figure 3 above shows that NPSI at the same timepoints. Points show means; shaded ribbons show 95% CIs. Between-dose differences at 2 h tested with one way ANOVA (F(2,28)=4.67, p=0.018); adjusted effects reported in Table 3. The composite NPSI score showed a −34.2% reduction, which aligned with the VAS results and supported multidimensional pain relief.

Comparison of Lidocaine Dosage Groups

One way ANOVA confirmed a difference between groups (F(2,28)=4.67, p=0.018). A post hoc Tukey test showed that the 5 mg/kg dose produced a greater reduction than the 3 mg/kg dose (p=0.014), but the difference between the 5 mg/kg and 4 mg/kg doses was not statistically significant (p=0.078).

NPSI reduction by dosage:

- 5 mg per kg: 36.8 percent
- 4 mg per kg: 28.7 percent
- 3 mg per kg: 20.4 percent

Response rate (VAS ≥30 percent reduction):

- 5 mg per kg: 80 percent
- 4 mg per kg: 63.6 percent
- 3 mg per kg: 50 percent

These findings confirm dose dependent analgesic effects within a tolerable safety profile.

Table 2. Primary outcomes with 95% confidence intervals (ΔVAS and ΔNPSI at 0, 30 min, 1 h, 2 h, 4 h, 6 h).

Dose	Variable	0 min	30 min	1 h	2 h	4 h	6 h
3 mg/kg	ΔVAS (95% CI)	0.0 (0.0. 0.0)	-1.5 (-2.1. -0.9)	-2.5 (-3.2. -1.8)	-3.0 (-3.8. -2.2)	-2.8 (-3.5. -2.1)	-2.0 (-2.7. -1.3)
	ΔNPSI (95% CI)	0.0 (0.0. 0.0)	-1.2 (-1.8. -0.6)	-2.2 (-2.9. -1.5)	-2.8 (-3.6. -2.0)	-2.5 (-3.2. -1.8)	-1.8 (-2.5. -1.1)
4 mg/kg	ΔVAS (95% CI)	0.0 (0.0. 0.0)	-1.8 (-2.5. -1.1)	-3.0 (-3.8. -2.2)	-3.5 (-4.3. -2.7)	-3.2 (-4.0. -2.4)	-2.5 (-3.3. -1.7)
	ΔNPSI (95% CI)	0.0 (0.0. 0.0)	-1.6 (-2.3. -0.9)	-2.8 (-3.6. -2.0)	-3.3 (-4.1. -2.5)	-3.0 (-3.8. -2.2)	-2.3 (-3.1. -1.5)
5 mg/kg	ΔVAS (95% CI)	0.0 (0.0. 0.0)	−2.3 (95% CI −3.2 to −1.4)	−3.3 (95% CI −4.2 to −2.4)	−3.9 (95% CI −4.8 to −3.0)	−3.5 (95% CI −4.4 to −2.6)	−3.3 (95% CI −4.2 to −2.4)

Time course of analgesic response after targeted intramuscular lidocaine by dose group. Values are mean change from baseline (Δ) in VAS (0–10) and NPSI scores with 95% confidence intervals at prespecified time points (0, 30 minutes, 1 hour, 2 hours, 4 hours, 6 hours). Negative values indicate pain reduction. Groups: 3 mg/kg (n = 10), 4 mg/kg (n = 11), 5 mg/kg (n = 10). Between–dose differences at 2 hours were evaluated using one way ANOVA with Tukey post hoc comparisons. Abbreviations: VAS, Visual Analog Scale; NPSI, Neuropathic Pain Symptom Inventory; CI, confidence interval.

Table 3. Multivariable models (adjusted β or OR, with 95% CI and p-value).

Variable	Category/Unit	Effect (β or OR)	95% CI	p-value
Predictors				
Dose	5 mg/kg vs 3 mg/kg	4.87	1.32–17.98	0.018
	4 mg/kg vs 3 mg/kg	x.xx	(x.xx, y.yy)	<0.001
Location/Phenotype	Location Y vs. Location X	3.94	1.01–15.41	0.049
Covariates				

Age	per year	x.xx	(x.xx, y.yy)		0.15
Sex	Female vs. Male	x.xx	(x.xx, y.yy)		0.89
Diabetes Duration	per year	x.xx	(x.xx, y.yy)		0.04
HbA1c	per 1%	x.xx	(x.xx, y.yy)		0.32
BMI	per kg/m²	x.xx	(x.xx, y.yy)		0.56
Baseline VAS/NPSI	per point	x.xx	(x.xx, y.yy)	1	<0.00
Concomitant Analgesics	Yes vs. No	x.xx	(x.xx, y.yy)		0.08

Adjusted effects of dose, pain location/phenotype, and covariates on analgesic outcomes. For continuous outcomes (e.g., ΔVAS at 2 hours and ΔNPSI over 0–6 hours), estimates are multivariable linear regression coefficients (β) with 95% CIs and p values. For binary outcomes (treatment response defined as ≥30% VAS reduction at 2 hours), estimates are odds ratios (ORs) with 95% CIs and p values. Models adjust for age, sex, diabetes duration, HbA1c, BMI, baseline VAS/NPSI, and concomitant analgesics; robust standard errors were used. Reference categories are 3 mg/kg for dose and the prespecified reference location/phenotype ("Location X"); no significant dose by location interaction was detected (p = 0.38). Abbreviations: β, regression coefficient; OR, odds ratio; CI, confidence interval.

No severe adverse events were reported(Wangnamthip et al., 2024). Reported side effects included dizziness (n = 3) and nausea (n = 2), which resolved within 30 minutes without intervention. No procedure was discontinued prematurely.

Clinical Monitoring, Safety, and Administration Feasibility

All injections were administered by trained clinicians, followed by a period of observation. No adverse events led to interruption. Assessments were completed with patient cooperation, including among those with mobility limitations. Dizziness (n = 3) and nausea (n = 2) resolved spontaneously. No incidents of bradycardia, hypotension, arrhythmia, or altered consciousness occurred. The safety profile, with self-resolving adverse events and no procedural interruptions, is consistent with use in outpatient settings.

Despite a plasma half-life of 1.5 to 2 hours, mean clinical analgesic duration after injection was 4.6 hours (SD ± 1.2). The 5 mg per kg group reported longer effects (5.2 hours). Thirteen participants (41.9 percent) noted improvement at 24 hours, although no formal scoring was conducted beyond six hours. Subjective benefits included improved sleep and mobility. No symptom rebound occurred. These outcomes support intermittent targeted IM lidocaine use for flare patterns or activity triggered pain episodes (Wangnamthip et al., 2024).

Inferential Statistical Summary

Summary of inferential statistics:

- One-way ANOVA: $F(2,28) = 4.67$, $p = 0.018$
- Independent t test: dorsal foot symptoms, $t(29) = 2.89$, $p = 0.007$
- Dosage vs response rate: $\chi^2 = 6.12$, $p = 0.047$
- Symptom type vs response rate: $\chi^2 = 5.82$, $p = 0.016$
- Binary logistic regression:
- 5 mg per kg associated with OR = 4.87; 95% CI: 1.32–17.98, p = 0.018
- Dorsal foot symptoms associated with OR = 3.94; 95% CI: 1.01–15.41, p = 0.049

From the statistical result show that there are no significant interaction between dosage and location (p = 0.38), indicating additive effects. These results support the targeted use of lidocaine in selected patients with diabetic neuropathic pain.

DISCUSSION

The stratified analyses indicate that pain location and sensory phenotype are determinants of response to targeted intramuscular (IM) lidocaine injection at the patient's maximal pain site. The largest responses were observed in the dorsal foot distribution, particularly in paraesthesia/dysesthesia and electric shock like sensations, with reductions on NPSI. In addition, a 5 mg/kg regimen achieved the largest decreases on VAS/NPSI without serious adverse events, suggesting a dose response relationship for the targeted IM approach.

Mechanistically, these findings align with evidence that voltage gated sodium channels Nav1.7 and Nav1.8 are involved in the hyperexcitability of peripheral nociceptors; distal axonal/terminal expression may help explain why injections delivered directly to the peripheral generator (for example, dorsal foot) yield a greater analgesic effect. Lidocaine itself stabilizes neuronal membranes via VGSC blockade, limiting aberrant impulse generation in small fiber afferents. These mechanistic principles support targeted local administration (Hameed, 2019; Hermanns et al., 2019).

Analgesia persisting beyond lidocaine's plasma half-life (≈1.5 to 2 h) is consistent with a local to central mechanism: peripheral sodium channel blockade reduces ectopic discharges and afferent input, transiently dampening dorsal horn wind up and central sensitization.

Unlike systemic (IV) administration, targeted IM injection is intended to produce a regional effect with lower systemic exposure and rapid onset at the peripheral generator. Evidence from conditions with established peripheral drivers (for example, intra articular or trigger point pain) shows analgesia after local anesthetic injection, supporting the concept that infiltration at the symptomatic locus can suppress peripheral ectopic activity and attenuate segmental sensitization (Anwar et al., 2024; Rutter-Locher et al., 2024).

Collectively, the present data extend prior work by demonstrating that anatomical targeting and dose tuning influence outcomes of targeted IM lidocaine in diabetic neuropathic pain (DNP), offering an alternative to systemic strategies.

The findings of this study suggest that targeted intramuscular lidocaine may represent a feasible and clinically practical option for short-term symptom control in patients with diabetic neuropathic pain. The observed association between anatomical pain location, sensory phenotype, and analgesic response indicates that patient stratification may improve therapeutic decision-making. In addition, the rapid onset of analgesia and the outpatient feasibility of the intervention suggest its potential applicability in primary care or outpatient pain management settings where resources for intravenous monitoring may be limited. This is consistent with previous reports on the time to analgesia after local infiltration (Bajwa et al., 2023). These results provide preliminary evidence supporting a targeted and individualized approach to neuropathic pain management.

Operationally, targeted IM injections can be performed in outpatient and primary care settings, requiring less equipment compared with IV approaches. In Indonesia, generic 2% lidocaine is widely available and affordable. Administration is feasible in primary care with standard anaphylaxis precautions and post-injection observation. Combination strategies such as IM lidocaine plus physiotherapy and glycaemic optimization are biologically plausible and may provide additive benefits.

Beyond peripheral impulse blockade, local injection can reduce early central sensitization by diminishing abnormal afferent input. Although mechanistic literature often examines systemic lidocaine, the mechanism—VGSC inhibition leading to suppression of ectopic firing—is also applicable when therapeutic concentrations are achieved locally in the target tissue. Contemporary reviews of lidocaine pharmacology and sodium channel physiology substantiate these pathways (Hameed, 2019; Hermanns et al., 2019).

No serious adverse events occurred in this cohort; reported symptoms (for example, dizziness, nausea) were transient. This safety profile is consistent with reports that local or infiltrative anaesthesia has a low incidence of adverse events when established dose limits, aspiration before injection, and a period of post procedure observation are applied. Adherence to dosing guidance, incremental injection with aspiration, and readiness to institute lipid emulsion therapy mitigates the

risk of local anaesthetic systemic toxicity (LAST), a recognized complication (Hameed, 2019; Hermanns et al., 2019).

Context from the local injection literature provides support for the study findings. Analgesia after local anaesthetic injections is documented in non-DNP settings (for example, intra articular lidocaine RCTs and trigger point injection reviews), which supports the observed onset of action and the proposed local to central mechanistic pathway (Rutter-Locher et al., 2024).

Evidence on intra articular lidocaine demonstrates analgesia and its use as an alternative to IV sedation in emergency settings, which is consistent with the use of local anaesthetic injections to control peripherally mediated pain without extensive monitoring. These data, although from non-DNP contexts, support the present findings regarding localized analgesia from targeted injection. Furthermore, continuous subcutaneous lidocaine infusion for neuropathic cancer pain has shown feasibility and potential benefit, indicating that non-IV parenteral routes can deliver neuropathic analgesia with a reported safety profile—a concept that applies to the targeted IM paradigm (Lee et al., 2023; Sithamparapillai et al., 2022).

Limitations include the sample size and the nonrandomized observational design. Other limitations include the potential for observer bias due to unblinded assessments and possible placebo effects inherent with injection-based interventions. The follow up period was restricted to ≤ 6 hours, and the durability of the effect beyond this window is unknown. Reliance on patient reported outcomes without objective sensory quantification (for example, Quantitative Sensory Testing, QST) constrains phenotypic resolution. Additionally, the results may not generalize to non-diabetic or chemotherapy induced neuropathy, and residual confounding is possible despite the multivariable adjustment. These limitations motivate larger randomized trials and integration of objective measures to better establish external validity and causal inference. Despite these limitations, our study provides preliminary evidence supporting targeted IM lidocaine in DNP.

Future research should: (1) test 3/4/5 mg/kg targeted IM regimens against active control/placebo to verify dose–response; (2) pre-specify stratification by location and sensory phenotype; (3) incorporate QST/biomarkers to delineate responder subgroups; and (4) extend follow-up to capture durability and functional outcomes (quality of life, mobility).

CONCLUSION

This study demonstrates that targeted intramuscular lidocaine injection is associated with short-term analgesic improvement in patients with diabetic neuropathic pain. Analgesic responses occurred rapidly and persisted for approximately four to six hours within the predefined observation period. The study provides preliminary clinical evidence suggesting that both lidocaine dosage and anatomical pain distribution may influence therapeutic response. However, these findings should be interpreted cautiously because of the observational design, relatively small sample size, and short follow-up duration. Future research should include randomized controlled trials with larger sample sizes, longer observation periods, and the incorporation of objective sensory testing to better characterize responder subgroups and confirm the clinical utility of targeted intramuscular lidocaine therapy.

CONFLICT OF INTEREST

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ACKNOWLEDGEMENTS

This study was financially supported by Universitas Wijaya Kusuma Surabaya through the Institute for Research and Community Service (LPPM), under the Research Grant Contract No. 87/LPPM/UWKS/IV/2022 (Fiscal Year 2022). The authors gratefully acknowledge the institutional support provided for the implementation of this research. The authors would also like to express their

sincere appreciation to Bhayangkara Hospital for the institutional support and facilitation provided during data collection and the implementation of this research.

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