e-ISSN (online): 2745-9497

Journal of Anesthesiology and Clinical Research (JACR)

Journal website: https://hmpublisher.com/index.php/jacr

Efficacy of Particulate versus Non-Particulate Corticosteroids as Adjuvants for Popliteal Sciatic Nerve Block: A Randomized Controlled Superiority Trial

Erma Rosita[1*], Taufiq Agus Siswagama[1], Rudy Vitraludyono[1], Buyung Hartiyo Laksono[1]

[1]Department of Anesthesiology, Faculty of Medicine, Universitas Brawijaya, Malang, Indonesia

ARTICLE INFO

Keywords:
Depot effect
Dexamethasone
Methylprednisolone
Popliteal sciatic block
Ropivacaine

***Corresponding author:**
Erma Rosita

E-mail address:
ermarosita87@gmail.com

All authors have reviewed and approved the final version of the manuscript.

https://doi.org/10.37275/jacr.v7i1.853

A B S T R A C T

Introduction: Single-shot ultrasound-guided popliteal sciatic nerve blocks are the gold standard for distal lower limb analgesia but are limited by a finite duration, often necessitating adjuvants. While dexamethasone (non-particulate) is the standard of care, methylprednisolone (particulate) theoretically offers a depot effect for sustained release. This study aimed to determine if perineural methylprednisolone provides superior analgesic duration compared to dexamethasone. **Methods:** In this prospective, double-blind, randomized controlled trial, 36 ASA I-III patients undergoing distal lower limb surgery were randomized (1:1) to receive 20 mL of 0.5% Ropivacaine with either Dexamethasone 8 mg (Group D) or Methylprednisolone 40 mg (Group M). To ensure blinding, solutions were prepared by an independent pharmacist and administered via opaque syringes. The primary outcome was the duration of analgesia (time to Numeric Rating Scale [NRS] greater than 3), analyzed using Kaplan-Meier survival curves and Log-Rank tests. Secondary outcomes included cumulative opioid consumption, rebound pain severity, and block onset time. The study was powered for superiority with a clinically significant difference of 4 hours. **Results:** Thirty-six patients completed the study. Demographic and surgical characteristics were comparable. The median duration of analgesia was 18.4 (SD 3.2) hours in Group D and 19.1 (SD 3.5) hours in Group M (p = 0.58; Log-Rank p = 0.61). Pain scores at 12, 24, and 48 hours showed no significant difference, with both groups demonstrating a floor effect due to multimodal analgesia (Median NRS less than 2). No adverse events, including neurotoxicity or infection, were observed. **Conclusion:** Perineural methylprednisolone failed to demonstrate superior analgesic duration compared to dexamethasone in this cohort. The theoretical depot advantage did not translate to clinical superiority, likely due to vascular clearance in the popliteal fossa. Given the comparable efficacy but superior safety profile of non-particulate agents, dexamethasone remains the preferred adjuvant. Methylprednisolone serves as a viable alternative only when non-particulate options are unavailable.

1. Introduction

The management of postoperative pain following distal lower limb surgery presents a unique challenge to the anesthesiologist. Procedures involving the foot and ankle, such as open reduction and internal fixation (ORIF) of ankle fractures, calcaneal osteotomies, and complex forefoot reconstructions, are associated with severe, dynamic nociceptive input.[1] This pain is driven by a convergence of somatic input from the cutaneous innervation and deep osteoarticular pain from periosteal stripping and bone instrumentation. Inadequate analgesia in this setting not only impedes early mobilization and delays hospital discharge but also serves as a potent catalyst for the development of chronic post-surgical pain (CPSP), a debilitating complication estimated to affect up to 30% of foot and ankle surgery patients.[2]

The ultrasound-guided popliteal sciatic nerve block (PSNB) has firmly established itself as the gold standard analgesic modality for these procedures.[3] By depositing local anesthetic within the paraneural sheath at the bifurcation of the sciatic nerve, the PSNB provides dense, site-specific anesthesia that is superior to parenteral opioids. It effectively blunts the neuroendocrine stress response, minimizes opioid-related side effects such as nausea and respiratory depression, and facilitates rapid recovery. However, the utility of single-shot peripheral nerve blocks is intrinsically limited by the pharmacokinetics of the local anesthetic employed. Even long-acting amide local anesthetics, such as ropivacaine or bupivacaine, typically provide sensory blockade for a maximum of 12 to 16 hours.[4]

The regression of the nerve block often coincides with the first postoperative night—a period of reduced nursing surveillance and patient vulnerability. This abrupt transition from complete anesthesia to full nociception is known as rebound pain. Rebound pain is not merely the return of sensation; it is a hyperalgesic state characterized by a rapid, often unmanageable escalation in pain intensity that can exceed the pain levels experienced by patients who never received a block.[5] To mitigate this, perineural catheters have been utilized to provide continuous infusions. While effective, catheters are resource-intensive, technically demanding, and fraught with complications such as dislodgement, leakage, and infection, limiting their routine use in high-throughput ambulatory settings.[6]

Consequently, the pharmacological extension of single-shot blocks using perineural adjuvants has become a primary research imperative in regional anesthesia.[7] A diverse array of agents—including alpha-2 agonists, opioids, and NMDA antagonists—has been investigated. Among these, corticosteroids have emerged as the most consistent and efficacious class of adjuvants. Their mechanism of action is multifaceted, involving the suppression of ectopic neuronal discharge in C-fibers, the inhibition of phospholipase A2, and the modulation of potassium channels. Dexamethasone, a potent, non-particulate glucocorticoid, is currently the most widely used agent, with meta-analyses confirming its ability to prolong analgesia by 6 to 8 hours.

Despite the efficacy of dexamethasone, its duration is finite. This limitation has reignited interest in alternative corticosteroid formulations, specifically particulate steroids such as methylprednisolone acetate. The depot hypothesis posits that the low solubility of particulate steroids allows them to precipitate at the injection site, forming a drug reservoir that provides a slow, sustained release of the active moiety over days or weeks. This pharmacokinetic property has been successfully exploited in epidural steroid injections and intra-articular therapies. Recent evidence in fascial plane blocks, such as the transversus abdominis plane (TAP) block, suggested that methylprednisolone might indeed offer superior long-term analgesia compared to dexamethasone.[8]

However, the extrapolation of these findings to the perineural space of the sciatic nerve is problematic. The pharmacokinetic environment of a distinct nerve sheath differs vastly from a fascial plane or a joint space. Furthermore, the use of particulate steroids carries significant safety implications. Insoluble particles pose a theoretical risk of embolic infarction of the vasa nervorum or direct neurotoxicity if injected intraneurally—a risk profile that is notably higher than that of non-particulate dexamethasone.[9] Therefore, the use of a particulate agent is only justifiable if it demonstrates a substantial clinical superiority in analgesic duration.

To date, robust head-to-head comparisons of methylprednisolone versus dexamethasone in popliteal sciatic nerve blocks are scarce, particularly in Southeast Asian populations where genetic polymorphisms in drug metabolism may influence outcomes. This study addresses this critical gap in the literature. We designed a rigorous, prospective, double-blind, randomized controlled trial to evaluate the comparative efficacy of these two agents.[10]

The primary aim of this study was to determine if the addition of 40 mg of particulate methylprednisolone to 0.5% ropivacaine results in a superior duration of analgesia compared to 8 mg of non-particulate dexamethasone in ultrasound-guided popliteal sciatic nerve blocks. The novelty of this research lies in: (1) testing the depot hypothesis in a peripheral nerve model: challenging the assumption that particulate

insolubility translates to prolonged perineural effect in the highly vascularized popliteal fossa; (2) resource-stratified pharmacology: providing evidence for alternative adjuvant strategies in resource-limited settings (common in developing nations) where drug supply chains are volatile, and the standard of care (dexamethasone) may not always be available.

2. Methods

This was a single-center, prospective, double-blind, randomized controlled superiority trial conducted at Dr. Saiful Anwar Regional General Hospital, Malang, Indonesia, a tertiary academic medical center, from March 2025 to September 2025. The study protocol strictly adhered to the Consolidated Standards of Reporting Trials (CONSORT) guidelines and the ethical principles outlined in the Declaration of Helsinki. Ethical approval was granted by the Institutional Review Board of the Faculty of Medicine, Universitas Brawijaya. The trial was registered in the local institutional registry prior to patient enrollment. Written informed consent was obtained from all participating subjects.

The study enrolled adult patients aged 18 to 65 years, classified as American Society of Anesthesiologists (ASA) physical status I, II, or III, who were scheduled for elective distal lower limb surgery requiring a sciatic nerve block. Eligible surgical procedures included open reduction and internal fixation of ankle fractures, hallux valgus correction (bunionectomy), metatarsal surgeries, and calcaneal spur excisions. To ensure patient safety and data homogeneity, strict exclusion criteria were applied: (1) Contraindications to regional anesthesia: Patient refusal, infection at the injection site, or significant coagulopathy (INR greater than 1.5, Platelets less than 80,000 per microliter); (2) Neurological factors: Pre-existing peripheral neuropathy (such as diabetic neuropathy), neurological deficits in the operative limb, or active lumbar radiculopathy; (3) Endocrine and metabolic factors: Uncontrolled diabetes mellitus (HbA1c greater than 8.0%) due to the risk of steroid-induced hyperglycemia; (4) Pharmacological factors: Known allergy to amide local anesthetics or corticosteroids; chronic opioid use (defined as daily opioid consumption for more than 3 months); or current use of systemic corticosteroids.

Patients were randomly allocated in a 1:1 ratio to one of two groups using a computer-generated randomization sequence (generated via simple randomization on www.randomization.com) with a block size of 4 to ensure equal distribution over time; (i) Group D (Dexamethasone): Received 20 mL of admixture containing 19 mL of Ropivacaine 0.5% plus 1 mL (8 mg) of Dexamethasone Sodium Phosphate (non-particulate); (ii) Group M (Methylprednisolone): Received 20 mL of admixture containing 19 mL of Ropivacaine 0.5% plus 1 mL (40 mg) of Methylprednisolone Acetate (particulate).

Maintaining the double-blind integrity was critical due to the visual difference between the clear dexamethasone solution and the cloudy or milky methylprednisolone suspension. An independent pharmacist, not involved in the perioperative care or data collection, prepared the study solutions. The prepared solutions were loaded into identical 20 mL syringes. To mask the visual appearance, the barrel of each syringe was completely wrapped in opaque surgical tape. The extension tubing connecting the syringe to the nerve block needle was also opaque. During the block performance, the ultrasound screen was positioned such that the patient could not see the screen or the injectate. The anesthesiologist performing the block was blinded to the drug identity, as the tactile feedback during injection is indistinguishable between the two mixtures. The postoperative outcomes were assessed by a dedicated research nurse who was blinded to group allocation.

All patients received standard ASA monitoring. Intravenous access was established, and midazolam (0.05 mg/kg) was administered for anxiolysis. The ultrasound-guided popliteal sciatic nerve block procedure was performed with the patient in the lateral decubitus position (operative side up). A high-frequency linear ultrasound transducer (10–15 MHz, GE Logiq e) was placed at the popliteal fossa. The sciatic nerve was identified in the short-axis view at the bifurcation level where the Tibial Nerve (TN) and Common Peroneal Nerve (CPN) diverge. Using an in-plane approach, a 22G, 100 mm echogenic insulated needle (Stimuplex

Ultra, B. Braun) was advanced toward the Vloka's sheath (paraneural sheath) common to both nerves. The target injection point was the subparaneural space between the TN and CPN. Upon negative aspiration for blood, the 20 mL study solution was injected in fractionated aliquots. The endpoint of successful injection was the visualization of the donut sign—the circumferential spread of local anesthetic separating the TN and CPN components within the sheath. Following the block, spinal anesthesia was performed (Bupivacaine Heavy 0.5%, 10-12.5 mg) to ensure surgical immobility and cover tourniquet pain. The sciatic block was performed pre-operatively to accurately assess onset time. If the surgical incision involved the medial malleolus (saphenous nerve territory), a separate adductor canal block was performed with 10 mL of Ropivacaine 0.375% (without steroid) to cover the saphenous nerve distribution.

To isolate the effect of the nerve block, all patients received a standardized multimodal analgesic regimen: (1) Paracetamol: 1 gram IV every 8 hours for 24 hours, then orally; (2) Ketorolac: 30 mg IV every 8 hours for 24 hours (if renal function permitted), followed by Ibuprofen 400 mg orally every 8 hours; (3) Rescue Analgesia: Intravenous tramadol 50 mg was administered for breakthrough pain, defined as a numeric rating scale (NRS) score greater than 3. The duration of analgesia, defined as the time interval (in hours) from the completion of the block injection to the first patient report of pain intensity greater than 3 on the NRS (0-10 scale) or the first request for rescue analgesia.

Secondary outcomes encompassed a comprehensive evaluation of both pharmacodynamic parameters and clinical efficacy. Block onset time was rigorously assessed via pinprick sensation testing in the sural and superficial peroneal nerve distributions at two-minute intervals until sensory loss was complete. Postoperative pain severity was longitudinally monitored using the Numeric Rating Scale (NRS) at 12, 24, and 48 hours, while the cumulative analgesic requirement was quantified by the total milligram consumption of tramadol over the 48-hour postoperative period. Furthermore, the study evaluated the incidence of rebound pain, operationalized as a rapid escalation in pain intensity from an NRS score of less than 3 to greater than 7 within two hours of block resolution. Finally, the safety profile was established by recording the incidence of adverse events, specifically local anesthetic systemic toxicity (LAST), injection site infection, or neurological sequelae defined as paresthesia persisting longer than seven days.

The sample size was calculated based on a superiority hypothesis. Based on previous literature, the mean duration of analgesia for a ropivacaine-dexamethasone sciatic block is approximately 18 (SD 3.5) hours. To justify the use of a particulate steroid with a higher theoretical risk profile, we determined that a clinically significant increase in duration would be 4 hours (Delta). Using an independent t-test power analysis with alpha = 0.05 (two-sided) and Power (1-beta) = 0.80, the required sample size was 16 patients per group. To account for potential dropouts, we recruited 36 patients (18 per group). This study was powered to detect a large effect size (Delta = 4 hours). The study is strictly powered for superiority and not for equivalence or non-inferiority.

Statistical analysis was performed using IBM SPSS Statistics for Windows, version 26.0 (IBM Corp., Armonk, NY). The normality of continuous data distribution was rigorously assessed using the Shapiro-Wilk test. Given the time-to-event nature of the primary outcome—the duration of analgesia—a Kaplan-Meier survival analysis was employed to estimate the median duration. The survival distributions between the two groups were subsequently compared using the Log-Rank (Mantel-Cox) test. This methodological approach was selected to provide a more robust assessment of block regression dynamics compared to simple mean comparison, as it appropriately accounts for the temporal aspect of the analgesic effect. For secondary continuous variables, between-group comparisons were conducted using the Independent Samples T-test for normally distributed data, while the Mann-Whitney U test was utilized for non-normally distributed data or ordinal variables, specifically the NRS pain scores. Categorical variables were analyzed using the Pearson Chi-Square test or Fisher's Exact test, contingent upon expected cell frequencies. All statistical tests were two-

tailed, and a p-value of less than 0.05 was considered statistically significant.

3. Results

A total of 40 patients were assessed for eligibility. Four patients were excluded (2 declined participation, 2 were on therapeutic anticoagulation). Thirty-six patients were randomized (18 in Group D, 18 in Group M) and all completed the study protocol. There were no protocol deviations or losses to follow-up. Baseline demographic characteristics, including age, gender, Body Mass Index (BMI), and surgical duration, were comparable between the two groups ($p > 0.05$), indicating successful randomization (Table 1).

Table 1. Demographic and Surgical Characteristics

Characteristic	Group D (Dexamethasone) (n=18)	Group M (Methylprednisolone) (n=18)	P-value (2-tailed)
Age (Years, Mean ± SD)	45.2 ± 11.4	47.1 ± 10.8	**0.62**
Gender (Male / Female)	8 / 10	11 / 7	**0.31**
BMI (kg/m², Mean ± SD)	24.5 ± 3.1	25.1 ± 2.8	**0.54**
ASA Physical Status			**0.85**
- ASA I	8	7	
- ASA II	9	9	
- ASA III	1	2	
Duration of Surgery (min)	85.4 ± 15.2	82.1 ± 18.5	**0.59**

Note: Data are presented as Mean ± Standard Deviation (SD) or frequency (n).
Abbreviations: *BMI* = Body Mass Index; *ASA* = American Society of Anesthesiologists.
P-values were calculated using the Independent T-test for continuous variables and Chi-Square test for categorical variables. No statistically significant differences were observed between groups at baseline.

Table 2 outlines the comparative pharmacodynamic characteristics and the primary efficacy endpoint for the two study groups. Regarding the establishment of anesthesia, the addition of methylprednisolone did not alter the speed of block engagement compared to dexamethasone. The median time to sensory onset was comparable between the dexamethasone and methylprednisolone groups (14.5 minutes vs. 15.0 minutes; $p = 0.52$), as was the time to complete motor blockade (18.0 minutes vs. 19.5 minutes; $p = 0.34$). Critically, the analysis of the primary outcome—the duration of analgesia—demonstrated no statistically significant difference between the two adjuvants. Patients in the methylprednisolone group experienced a mean analgesic duration of 19.1 ± 3.5 hours, compared to 18.4 ± 3.2 hours in the dexamethasone group. The mean difference of 0.7 hours (95% CI: -1.5 to 2.9) was neither clinically substantial nor statistically significant ($p = 0.58$). This finding was further corroborated by the Kaplan-Meier survival analysis using the Log-Rank test ($p = 0.61$), confirming that the particulate steroid failed to provide a superior depot effect relative to the non-particulate standard of care in this cohort (Figure 1).

Table 2. Block Characteristics and Primary Outcome

Parameter	Group D (Dexamethasone) (n=18)	Group M (Methylprednisolone) (n=18)	Mean Difference (95% CI)	P-value
Sensory Onset (min) Median [IQR]	14.5 [12 - 18]	15.0 [12 - 19]	—	0.52[a]
Motor Onset (min) Median [IQR]	18.0 [15 - 22]	19.5 [16 - 24]	—	0.34[a]
Duration of Analgesia (hours) Mean ± SD	**18.4 ± 3.2**	**19.1 ± 3.5**	0.7 (-1.5 to 2.9)	0.58[b]
Kaplan-Meier Analysis (Log-Rank)		*Chi-Square = 0.26*		0.61[c]

Note: Data are presented as Mean ± Standard Deviation (SD) for normally distributed variables or Median [Interquartile Range, IQR] for non-parametric data.
Abbreviations: *CI* = Confidence Interval; *SD* = Standard Deviation.
Statistical Tests: [a]Mann-Whitney U Test; [b]Independent Samples T-Test; [c]Log-Rank (Mantel-Cox) Test.
The primary outcome (Duration of Analgesia) showed no statistically significant difference between groups.

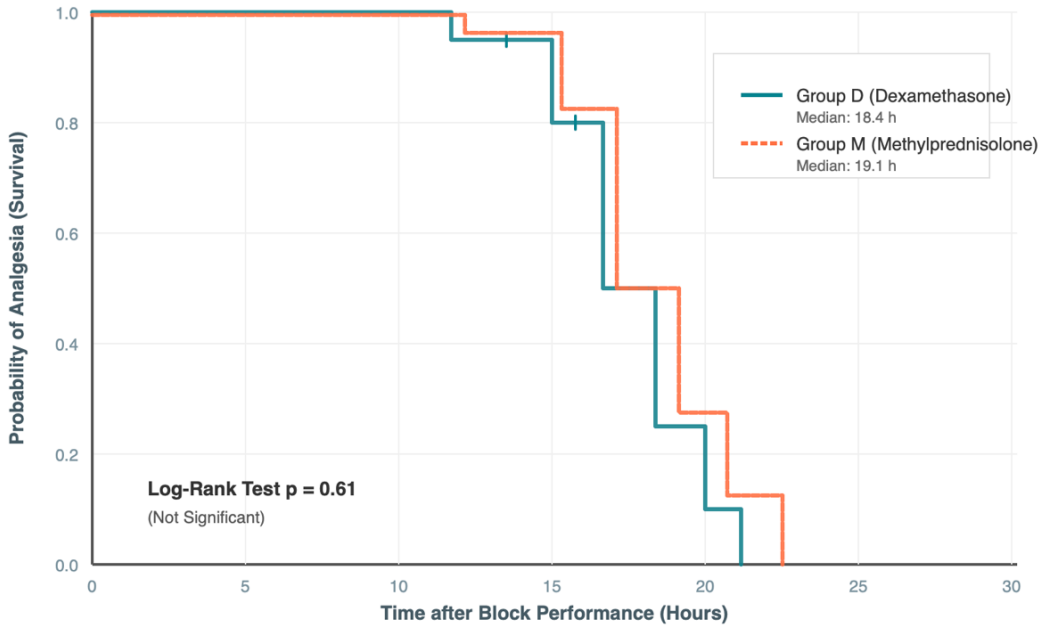

Figure 1. Kaplan-Meier survival curves for duration of analgesia.

Figure 2 delineates the secondary efficacy endpoints, providing a composite view of subjective pain intensity and objective analgesic consumption. Panel A illustrates the temporal trajectory of postoperative pain using the numeric rating scale (NRS). Both the dexamethasone and methylprednisolone groups demonstrated a pronounced floor effect across the 48-hour observation period, a finding attributable to the effective nerve blockade combined with the standardized multimodal analgesic regimen. Median

NRS scores remained consistently low (less than or equal to 2) at all time points, with overlapping interquartile ranges. Statistical analysis confirmed no significant differences in pain severity between the groups at 12, 24, or 48 hours ($p > 0.05$). Panel B corroborates these findings by presenting the incidence of rescue analgesia requirements. The need for breakthrough opioid therapy (intravenous tramadol) was negligible; only 11.1% of patients in the dexamethasone group and 5.6% in the methylprednisolone group required rescue medication. This difference was not statistically significant ($p = 0.65$). Collectively, these panels indicate that while both adjuvants facilitate excellent postoperative comfort, the particulate steroid offered no advantage over the non-particulate standard in terms of reducing pain intensity or opioid consumption.

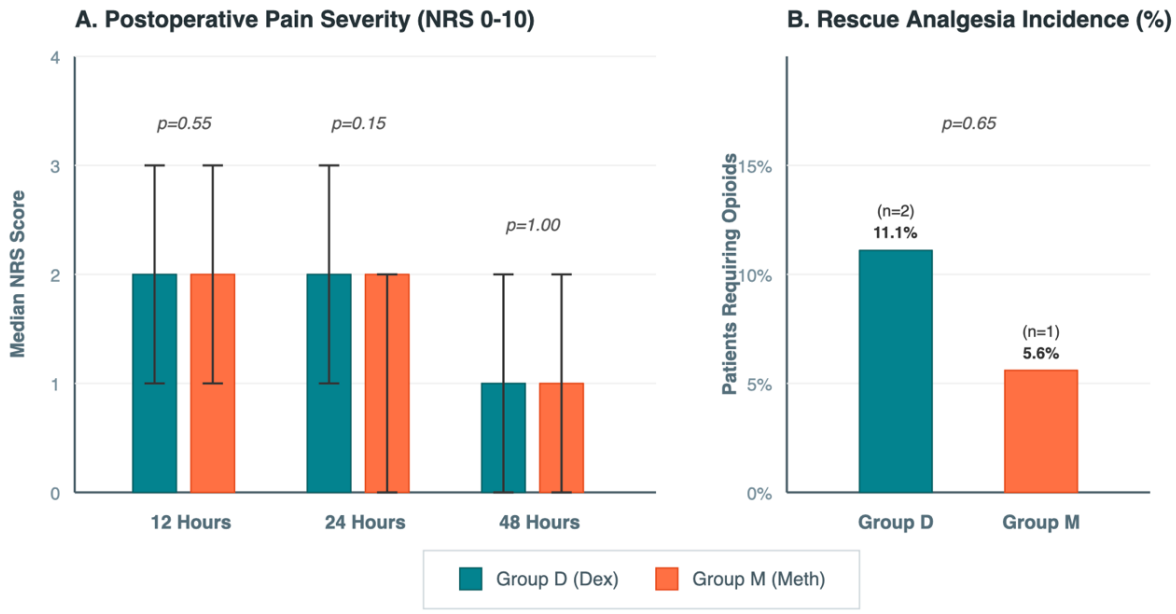

Figure 2. Secondary Outcomes Analysis.
(A) Postoperative pain severity assessed via Numeric Rating Scale (NRS, 0-10) at 12, 24, and 48 hours. Bars represent Median values; error bars represent the Interquartile Range (IQR). Both groups demonstrated a "floor effect" with minimal pain. **(B)** Incidence of rescue analgesia (Tramadol) requirement within the first 48 hours. No statistically significant differences were observed between Group D (Dexamethasone) and Group M (Methylprednisolone) in either pain scores or opioid consumption.

The safety profile was benign across both study groups, with no immediate or delayed complications recorded. Specifically, there were no observed cases of local anesthetic systemic toxicity (LAST) or injection site infection. Neurological surveillance confirmed the absence of neurotoxicity; no patient exhibited persistent paresthesia or motor deficits extending beyond the expected duration of the block. Additionally, although blood glucose was not a formal outcome measure, no clinical evidence of steroid-induced hyperglycemia requiring medical intervention was reported. These findings suggest that both particulate and non-particulate adjuvants were well-tolerated within the specific context of this protocol.

4. Discussion

The principal finding of this prospective, double-blind, randomized controlled trial is that the perineural administration of 40 mg of particulate methylprednisolone failed to demonstrate superiority over 8 mg of non-particulate dexamethasone when used as an adjuvant to ropivacaine in ultrasound-guided

popliteal sciatic nerve blocks. Despite the theoretical pharmacokinetic advantage associated with the low solubility of methylprednisolone, our results showed a mean analgesic duration of approximately 19.1 hours in the methylprednisolone group versus 18.4 hours in the dexamethasone group. The observed difference of 0.7 hours was neither statistically significant nor clinically meaningful, leading to the rejection of our primary hypothesis that the particulate depot effect would extend the duration of sensory blockade beyond that of the standard non-particulate agent.[11] Furthermore, secondary outcomes, including postoperative opioid consumption and pain severity scores at 48 hours, were comparable between groups, suggesting that both adjuvants effectively facilitate a smooth transition to oral analgesia. These findings challenge the utility of selecting a particulate steroid solely for the purpose of extending block duration in this specific anatomical context.[12]

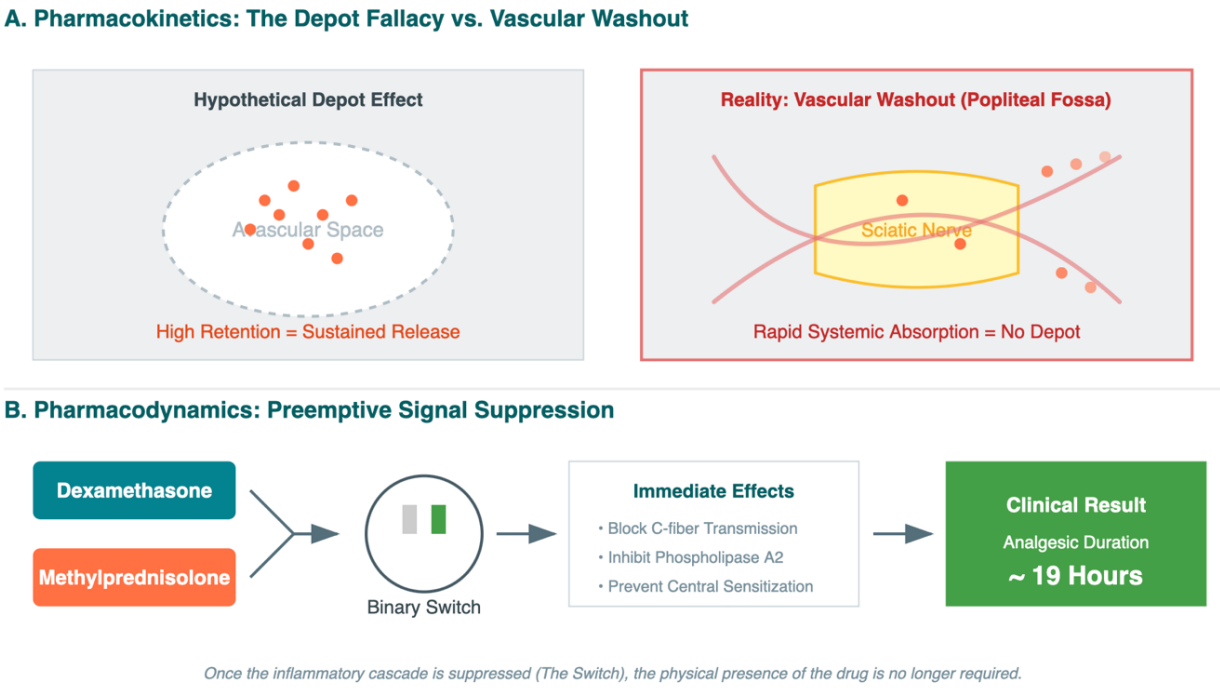

Figure 3. Proposed pathophysiological mechanism.

The conceptual framework of this study was predicated on the depot hypothesis—the pharmacological assumption that the physicochemical properties of methylprednisolone acetate, specifically its low solubility and micro-crystalline structure, would create a drug reservoir at the nerve sheath (Figure 3). In theory, this reservoir should elute the active corticosteroid moiety over an extended period, maintaining therapeutic perineural concentrations long after a soluble agent like dexamethasone would have been cleared. This mechanism is well-established in other clinical domains; for example, in intra-articular injections, the avascular nature of synovial fluid allows particulate depots to persist and exert anti-inflammatory effects for weeks.[13] However, our results suggest that this hypothesis implies a false equivalence between different anatomical compartments and does not hold true for the popliteal sciatic nerve block.

We propose a vascular washout mechanism to explain this failure of translation. Unlike the closed, avascular compartment of a joint, the popliteal fossa is a loose connective tissue space containing a rich vascular network surrounding the sciatic nerve. It is highly probable that the carrier suspension of the

methylprednisolone is rapidly absorbed into the systemic circulation. Alternatively, the localized inflammatory response to the foreign micro-crystals may recruit macrophages that clear the particulate matter significantly faster than the elution rate required to maintain prolonged neural blockade. Consequently, the depot is likely washed out or metabolized before it can provide the extended durability observed in fascial plane blocks or intra-articular applications.[14]

Furthermore, the fundamental mechanism of steroid-induced analgesia likely relies on preemptive signal suppression rather than continuous drug presence. Corticosteroids act via a complex mechanism involving the inhibition of phospholipase A2 (preventing the release of arachidonic acid) and the direct modulation of potassium channels on nociceptive C-fibers. This effect suppresses the ectopic neuronal discharge and inhibits the upregulation of pro-inflammatory neuropeptides, such as Substance P and Calcitonin Gene-Related Peptide (CGRP), in the dorsal root ganglion.[15] We hypothesize that this pharmacological effect operates as a binary switch—once the initial high concentration of steroid (whether dexamethasone or methylprednisolone) triggers the anti-inflammatory cascade and suppresses the initial sensitization of the nerve, the biological effect is locked in. Once this threshold of signal suppression is achieved, the physical persistence of the drug molecules may be irrelevant. The durability of the analgesia observed in our study (approx. 19 hours) is likely a reflection of the initial suppression of the wind-up phenomenon and the time required for the nerve to recover its excitability, rather than a function of how long the steroid crystals remained adjacent to the epineurium.

A critical methodological aspect of this study, which dictates the interpretation of our results, is the sample size calculation and the chosen study design.[16] We powered this trial specifically to detect a large effect size—a difference (Delta) of 4 hours—to justify the use of a riskier particulate agent. The rationale was that for a clinician to choose methylprednisolone (which carries a theoretical risk of embolic injury) over dexamethasone (which is inherently safer), the analgesic reward must be substantial. A marginal gain of 1 or 2 hours would arguably not justify the increased risk profile. By finding a difference of only 0.7 hours with a p-value of 0.58, we find ourselves in a statistical grey zone. It is imperative to clarify that our failure to demonstrate superiority is not statistically the same as proving equivalence. Because we did not perform a non-inferiority trial with a tight margin (1 hour), we cannot strictly claim the drugs are identical. It remains statistically possible that Methylprednisolone provides a modest benefit (1.5 hours) that our study (n=36) was underpowered to detect, representing a potential Type II error.

However, statistical significance must be weighed against clinical relevance. From a pragmatic clinical standpoint, a difference in analgesic duration of less than 2 hours is unlikely to alter postoperative management or patient outcomes. In the context of a 19-hour block, an additional hour of numbness does not typically confer a benefit regarding sleep quality or discharge readiness, particularly when effective oral analgesics are available. Therefore, while we statistically report a failure to show superiority, clinically, the performance of the two drugs appears effectively similar. Both agents, when combined with a multimodal analgesic regimen, provided excellent pain control well beyond the duration of the surgical stimulus. Thus, the decision to use one agent over the other should not be based on efficacy, as they are functionally indistinguishable in this cohort, but rather on safety and availability.[17]

The safety profile of perineural corticosteroids remains a subject of intense debate and is the most significant factor differentiating the two study drugs.[18] The distinction lies in their physical formulation: dexamethasone sodium phosphate is a non-particulate solution, whereas methylprednisolone acetate is a particulate suspension containing macroscopic crystals. This physical difference dictates their toxicity profile. If a particulate steroid is accidentally injected into a radicular artery or a nutritive artery of the nerve (vasa nervorum), the crystals can act as embolic debris. This embolization can cause mechanical occlusion of the blood vessel, leading to ischemia, subsequent nerve infarction, and catastrophic neurological sequelae such as

paraplegia—complications that have been well-documented in the literature regarding transforaminal epidural injections. Conversely, non-particulate dexamethasone carries no risk of embolic occlusion, even in the event of intravascular injection, making it the safer choice for perineural administration.

In our study, we observed zero adverse events, no neurological complications, and no signs of infection in either group (n=18 per group). However, it is crucial to interpret this absence of complications with caution. The rule of 3 in medical statistics suggests that observing zero events in a sample of 36 patients (or 18 per group) does not mean the risk is zero; rather, it implies that the upper limit of the 95% confidence interval for the risk could still be as high as 17%. Therefore, our study was statistically incapable of proving that methylprednisolone is safe; it merely demonstrates that complications are not extremely frequent.

This leads to a critical risk-benefit analysis. Given that Methylprednisolone failed to provide the reward of significantly longer analgesia (the hypothesis of the study) to offset its theoretical risk, the justification for its routine use diminishes. Dexamethasone should unequivocally remain the first-line adjuvant for popliteal sciatic nerve blocks due to its comparable efficacy and superior safety profile. However, our findings are highly relevant for resource-limited settings, such as hospitals in developing nations, where drug shortages are common. In scenarios where preservative-free, non-particulate dexamethasone is unavailable, our data support methylprednisolone as a viable, robust analgesic alternative. Clinicians in such settings can use methylprednisolone with the knowledge that it provides effective block prolongation, provided they exercise extreme caution to avoid intravascular injection (using ultrasound guidance, aspiration, and test doses).[19]

Our study is subject to several limitations that warrant discussion. First, as previously noted, the sample size was calculated based on a superiority design with a large effect size. Consequently, the study was underpowered to detect smaller, potentially subtle differences in analgesic duration (< 4 hours) between the groups. While we deem these smaller differences clinically negligible, a larger trial would be required to statistically rule them out. Second, the robust nature of our background multimodal analgesic regimen (scheduled Paracetamol and Ketorolac) resulted in very low pain scores across both groups. This created a floor effect, potentially masking any subtle analgesic superiority of one adjuvant over the other. While this multimodal approach is ethical and standard of care, it reduces the assay sensitivity of the trial regarding the nerve block's specific contribution to late-phase analgesia. Finally, we did not measure plasma concentrations of the steroids or local anesthetics. The lack of pharmacokinetic monitoring limits our ability to definitively confirm the vascular washout hypothesis or correlate systemic absorption rates with clinical analgesic duration.[20] Future research should focus on dose-finding studies to establish the minimum effective dose of methylprednisolone to further enhance safety margins if it is to be used as an alternative agent.

5. Conclusion

In conclusion, this prospective, double-blind, randomized controlled trial demonstrates that the perineural administration of particulate methylprednisolone (40 mg) failed to result in a superior duration of analgesia compared to non-particulate dexamethasone (8 mg) when used as adjuvants to ropivacaine in ultrasound-guided popliteal sciatic nerve blocks. The hypothesized depot effect, which posits that the low solubility of particulate steroids leads to sustained local release and prolonged blockade, was not clinically evident in the vascularized tissue of the popliteal fossa. Both corticosteroid adjuvants, when incorporated into a multimodal analgesic pathway, facilitated excellent postoperative pain control with minimal opioid consumption and high patient satisfaction.

However, the similar efficacy profile of these two agents implies that the choice of adjuvant must be dictated by safety considerations rather than potency. Given the theoretical risks of embolic events associated with particulate suspensions, non-particulate dexamethasone remains the preferred first-line adjuvant for peripheral nerve blockade. Methylprednisolone represents a viable and

effective alternative, particularly valuable in resource-constrained environments where dexamethasone may be inaccessible, but its use requires a conscious acknowledgement of the safety profile and strict adherence to injection safety protocols.

6. References

1. Noikham A, Tivirach W, Pongraweewan O, Suphathamwit A, Puangpunngam N, Jirativanont T. Popliteal sciatic nerve block for high-risk patients undergoing lower limb angioplasty: a prospective double-blinded randomized controlled trial. Medicine (Baltimore). 2023; 102(18): e33690.
2. Olofsson M, Nguyen A, Rossel J-B, Albrecht E. Duration of analgesia after forefoot surgery compared between an ankle and a sciatic nerve block at the popliteal crease: a randomised controlled single-blinded trial. Eur J Anaesthesiol. 2024; 41(1): 55–60.
3. Prasad G, Misquith JCR, Ribeiro KNS, Naik SA. Comparison of the analgesic duration using ultrasound-guided popliteal sciatic nerve block between diabetics with neuropathy and nondiabetics without neuropathy. Ann Afr Med. 2024; 23(4): 663–8.
4. Eman A, Balaban O, Pekşen Ö, Erkin A. Ultrasound-guided popliteal sciatic nerve block for surgical anesthesia in wound care patients with ongoing anticoagulant/antiaggregant therapy: a single-center, prospective study. Medicine (Baltimore). 2024; 103(44): e40311.
5. Pulitanò R, Giudice M, La Verde F, Di Sabatino E, Carassiti M, Pascarella G. Ropivacaine and magnesium sulfate in sciatic nerve block at the popliteal level: randomized double-blind study. Minerva Anestesiol. 2024; 90(12): 1090–7.
6. Soor B, Garg I. A case report of an ultrasound-guided popliteal sciatic nerve block: an asset for emergency lower limb debridement in a high-risk patient. Cureus. 2024; 16(4): e57752.
7. Lei G, Yang S, Wu L, Yin Y, Zhang S, Wang G. Intravenous injection of dexamethasone is non-inferior to perineural administration for popliteal sciatic nerve and saphenous nerve blocks: a randomized, controlled, triple-blind study. Heliyon. 2024; 10(7): e28304.
8. Coviello A, Iacovazzo C, Cirillo D, Bernasconi A, Marra A, Squillacioti F, et al. Dexamethasone versus dexmedetomidine as adjuvants in ultrasound popliteal sciatic nerve block for hallux Valgus surgery: a mono-centric retrospective comparative study. Drug Des Devel Ther. 2024; 18: 1231–45.
9. Clipet-Jensen A, Fjeldsøe-Nielsen H, Roy Kirkegaard P. Foot drop following a popliteal sciatic nerve block with ropivacaine, a case report and literature review. Local Reg Anesth. 2024; 17: 87–91.
10. Yanaki M, Koide S, Mori H, Taketomi T, Yanaki F. Ultrasound-guided popliteal sciatic nerve block in home palliative care: Two patients with necrotic lower limb pain caused by peripheral circulatory disorders. Palliat Care Res. 2025; 20(3): 181–5.
11. Park YU, Joe HB, Lee JW, Seo YW. Analgesic effectiveness of continuous versus single-injection adductor canal block in addition to continuous popliteal sciatic nerve block for bimalleolar and trimalleolar ankle fracture surgery: Prospective randomized controlled trial. J Orthop Sci. 2025; 30(1): 159–63.
12. Biradar V, Konnur S, Sancheti A. Combining ultrasound-guided popliteal sciatic and adductor canal block as a lifesaver for high-risk patients scheduled for emergency below knee surgery: a case series. Archives of Anesthesia and Critical Care. 2025.
13. Reysner T, Pietraszek P, Shadi M, Musielak B, Kowalski G, Daroszewski P, et al. Effect of perineural dexamethasone versus dexmedetomidine as adjuvants to ropivacaine on analgesic duration in pediatric popliteal sciatic nerve blocks: a randomized, triple-blinded, placebo-controlled trial. Reg Anesth Pain Med. 2025; rapm-2025-107096.
14. Yao J, Cai J, Lu Q, Huang X. Ultrasound-guided sural nerve and tibial nerve block provides comparable analgesia to popliteal sciatic nerve block following calcaneal surgery:

a single center randomized controlled double-blind study. J Pain Res. 2025; 18: 1765–73.

15. Zhang J, Zhao Z. Ultrasound-guided popliteal sciatic nerve block versus traditional analgesia for early perioperative pain relief in severe chronic lower extremity arterial occlusive disease: a retrospective study. Vascular. 2025; (17085381251339937): 17085381251339937.
16. Lei G, Wu L, Yin Y, Zhang S, Wang G. Perineural dexamethasone is more efficient than perineural dexmedetomidine in prolonging popliteal sciatic and saphenous nerve blocks: a single-center, prospective, double-blinded, randomized controlled trial. Local Reg Anesth. 2025; 18: 27–38.
17. Patil SS, Parikh DA, Jain RA. Ultrasound-guided supine lateral CAPS (crosswise approach to popliteal sciatic) block for below-knee surgeries in high-risk patients: a retrospective case series. Indian J Anaesth. 2025; 69(7): 729–32.
18. Si G, Wang L, Deng M, Sun Y, Cao Y, Fan J, et al. Popliteal sciatic nerve block versus intrathecal anesthesia for Achilles tendon rupture repair surgery: a mono-centric retrospective comparative study. Front Med (Lausanne). 2025; 12(1516874): 1516874.
19. Knecht S, Tamine L, Faure N, Tran P, Orban J-C, Bronsard N, et al. Effectiveness of adductor canal block combined with posterior capsular infiltration on pain and return to walking after total knee arthroplasty: comparative analysis with femoral and popliteal sciatic nerves blocks. Orthop Traumatol Surg Res. 2025; 111(5): 104082.
20. Yoo S, Choi B-M, Kim DJ, Kim J-T. Plasma concentrations of total and unbound ropivacaine and its metabolite 2',6'-pipecoloxylidide after popliteal sciatic nerve block in chronic kidney disease patients not receiving haemodialysis: a population pharmacokinetic analysis. Eur J Anaesthesiol. 2025; 42(8): 751–3.